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ORIGINAL ARTICLES.

THE LEUKOCYTIC PICTURE IN INFLUENZA.

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The two recent epidemics of influenza have given opportunity for restudying the blood changes in this disease. Yet such study, judging from the reports, has been for the most part incidental to a general clinical study and has not been sufficient to establish the leukocytic picture in the infection. At least I have found but one paper, that of Adler,[1] of Zurich, in which the blood findings have been a matter of primary interest and have received adequate consideration.

In the text-books on clinical diagnosis and on medicine commonly available to students the notes on the leukocytic picture of influenza are hazy and contradictory. These books, as a matter of course, have not had the benefit of the findings in the recent epidemics. Further, in many cases, their statistics seem to have been compiled from single counts in a patient, without reference to the day of the disease, or without accurate determination of the presence or absence of complications in the patient. Thus, Cabot[2] states that five-sixths of his cases had a normal leukocyte count, and of the eleven with leukocytosis one or more had complications. Emerson[3] reports that after an early low leukocyte count one-half of his cases showed a count of over 10,000 cells, some even reaching a count of 20,000. Yet in his statement that "influenza covers a wide group

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[1] Folia Hæmatologica, November, 1919, xxv, 16.
[2] Clinical Examination of the Blood, 2d edition, 1898, p. 214.
[3] Clinical Diagnosis, 2d edition, 1908, p. 528.

of cases," one has evidence that at the time of publication (1908) he did not have a clear-cut idea as to the specificity of the infection. Simon[4] states that in uncomplicated cases the leukocytes are commonly diminished but may be normal, and that with a count of over 15,000 cells some complication is present. During the course of the disease he records a lymphocytosis with low neutrophile and eosinophile values, and a return of neutrophile values to normal with convalescence. Webster[5] states that there is usually a diminution in white cells, though a normal count may be found. Bass and Johns[6] tabulate little or no increase in leukocytes, with a differential increase in both neutrophiles and small mononuclears. Sahli[7] makes no note of the blood picture because of the vague conceptions of the disease. The blood changes are apparently considered by some to have no importance in diagnosis, as no note is found concerning them in Albutt, in *Monographic Medicine*, or in Musser. Lord,[8] in Osler's *Modern Medicine*, reports that in 167 cases representing the simple acute form of the disease with slight respiratory disturbance the leukocytes did not exceed 12,000 in 70 per cent., and in the other 30 per cent. the greater leukocytosis could not be accounted for by complications. With deeper involvement of the respiratory tract, one-half of 54 cases with bronchitis and two-thirds of twelve cases with pneumonia gave a count of more than 12,000.

In the journal reports of the 1918 epidemic, chiefly from the army camps, the statements of blood-findings are much sharper and show closer agreement.[9] Keeton and Cushman found a leukopenia (with a minimum count of 900 cells) in 46.6 per cent. of their cases and a normal count in 24.7 per cent.; in the cases with recovery after bronchopneumonia there was a leukocytosis in 62.2 per cent.; and in the bronchopneumonia cases with fatal outcome a leukocytosis in but 41.3 per cent. Brem, Bolling and Casper[10] found a leukopenia practically always, in the influenzal stage, and they concluded that the initial infection produced a depression of the bone-marrow, but that the latter was capable of stimulation in secondary pyogenic infection. Ross and Hund[11] found a leukopenia with a count from 1800 to 3000 in their desperately ill influenza-pneumonia cases. Dever, Boles and Case[12] found a tendency toward leukopenia well marked in some cases of uncomplicated influenza and a leukocytosis in the majority of the cases with a complicating pneumonia. Zeedick[13] found a normal count or a leukopenia in most of the uncomplicated cases and is much inclined to the opinion that any count above normal means a secondary bacterial invasion. In his

[4] Clinical Diagnosis, 6th edition, 1907, p. 100.
[5] Diagnostic Methods, 3d edition, 1913, p. 499.
[6] Laboratory Diagnosis, 1917, p. 57.
[7] Clinical Diagnosis, 2d edition, (Potter), 1911, p. 801.
[8] Modern Medicine, 1907, ii, 481.
[9] Jour. Am. Med. Assn., 1919, lxxii, 640.
[10] Ibid., 1918, lxxi, 2138.   [11] Ibid., 1919, lxxii, 640.   [12] Ibid., 1919, lxxii, 265.
[13] Studies in Epidemic Influenza, Univ. of Pittsburgh, 1919.

opinion leukocytosis at the end of the course is not a part of the blood picture, but there is instead a gradual return to the normal count in convalescence; while with pneumonia there is, as a rule, a very moderate leukocytosis if there is not a leukopenia. Kinsella and Broun[14] have emphasized, in addition to these leukocyte pictures, the great reduction in blood-platelets that occurs in the disease.

Adler,[15] whose paper came to hand after the completion of the study to be reported here, has attempted to construct the leukocytic picture of the disease by daily total and differential counts on the patients. He finds an increase in leukocytes during the prodromal stage and on the first febrile day. This is followed by a leukopenia, with reduction in neutrophiles, eosinophiles and basophiles which is due to marrow inhibition. This is succeeded by a positive marrow reaction, until, on the fourth or sixth day, the blood-picture approaches the normal. There is also an early absolute reduction in number of lymphocytes, followed by a reactive lymphocytosis. Adler insists that a disease with a constant leukocytosis cannot be influenza. He draws a further sweeping conclusion, possibly not entirely justified, that diseases which result in immunity show in their course a leukopenia, diseases without an immunity a leukocytosis. Two apparently striking exceptions, scarlet fever and smallpox, he explains on the dominance of the picture by the secondary streptococcic invader.

One may summarize these more recent reports by stating that in influenza there is an early inhibition (not exhaustion) of the marrow activity by the infecting agent, resulting in a leukopenia which is characteristic of the disease. The marrow is capable of stimulation upon pyogenic infection as a complication, and there results a leukocytosis usually of moderate degree.

During the 1920 epidemic of influenza among the students of the University of Wisconsin the author made a daily study of the differential leukocyte picture in a short series of cases treated in the University Infirmary. This study was made with no thought of a publication of statistical results, but merely with the hope that it might throw some light on the nature of the disease and on some of its phenomena. I realize the series of cases is short and publication is hardly justified from the standpoint of statistics. Yet conclusions that may be drawn from the uniformity of findings (within the limits of individual variation), and, further, certain practical points in the care of patients, indicated by the blood findings, seem to justify reporting the work. I wish to express here my indebtedness to Dr. W. S. Middleton for the clinical notes, and to Miss Hazel Gray for the great majority of the total leukocyte counts.

In the hope of obtaining the leukocytic picture of the primary infection, cases were selected which showed no signs of deep respiratory infection upon admission. As it happened no case which was

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[14] Jour. Am. Med. Assn., 1920, lxxiv, 1070.   [15] Loc. cit.

selected terminated fatally, but several cases did show complications in the course of the disease. Some had very mild attacks and were sent from the hospital to their rooms as soon as afebrile, but before their blood picture had returned to normal. This was necessitated by the extent of the epidemic and the demand for beds for the very sick, and is not to be construed as the general practice in regard to the student sick or as a practice to be recommended. In fact, the main practical point that comes from a study of the blood picture in influenza is that patients should be carefully attended until the blood does return practically to normal.

In making the daily differential counts it has been thought sufficient to count 200 cells, if the two hundreds, as such, did not materially differ from each other in proportion of cells. If there was marked difference an increased number was counted. It is realized that in single counts no number less than 500 cells will give an accurate percentage for the cells which exist in the circulation in small proportion, as the eosinophiles and basophiles. In repeated counts, however, and where the main interest is in the cells largely represented, as neutrophiles and lymphocytes, the smaller number gives close accuracy in well-made cover-slip smears. The cells have been classed into seven groups: neutrophiles, eosinophiles, basophiles, small lymphocytes, large lymphocytes, large mononuclear cells and transitionals. But one or two of these groups need explanation. The cell classified as a large lymphocyte is the lymphocyte with considerable protoplasm which has usually a somewhat acidophilic reaction and contains commonly a few coarse azurophile sometimes rod-like granules when stained by Wright's stain. This has been considered by the author to be a more mature small lymphocyte and is found normally in the blood stream. The large mononuclear is a large cell with round or oval nucleus and has been considered an immature form of the so-called transitional which has a polymorphous nucleus. If we may trust the oxidase reactions these are both chiefly of marrow origin in the normal blood.

The cases and their blood counts follow. The first group of five cases consists of those with light attacks and with no pulmonary complications.

CASE I.—Mr. E.

1920.	Total count.	Neutrophiles.		Eosinophiles.		Basophiles.		Small lymphocytes.		Large lymphocytes.		Large mononuclears.		Transitionals.	
		Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.
Jan. 21	13,000	76.5	9945	0.0	0.0	0.5	65	9.5	1235	1.5	195	0.0	0.0	12	1560
22	7,000	35.5	2485	1.0	70	1.5	105	39.5	2695	2.5	175	1.0	70.0	19	1330
23	6,800	42.0	2856	3.5	238	1.5	102	36.5	2482	4.0	272	0.0	0.0	18.5	1250

Blood-platelets distinctly fewer than normal on all smears. Patient admitted with temperature of 102.8° on the morning of January 21. Afebrile on January 22; discharged January 24. No pulmonary symptoms or findings, no complications.

Case II.—Miss H. G.

1920.	Total count.	Neutro-philes.		Eosino-philes.		Baso-philes.		Small lymphocytes.		Large lymphocytes.		Large mononu-clears.		Transi-tionals.	
		Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.
Jan. 25	7800	79.0	6162	0.0	0.0	0.0	0.0	12	936	0.5	39	0.0	0.0	7.5	585
26	5000	58.5	2925	0.5	25.0	0.5	25.0	25	1250	3.0	150	0.0	0.0	12.5	625
27	4200	46.5	1953	0.5	21.0	2.0	84.0	32	1344	4.0	168	0.5	21.0	14.5	609

Blood-platelets distinctly diminished after the first day. Patient admitted during evening of January 24 with temperature of 103.2°; afebrile on January 28.

Case III.—Miss H.

1920.	Total count.	Neutro-philes.		Eosino-philes.		Baso-philes.		Small lymphocytes.		Large lymphocytes.		Large mononu-clears.		Transi-tionals.	
		Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.
Jan. 20	...	58.0	..	0.9	..	0.0	..	29.3	..	4	..	2.3	..	6.3	
21	5200	55.5	2886	0.5	26	0.0	0.0	32.5	1690	4	208	1.0	52	6.5	348
22	6000	70.0	4200	0.0	0.0	0.0	0.0	20.5	1230	1	60	0.0	0.0	8.5	510

Platelets extremely few until January 22. Patient admitted January 20 with temperature of 100°. Afebrile afternoon of January 21. No complications or pulmonary signs. Discharged January 23. In the confusion attendant upon the rush of patients on January 20, a number of the total leukocyte counts were not recorded. In this case there was evidently a leukopenia or normal count, judging from the differential.

Case IV.—Mr. M.

1920.	Total count.	Neutro-philes.		Eosino-philes.		Baso-philes.		Small lymphocytes.		Large lymphocytes.		Large mononu-clears.		Transi-tionals.	
		Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.
Jan. 25	6800	61.5	4182	0.0	00	0.0	00	23.0	1564	2.0	136	0.0	00	13.5	918
26	6200	36.5	2263	0.5	41	0.5	31	44.5	2759	6.5	403	1.5	93	10.0	620
27	8400	43.0	3612	0.5	42	0.0	00	37.0	3118	12.0	1008	3.0	252	4.5	378

Platelets few after January 25. Patient admitted evening of January 24 with temperature of 101.2°. Afebrile afternoon of January 26. Discharged January 28. No complications and no signs of pulmonary involvements.

Case V.—Dr. M.

1920.	Total count.	Neutro-philes.		Eosino-philes.		Baso-philes.		Small lymphocytes.		Large lymphocytes.		Large mononu-clears.		Transi-tionals.	
		Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.
Jan. 25	7300	70.0	5110	0.0	00	1.0	73	16.5	1204	4.0	292	0.0	00	8.5	621
26	6000	52.5	7150	2.5	150	1.0	60	24.5	1470	6.5	390	0.0	00	13.0	780
27	6400	59.5	3808	6.0	384	0.5	32	18.0	1152	6.0	384	0.0	00	10.0	640

Platelets few throughout. Pseudopodial forms noted. Patient admitted on second febrile day. Afebrile after noon of January 26. Discharged evening of January 27. No complications or pulmonary signs.

In this group of mild attacks of the disease there was a moderately sharp fever on the first day of definite illness, and a rapid decline of temperature, with recovery on the third or fourth day, without complications. From the standpoint of the leukocytes it is evident that there may be a moderate leukocytosis at the outset of the attack. Even without a definite or marked increase in total leukocytes there is a relative neutrophile leukocytosis in those cases seen early enough. This is followed by a sharp drop in total leukocyte count due, in chief, to a pronounced fall in the number of polymorphonuclear neutrophiles, the total number of which per unit of circulation may be but from 25 to 50 per cent. of that on the previous day. The lymphocytes, on the other hand, show both a relative and and absolute increase in number. Large mononuclears and transitionals vary slightly in reaction in the different cases, there being either a slight fall in number or practically a constant number. Eosinophiles and basophiles are either absent from the circulation or present in very small numbers. Blood-platelets show a sharp decrease, as estimated from the blood smear. In Case III they were extremely few, and the formation of platelet-like bodies from the large lymphocytes, as reported in another paper,[16] was noted.

On the third day of disease in these mild cases we find, except in one case, a slight increase in total number of neutrophiles; some variation in the lymphocyte numbers, but usually an indication that the peak of reaction has been passed; little change in the large mononuclear group; a low count of eosinophiles in three cases, with a slight eosinophilia in two.   ·

The next two cases ran a somewhat more severe course but without any pneumonia patches, although one had bronchial rales throughout.

Case VI.—Miss E. H.

1920.	Total count.	Neutrophiles.		Eosinophiles.		Basophiles.		Small lymphocytes.		Large lymphocytes.		Large mononuclears.		Transitionals.	
		Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.
Jan. 21	10,600	73.5	7791	0.5	53	0.5	53	13.5	1431	2.0	212	0.0	00	10.0	1060
22	4,400	41.5	1826	0.0	00	0.5	22	36.5	1606	2.0	88	1.0	44	17.5	770
23	6,400	49.0	3136	0.0	00	0.5	32	34.0	2176	1.5	96	2.0	128	13.0	830
25	6,200	43.0	2666	0.0	00	0.0	00	45.0	2790	2.0	124	1.5	93	8.5	527
26	8,000	48.5	3880	0.0	00	0.5	40	35.5	2840	5.5	440	2.5	200	8.0	640
27	4,600	38.0	1748	0.5	23	0.5	23	43.0	1978	5.5	253	1.0	46	11.5	539

Platelets numerous January 21, then diminished until Janury 25, when increase apparent. Patient admitted January 21 with temperature of 102.4°. Gradual decline until January 25 when afebrile. No complications. Discharged January 27.

[16] Johns Hopkins Hosp. Bull., 1920, xxxi, 439.

Case VII.—Miss E.

1920.	Total count.	Neutrophiles.		Eosinophiles.		Basophiles.		Small lymphocytes.		Large lymphocytes.		Large mononuclears.		Transitionals.	
		Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.
Jan. 20	...	53.0	..	0.5	..	0.5	..	21.5	..	13.5	..	0.5	..	10.5	
21	6200	40.5	2511	0.5	31	0.0	00	34.0	2108	13.0	716	0.5	31	11.5	713
22	3400	41.0	1394	1.0	34	0.0	00	37.0	1258	10.5	357	0.5	17	10.0	340
23	3600	43.5	1566	1.0	36	0.0	00	32.5	1160	11.0	396	1.5	54	10.5	378
24	2600	42.0	1092	0.0	00	1.0	26	37.0	962	10.5	273	0.5	13	9.0	234
25	9000	47.5	4275	0.0	00	0.0	00	30.0	2700	11.5	1035	1.0	90	10.0	900
26	6000	52.0	3120	0.5	30	0.0	00	30.5	1830	9.5	570	2.5	150	5.0	300
27	...	56.0	..	0.0	00	0.5	00	32.0	..	5.0	..	1.5	..	5.0	

Platelets relatively few throughout. Patient admitted January 19 with evening temperature of 101°. Temperature ranged between 101.4° and 99° until January 26 when afebrile. No complications beyond the presence of rales at left apex from onset. Moderately severe course. Discharged January 27.

In these two cases we have the same features as shown in the earlier cases, but they are more pronounced, especially as far as the fall in neutrophile leukocytes is concerned. This leukopenia is also more persistent.

The following cases developed pneumonic patches and other complications during the course of their illness, but showed eventual recovery.

Case VIII.—Miss V.

1920.	Total count.	Neutrophiles.		Eosinophiles.		Basophiles.		Small lymphocytes.		Large lymphocytes.		Large mononuclears.		Transitionals.	
		Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.
Jan. 21	6,600	71.0	4,686	0.0	00	0.5	33	8.5	561	3.0	198	1.5	99	15.0	990
22	4,400	30.5	1,342	0.0	00	0.5	22	35.0	1540	1.0	44	2.5	110	21.5	946
23	9,600	66.0	6,336	1.0	96	0.5	48	16.0	1536	7.0	672	1.0	96	8.5	816
24	5,400	71.0	3,834	0.0	00	0.0	00	14.0	756	3.5	189	0.5	27	11.0	594
25	9,600	73.5	7,056	0.0	00	0.0	00	6.0	576	5.0	480	0.5	48	15.0	1440
26	14,000	76.0	10,640	0.0	00	0.0	00	7.5	1050	1.5	210	2.0	280	13.0	1820
27	19,400	80.5	15,617	0.0	00	0.0	00	8.5	1649	0.0	00	0.5	97	10.5	2037
28	16,000	79.5	12,720	0.0	00	0.0	00	6.0	960	3.0	480	0.0	00	11.5	1840
29	17,800	73.0	12,994	0.0	00	0.0	00	7.0	1246	2.5	445	0.0	00	17.5	3115
30	15,000	70.5	10,545	0.0	00	0.0	00	8.5	1275	2.5	375	0.5	75	18.0	2700
31	14,200	67.5	9,585	0.0	00	0.5	71	12.5	1775	3.0	426	0.0	00	16.5	2343
Feb. 1	14,400	74.0	10,656	1.0	144	0.5	72	10.0	1440	1.0	144	0.0	00	13.5	1944
2	21,000	80.5	16,905	0.5	105	1.0	210	9.0	1890	2.0	420	0.0	00	7.0	1470
3	9,200?	76.0	6,992	0.5	46	0.5	46	12.5	1150	0.5	46	0.5	46	9.5	874
4	17,400	79.0	13,746	1.0	174	0.5	87	7.5	1305	3.0	592	0.0	00	9.0	1566

Platelets relatively few until January 27 increasing afterward to an apparent maximum on February 3 and 4. Patient admitted January 21 with temperature of 103.4°. Temperature normal January 22. On January 23 temperature rose to 100.8° in the afternoon, when a pleuritic friction rub was heard and patches of consolidation made out in the lower right lobe. Thereafter there was irregular fever with a maximum of 104.8° on January 28. Temperature declined from this point, but persisted until February 3. An otitis media had developed and the ear drum was incised on February 1.

Case IX.—Mr. S.

1920.	Total count.	Neutrophiles.		Eosinophiles.		Basophiles.		Small lymphocytes.		Large lymphocytes.		Large mononuclears.		Transitionals.	
		Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.
Jan. 24	6,600	41.0	2,706	0.5	33	0.5	33	36.0	2376	9.0	594	2.0	132	11.0	726
26	5,200	43.0	2,236	0.0	00	0.0	00	32.5	1690	7.0	364	1.0	52	16.5	858
28	5,400	34.0	1,836	1.5	81	0.0	00	42.0	2268	6.5	351	1.0	54	15.0	810
29	17,200	80.0	13,760	0.0	00	0.5	86	8.0	1376	2.5	431	0.5	86	8.5	1462
30	12,600	73.0	9,198	0.0	00	0.0	00	13.0	1638	3.0	378	0.5	63	10.5	1323
31	16,200	73.5	11,907	1.0	162	0.0	00	12.0	1944	0.5	81	0.0	00	13.0	1106

Platelets distinctly few until January 29, remaining above normal thereafter. Patient admitted on January 24 with temperature of 102°. Temperature normal on January 27 and 28. On January 29 temperature rose to 102.2° and a patch of decreased resonance and increased fremitus was found in the lower right lobe. Temperature normal on February 1; rose again on February 3, when patient was found to have parotitis Eventual recovery.

Case X.—Miss K.

1920.	Total count.	Neutrophiles.		Eosinophiles.		Basophiles.		Small lymphocytes.		Large lymphocytes.		Large mononuclears.		Transitionals.	
		Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.
Jan. 20	...	71.0	...	0.0	..	1.5	..	14.5	..	6.0	..	0.0	..	7.0	
21	...	57.0	...	1.0	..	0.0	..	27.0	..	7.5	..	1.5	..	6.0	
23	6,200	66.5	4123	0.0	00	0.0	00	21.0	1302	6.5	403	1.5	62	5.0	310
24	5,200	64.0	3328	0.0	00	0.5	26	24.0	1248	3.5	182	0.5	26	7.5	390
25	8,400	76.5	6426	0.0	00	0.0	00	15.0	1260	3.0	252	3.0	252	2.5	210
26	10,600	57.0	6042	0.0	00	0.5	53	28.0	2968	5.0	530	0.5	53	9.0	954
29	12,200	68.0	8296	0.5	61	0.0	00	17.5	2135	5.0	610	1.0	122	8.0	978

Platelets relatively few until January 29. Patient admitted January 19, with temperature of 101.2° with rales at both bases posteriorly. On January 21, a patch of consolidation in the lower right lobe was diagnosed. On January 25 consolidation was found at both bases. Temperature was normal on January 27. Convalescence was delayed by the development of new areas of consolidation in the right infrascapular region on February 5, with new febrile reaction which persisted until February 11. Recovery.

In two of these we have a characteristic behavior of the leukocytes in the early phases of the disease. The neutrophiles reach a low level in the circulating blood. Clinically the patients' temperature reached normal, and one might have expected immediate recovery; but there is a return of fever and, coincidently, a change in leukocytic picture to a neutrophile leukocytosis and an area of pulmonary consolidation is discovered. After a period of irregular but fairly high leukocytosis there is recovery. Case X, with a somewhat irregular leukocytic picture, yet with early characteristics that indicate its etiology, shows a much feebler response to the pulmonary infection, and clinically the case had a longer course.

There is a consistency in these blood findings which would seem to justify certain conclusions, if not from these cases alone, at least when they are taken in conjunction with the work of others. They show that uncomplicated influenza has a characteristic blood picture. The features of this are an early neutrophile leukocytosis followed by a sharp drop to a leukopenia, with a marked deficiency in cells of marrow origin and of blood platelets and with a lym-

phocytosis of varying degree. There is a gradual return toward a normal picture, but a cessation of fever and of symptoms may occur with the presence of a very abnormal blood count.

This leukopenia suggests somewhat that of typhoid fever and also somewhat that of measles. It indicates sharply that the primary infecting agent is not a pyogenic coccus. The leukopenia in influenza would appear to depend upon a marrow inhibition like that in typhoid fever and not upon a severe injury to the marrow or to its exhaustion for in both diseases, given a pyogenic stimulation of the marrow through secondary infection, there is immediate response with a neutrophile leukocytosis, at least in reactive individuals. Even in other cases, as in the last of the series, with low total count, marrow response is shown in the relative neutrophile increase. What the nature of this marrow inhibition or negative chemotaxis may be is not evident.

This great poverty in circulating neutrophilic leukocytes would seem to account for the frequency of pyogenic complications in influenza. The complications in Cases VIII and IX have followed directly upon a very low neutrophile blood content. These cases, taken in conjunction with observations in measles and other conditions in which there is a similar low content of neutrophiles and succeeding pyogenic complications, suggest strongly that there is a danger limit of neutrophile reduction beyond which we become a prey to coccus infection—either from those we harbor or from those received from others by contagion. This is the basis for the point emphasized earlier, that in practice, influenza patients should not be allowed to get up and resume their ordinary life immediately upon the cessation of fever, but should be kept quiet and isolated until their blood has approached at least the normal leukocytic formula, which apparently requires almost a week from the cessation of fever.

The great platelet decrease in the blood in influenza, apparent in blood-smears, but established by the actual counts of Kinsella and Broun,[17] is apparently responsible for the hemorrhagic character of the pneumonic exudate in that complication of the disease. Given endothelial injury through the secondary infection, one would expect a much prolonged bleeding time as a result of this platelet deficiency, also some deviation from normal in coagulation.

In view of the blood changes there arises an interesting theoretical question as to the nature of the cellular defense (if such there be) against the invading virus. Conquest of the infecting agent clearly is not brought about through the agency of the neutrophile leukocytes, as they remain particularly low throughout the uncomplicated attack. There is often, and probably, as a rule, a sharp lymphocytosis, but evidence from this series is not sufficient to credit this cell absolutely with the destruction of the infecting agent and the establishment of the immunity that is acquired.

[17] Loc. cit.

OBSERVATIONS ON THE BASAL METABOLISM ESTIMATIONS IN THE GOITER CLINIC OF THE UNIVERSITY HOSPITAL.

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Studies in basal metabolism have been of the greatest scientific value and interest in experimental physiology and research medicine. Our knowledge of the physiology and of the diseases of the thyroid gland is based primarily upon such studies. Is there a practical working value as well in the estimation of the basal metabolic rate; and in what ways are such estimations of value to the surgeon in the diagnosis, prognosis and treatment of cases of hyperthyroidism?

We have found the portable Benedict apparatus of the greatest practical value in this clinic because of its small size and simplicity. In the hands of an experienced operator the readings compare favorably with those taken by the more costly and time-consuming instruments. It has been our practice to take readings on all goiter cases before and after treatment, whether that consist in ligation or thyroidectomy. Before the initial reading is made the patient is run through the various steps in the procedure on one or more days, depending on her nervous state, until we are confident she is no longer alarmed by the experience. If the case comes to ligation as the initial step in treatment a second reading is taken either before leaving the hospital or when the patient returns for thyroidectomy several months later. The final reading, after all treatment is over, is usually made within a year from the last operation, when the patient returns for final observation.

For the convenience of study and analysis we have divided our cases into four groups, based on the metabolic rate.

Group 1.   Basal metabolic rate from 10 to 20 per cent.
Group 2.   "   "   "   " 20 to 40   "
Group 3.   "   "   "   " 40 to 60   "
Group 4.   "   "   "   " 60 and up.

As the same time we have graded our cases according to the symptomatic evidence of toxicity alone into four groups. This was done without a knowledge of the metabolic rate. In Group 1 we place the mildest cases, i. e., those with the lowest grade of toxicity, and in Group 4 the severest cases, i. e., those with the highest grade of toxicity. Groups 2 and 3 are intermediate. We find that there is a certain conformity between the groups graded by the

clinical picture and graded by the metabolic rate. Table I shows the percentage of cases in each group when classified by the two methods.

TABLE I.

	Per cent. of cases based on basal metabolism.	Per cent. of cases based on clinical pictures.
Group 1	26.4	30.9
Group 2	21.4	19.0
Group 3	30.9	33.3
Group 4	21.4	16.6

The largest percentage of cases fall in Group 3. The conformity between the several groups, as classified on the one hand by the clinical phenomena and on the other by the metabolic rate, is sufficient to enable us to say that in the majority of cases we have in the basal metabolic rate a numerical index of the patient's toxicity. The advantages of having a numerical index is self-evident; it gives us at once a means of classifying our patients, a guide to treatment and a measure of the improvement under any particular treatment. We do not as yet have sufficient confidence in the metabolic rate to allow it precedence over the clinical picture; we regard it merely as one link in the chain of evidence and still rely upon our own judgment as to operative risk and surgical toleration in the interpretation of the symptom-complex, attaching greater significance to loss of weight, emotional instability and pulse-rate.

The metabolic rate is of special value in diagnosis in that it offers a ready means of distinguishing cases of true hyperthyroidism from those cases of neurasthenia, cardiovascular disease or tuberculosis, who present the clinical picture of toxicity and who happen to have a simple adenomatous enlargement of the thyroid. These cases are often sent to the surgeon as a court of last resort. Such cases would naturally not be benefited by any operation and might be made a good deal worse.

The metabolic rate enables us to decide for or against operation in cases in which there is little or no perceptible enlargement of the thyroid gland and in which the only evidence of toxicity is tachycardia. We have had only one instance in which we disregarded a normal metabolic rate and relied upon our interpretation of the clinical picture and operated. On leaving the hospital this case showed clinical improvement, but sufficient time has not elapsed for us to judge of the ultimate result.

In distinguishing between cases of true Graves's disease, i. e., the hyperplastic toxic goiter, and cases of toxic adenoma the observations of the metabolic rates bear out our opinion based on clinical observation, namely, that for practical purposes the two should be treated alike. We find that the metabolic rate may be as high in one as in the other and the operative risks just as great. The distinction is purely a pathologic one, and for the present, at least, we see no reason for laying much stress on it.

In treatment we find that we may be guided by the metabolic rate in the choice of operations. Thus in Groups 1 and 2 we may proceed with a subtotal thyroidectomy at once. In Group 3, in the majority of instances, we first do a bipolar ligation; only occasionally a thyroidectomy as the initial procedure. In Group 4 we never do a thyroidectomy first but choose either unipolar or bipolar ligation.

The metabolic rate is also useful in determining the amount of improvement which any course of treatment may have effected. Table 2 shows the numerical reduction of the metabolic rates after ligation and after thyroidectomy.

TABLE II.—REDUCTION OF THE METABOLIC RATE.

	After ligation. Points.	After thyroidectomy. Points.
Maximum	61.9	60.0
Minimum	2.2	8.0
Average	31.7	28.3

It is interesting to note that after ligation the average reduction was greater than after thyroidectomy. That the two figures cannot be compared, and any deductions drawn as to the relative value of these two procedures is evident when we consider the type of case which is selected for ligation. Those cases which have a preliminary ligation have the highest metabolic rates. In reducing the metabolic rate it is as though we were reducing the height of a pyramid; much less effort is expended in taking away the top half, the labor increasing with each successive step. It is easier, therefore, to cut down the top half of a high metabolic rate by ligation than to remove the remainder, this more difficult part of the work being accomplished by the thyroidectomy. The reduction in total points, therefore, is less after thyroidectomy than after ligation.

Summary. Estimations of basal metabolism are of value in the following ways:

1. Positive. In eliminating those cases which will not be benefited, and might be made worse by operation.

2. Supplemental. (*a*) In offering confirmatory evidence of the degree of toxicity.

(*b*) In offering a quantitative rather than a qualitative index for use in diagnosis, prognosis and treatment.

3. Problematical. It may be possible to determine by the metabolic rate how much thyroid tissue may be removed. The reduction of the metabolic rate to points well below that of the normal range (–10) should imply that too much secreting substance had been removed. Such cases must be studied clinically for signs of hypothyroidism. We have had two patients whose metabolic rate after operation fell well below normal—in one to −17 per cent., the second to −30 per cent. Neither of these cases has shown signs of hypothyroidism.

CLINICAL OBSERVATIONS ON PAROXYSMAL AURICULAR FIBRILLATIONS AND FLUTTER.

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The following report is based on clinical observations made on paroxysmal auricular fibrillation and flutter. The close relationship of the mechanism of these two conditions, their appearance in the same type of cardiac conditions and their similar clinical significance will permit their being considered together.

A summary of the important features of the clinical histories of the eleven cases covered will be given.

1. *Paroxysmal auricular fibrillation as associated with chronic myocarditis, chronic valvular disease—aortic and mitral regurgitation—arteriosclerosis, hypertension, emphysema and chronic bronchitis.*

Mr. J., janitor, aged sixty, single, entered the Presbyterian Hospital on the service of Dr. Herrick, September 24, 1919. He complained of shortness of breath, cough, weakness and swelling of the feet. The cough had been present for many years during the winter months. The shortness of breath was first noticed in the fall of 1918. Since that time it had been growing progressively worse. In the last few weeks the feet had begun to swell.

Past History. He denied venereal infection. A bilateral herniotomy was done in 1911. At that time a hydrocele was aspirated and one testicle was removed. Later the other testicle was removed. The patient was unable to give any information as to why the testicle was removed other than that it was diseased.

Examination. The lips were cyanosed and there was a marked pulsation of the arteries of the neck. The breathing was shallow and labored. The chest was barrel-shaped. The breath tones were harsh and there were rales at the bases. The apex impulse was heaving and located in the sixth interspace in the anterior axillary line. A diastolic murmur was heard over the aortic area and to the left of the sternum. There was an apical systolic murmur that was transmitted to the axilla. The rhythm was regular except for an occasional premature contraction. The liver edge was palpable and tender. There was a purpuric rash on the legs that had been present at intervals for years. The ankles pitted. The brachial and radial arteries rolled readily under the fingers. The reflexes were present and equal.

Laboratory Findings. Blood: reds, 3,840,000; whites, 10,000; Hb., 70 per cent. Blood-pressure: systolic 190 and diastolic 88. The

Wassermann test on the blood and spinal fluid was negative.   The urine was negative.

The patient was given absolute rest in bed and the heart digitalized.   He, however, remained very short of breath for several days. On October 1 he had an attack of palpitation of the heart and the breathing became more difficult.   The heart-rate was 120 per minute and the rhythm was very irregular.   The electrocardiogram showed auricular fibrillation.   This attack lasted about twelve hours.   A sinus rhythm was maintained during his remaining stay in the hospital.   He was discharged in February much improved. Since this time he has been seen at frequent intervals in the Cardiac Clinic of the Central Free Dispensary and has remained free from attacks of rapid irregular heart action.

2. *Paroxysmal auricular fibrillation without much evidence of structural changes in the heart and bloodvessels.*

Dr. H., aged fifty-five, consulted Dr. Herrick for attacks of rapid, irregular heart action.   The attacks first appeared five years ago. At that time he had several attacks.   Each attack lasted from one to twelve hours.   He was not short of breath on exertion.   He felt tired most of the time.   Following this he grew strong, the cardiac attacks disappeared and for more than four years he did more work than at any other period during his life.   About eight months ago he began to feel tired again and the attacks reappeared.

Past History.   He had pneumonia at twenty-five and an appendectomy at forty-six.

Examination.   On examination the heart was slightly enlarged to the left.   The physical findings were otherwise negative.   The systolic blood-pressure was 160 mm. Hg and the diastolic 90 mm. Hg.   The urine was negative.   The electrocardiogram that was taken during an attack showed auricular fibrillation.

3. *Paroxysmal auricular fibrillation associated with mitral stenosis, arteriosclerosis, and focal infection of teeth and tonsils.*

Mrs. B., white woman, single, aged sixty-nine, entered Presbyterian Hospital on Dr. Herrick's service, June 23, 1919.   She complained of attacks of palpitation in which the heart-rate was very rapid and the rhythm irregular.   The first attack appeared in October, 1918. At first they appeared about every month or six weeks.   Lately, however, they were as frequent as three or four a week.   They lasted from a few hours to two days.   She always held that exertion precipitated an attack.   She was not apparently short of breath on exertion.   She was told four years ago that she had a systolic blood-pressure of 210 mm. Hg.

Past History.   Typhoid at twenty-four, erysipelas at forty-eight. She had frequent sore-throat during early life.   The family history was negative.

Physical Examination.   Eyes were negative.   The lower teeth were false.   The upper had several inlays and showed evidence of

pyorrhea. The neck and lungs were negative. The left border of the heart extended 12 cm. to the left of the midsternal line. There was a slight presystolic thrill at the apex and a presystolic and a systolic murmur were heard in this location. There was also a systolic murmur over the aortic area and the second tone was indistinct. The abdomen and extremities were negative except for some hardening of the radial and brachial arteries.

Laboratory Findings. Blood: reds, 3,420,000; whites, 6500; Hb., 58 per cent. Blood-pressure: systolic 168 and diastolic 95. The urine was negative except for a few leukocytes. The Wassermann on the blood and spinal fluid was negative.

During the first four weeks of her stay in the hospital she had frequent attacks of irregular heart action. Electrocardiograms showed the abnormal rhythm to be auricular fibrillation. These attacks lasted from one to twenty-four hours.

X-ray films of the upper teeth showed several small apical abscesses. On July 22 all the upper teeth were extracted. This was followed by a paroxysm of auricular fibrillation. Her tonsils showed evidence of chronic infection and were removed on August 6. She again had a paroxysm of auricular fibrillation. Since that time, *i. e.,* for a period of fourteen months, she has been free from attacks and feels better generally than she has in years.

4. *Paroxysmal auricular fibrillation, chronic nephritis, hypertension, arteriosclerosis and chronic myocarditis.*

Mrs. B., aged sixty-seven, was referred to the cardiac department of the Central Free Dispensary in April, 1920. She had been attending the dispensary at intervals since 1912. At that time she complained of headaches, dizziness and frequent urination. A trace of albumin and granular and hyalin casts were found in the urine. The blood-pressure was 170 systolic and 110 diastolic. At the time of the first examination in the cardiac department she complained of palpitation and rapid heart action. The heart-rate was 130 per minutes and very irregular. She stated that she had had similar attacks at intervals for a period of nine to ten years. At first they were a few minutes to two hours in duration, and appeared on the average of once a month. Lately they have been as frequent as one to two a week and may last from one to two days. The shortness of breath has been more marked in recent attacks and swelling of the feet has been first noticed.

Past History. She had typhoid at fourteen. Four children were living and well. There had been no miscarriages.

Examination. The eyes were negative. The teeth were gone except for a few uppers that were in bad condition. The tonsils were submerged and fibrous. There was a cervical adenopathy. The lungs were emphysematous. The breathing tones were harsh and numerous rales were heard at the bases. The left cardiac border was in the sixth interspace at the anterior axillary line. The tones

were faint. A systolic murmur was heard at the apex and was transmitted to the axilla. The aortic second tone was accentuated. The heart-rate was 120 per minute and the rhythm was very irregular. The liver extended two fingers below the costal margin. The blood-pressure was 170 systolic and 110 diastolic. The urine contained albumin and granular and hyalin casts. The Wassermann on the blood was negative.

The patient was seen the following day. The attack of auricular fibrillation had subsided and she was feeling fairly comfortable. Since this time the cardiac reserve has been built up by the administration of digitalis and by rest and the attacks of auricular fibrillation have been much less frequent.

5. *Paroxysmal auricular fibrillation, which later became permanent, associated with mitral stenosis.*

Mr. L., aged thirty-eight, had been treated at the Central Free Dispensary since 1917. He complained of pains in the joints and frequent sore-throats. At the time of his first visit it was noted that he had a very high-grade mitral stenosis. He had had an attack of rheumatic fever in 1913. Many joints were involved. The tonsils were removed in the summer of 1917. In May, 1919, he was transferred to the Cardiac Clinic. At this time he complained of palpitation, shortness of breath and precordial pain.

Examination. The head, neck and lungs were negative. The left cardiac border was 2 cm. outside of the midclavicular line. The apex impulse was diffuse. There was a marked thrill in this location. A harsh presystolic and a soft diastolic murmur were heard. The heart-rate was 74 per minute and the rhythm was regular except for an occasional premature contraction. The abdomen and extremities were negative.

Laboratory Findings. Blood: reds, 4,200,000; whites, 7800; Hb., 80. Blood-pressure: systolic 110 and diastolic 70. The urine was negative. The electrocardiogram showed a right ventricular preponderance and auricular premature contractions.

The patient improved with rest and digitalis. Later, however, he became more short of breath and complained of having short attacks of very rapid irregular heart action. An electrocardiogram was taken during one of these attacks and showed auricular fibrillation. About two months later the auricular fibrillation became permanent.

6. *Paroxysmal auricular fibrillation. Chronic myocarditis, diabetes and gangrene of the right foot.*

Mr. M., aged fifty-five, entered the Presbyterian Hospital on Dr. Herrick's service February 2, 1918. He was told at the Central Free Dispensary that he had sugar in his urine and was sent to the hospital for treatment. He said that he was often thirsty and drank a considerable quantity of water. There was apparently not much polyuria. He had been short of breath on slight exertion for about

two years and had been troubled with a dry cough for many years. He had a soft chancre at the age of twenty-five and three years later gonorrhea. The family history was negative.

Examination. The pupils were equal, regular and reacted to light and accommodation. All the teeth were missing. The chest was emphysematous. There were numerous moist musical rales in the bases of the lungs. In front the breath tones were harsh. The left cardiac border extended to the anterior axillary line. The tones were indistinct. A systolic murmur was heard at the apex. The rhythm was regular. There was a large umbilical hernia. The reflexes were normal. The red blood cells numbered 4,900,000, whites 7500, and the hemoglobin 85 per cent. The systolic blood-pressure was 204 and the diastolic 110. The urine contained 4.3 per cent. sugar; no albumin or casts. The blood Wassermann was negative.

On a carbohydrate-free diet the sugar disappeared from the urine on the second day. On March 3 he had an attack of rapid, irregular heart action. An electrocardiogram showed auricular fibrillation. The attack lasted about twelve hours. He had another attack of auricular fibrillation ten days later. The following day the rhythm was regular and the cardiac rate was 88 per minute. He was discharged from the hospital May 13, 1918. His urine had been free from sugar since the second day after admission to the hospital, and he felt much stronger generally.

He was sent to the hospital again May 30, 1919, by Dr. W. D. Sansum, from the diabetic clinic of the Central Free Dispensary. He complained of pain in the right foot and sugar had again appeared in the urine. Gangrene of the right foot developed rapidly. In the meantime the heart muscle became weak and the auricles began fibrillating. The condition gradually grew worse. Dr. Sansum finally decided to have the right foot amputated. The operation was performed by Dr. C. B. Davis, July 2, under gas anesthesia. The patient had a very stormy period following operation. The cardiac condition did not improve and the stump would not heal. Later, however, the cardiac condition began to improve and the stump gradually healed. On September 9, 1919, the patient was transferred back to Dr. Sansum. The heart had become competent. A sinus rhythm had been established and the urine was sugar-free. He remained in the hospital until May, 1920. During this time he maintained a sinus rhythm while at rest. On a few occasions, however, after slight exertion the auricular fibrillation reappeared with other symptoms of cardiac failure.

7. *Paroxysmal auricular flutter, mitral stenosis and hyperthyroidism.* Mrs. H., married, aged thirty-nine, entered the Presbyterian Hospital on Dr. Herrick's service, November, 1916. She complained of shortness of breath, palpitation of the heart, swelling of the feet, nausea and vomiting, nervousness and loss of weight. She had been

short of breath for about nine weeks. This was first noticed after doing a large washing. At this time she was conscious that her heart was beating rapidly. She first noticed that her feet were swollen three days prior to coming to the hospital. She was extremely nervous and had had difficulty in sleeping. There was no history of rheumatism. She had one child. There had been no miscarriages.

Examination. The eyes were prominent and there was a lagging of the lids. The isthmus and right lobe of the thyroid gland were enlarged. A few rales were heard in the bases of the lungs. The apex impulse was diffuse and most prominent in the fifth interspace. The left cardiac dulness extended out to the anterior axillary line. A palpable thrill was detected at the apex. A presystolic and
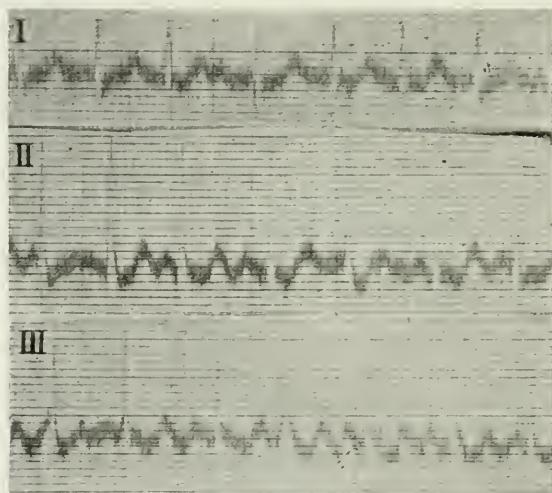
FIG. 1.—Case VII. This electrocardiogram was taken during the first cardiac attack. Some of the cycles of lead II, and especially lead III, resemble very much that of auricular flutter.

systolic murmur were heard in this location. The pulmonic second tone was accentuated. The heart-rate was 100 per minute. There was an occasional premature contraction. The liver was palpable and tender. There was a slight pitting of the ankles.

Laboratory Findings. Blood: reds, 4,200,000; whites, 9900; Hb., 85 per cent. Blood-pressure: systolic 135 and diastolic 70. The urine was negative.

On December 20 the patient suddenly became conscious of the rapid beating of her heart. She felt weak and was dyspneic. The heart-rate was about 160 per minute and the rhythm was very irregular. This was, according to the patient, the first attack of this nature. The electrocardiogram (Fig. 1) was taken. In some

cardiac cycles the auricular activity was suggestive of flutter, in others of fibrillation. She had a similar attack the following day. The electrocardiogram was the same as that taken during the first attack. She gradually improved under rest and general manage-
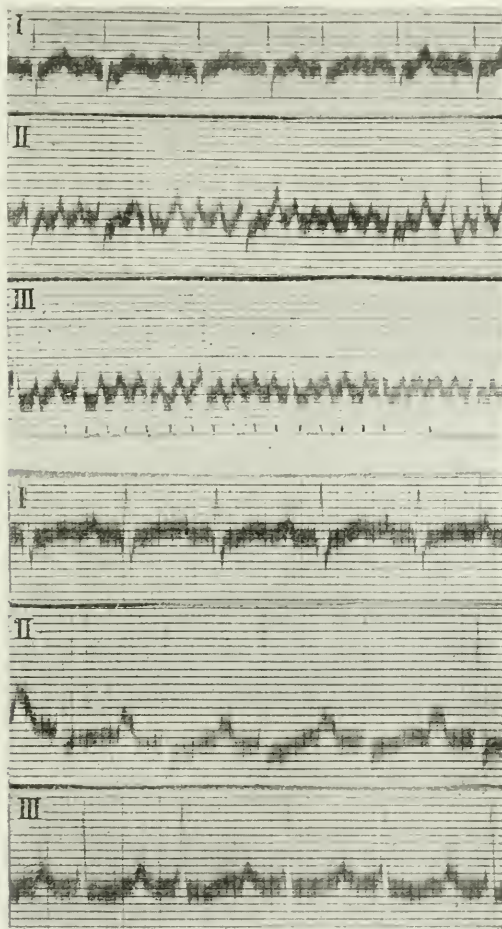
Fig. 2.—Case VII. Top: Taken during an attack after second admission to hospital. The ventricular rate was about 96 per minute. Bottom: Taken the following day after a sinus rhythm was established. The *PR* interval is about 0.2 second.

ment and was discharged from the hospital January 22, feeling fine. During this time she had had no more attacks of tachycardia.

She felt well until September, 1917, and was able to do light housework very comfortably. She was, however, short of breath on exertion. She contracted a cold at this time and a cough per-

sisted for several weeks. She became nervous again. The appetite was poor and she lost weight. She occasionally became nauseated and vomited. She felt so bad generally that she returned to the hospital in February, 1918. The physical findings were much the same as those on former admittance. The heart-rate was 80 and the rhythm was regular. On the following morning she became dizzy and faint and according to the nurse lost consciousness at one time. The intern was called. He found the heart-rate 40 per minute and the rhythm very irregular. An electrocardiogram taken on the same morning showed auricular flutter. During the next few days the patient had several attacks lasting from three to twelve hours. The rhythm was always irregular during an attack. The heart-rate gradually increased to about 100 per minute. An electrocardiogram taken during a period of sinus rhythm showed a prolonged *PR* interval (Fig. 2). The patient was very weak and at times irrational. She was unable to take food by mouth. She gradually improved the next few weeks and was discharged from the hospital May 27 in fairly good condition. Since this time she has occasionally seen Dr. Herrick at his office. She still has some symptoms of hyperthyroidism but has had no more attacks of cardiac irregularity to her knowledge.

8. *Paroxysmal auricular flutter, hypertension and cardiac asthma.* Mrs. M., white woman, aged forty-eight, married, entered the Presbyterian Hospital on Dr. Herrick's service March 3, 1920. She complained of high blood-pressure and attacks of dyspnea at night. She had been troubled with attacks of dyspnea during the night for about one and one-half years. They always appeared just at the time she fell asleep and lately had become so frequent that she got very little sleep. She had known that she had high blood-pressure for several years. She was short of breath on exertion.

Physical Examination. The head was negative. The pupils were equal and reacted to light and accommodation. Several teeth were missing and those that remained contained fillings and inlays. The tonsils were small with no evidence of infection. There was quite marked pulsation of the arteries of the neck. The lungs were negative. The apex impulse was just inside of the anterior axillary line in the sixth interspace and was heaving in character. There was a systolic murmur at the apex transmitted to the axilla. The aortic second tone was sharp and ringing. The rhythm was regular. The abdomen and extremities were negative.

Laboratory Examination. Blood: reds, 3,350,000; whites, 18,000; Hb., 45 per cent. Blood-pressure: systolic 206 and diastolic 122. Urine contained a trace of albumin at times and a few granular and hyalin casts. The Wassermann on the blood was negative. X-ray pictures of the teeth showed apical infection of two upper molars. These were extracted. The routine electrocardiogram (Fig. 3) showed the beginning of a short paroxysm of auricular flutter in lead II.

9. *Paroxysmal auricular flutter. Mitral stenosis and aortic regurgitation.*

Frank S., aged fifteen, messenger boy, visited the cardiac clinic of Rush Medical College in January, 1920. He complained of pain in the precordium, palpitation of the heart and rheumatism. He stated that the pain in the precordium was sticking in character and rarely lasted more than five to ten minutes at a time. It was always accompanied by palpitation. He had had four attacks in the last four years. The last attack appeared one month previous. He was short of breath on ordinary exertion.

Past History. He had a severe attack of rheumatic fever four years ago. He was confined to bed one month and many joints were involved. He had had three subsequent milder attacks.
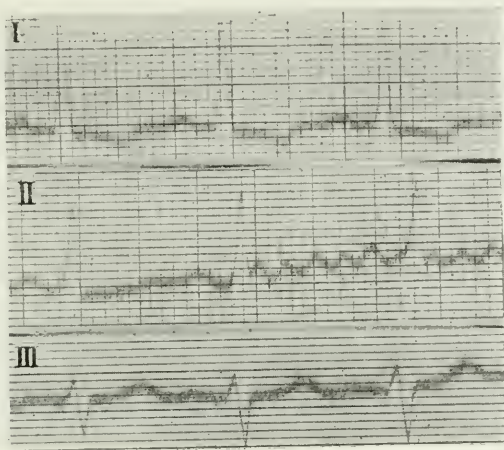
Fig. 3.—Case VIII. Lead II shows the beginning of a paroxysm of auricular flutter. The same ventricular rate is maintained. This attack evidently lasted only a few seconds, as lead III shows a sinus rhythm.

Examination. The eyes were negative. The tonsils were small and submerged. The teeth had been neglected and many were carious. The neck was normal. The lung findings were negative. The left cardiac border was 12 cm. from the midsternal line and the right border 3 cm. There was a rough presystolic murmur at the apex. A diastolic murmur was heard over the aortic area and to the left of the sternum. The pulmonic second tone was accentuated. The spleen was palpable. The reflexes were normal. The urinary findings and blood Wassermann were negative. An electrocardiogram (Fig. 4) taken the same day showed a peculiar auricular activity in lead III, which was though to be flutter. The ventricular rhythm remained regular in this lead and the rate the same as in the other two leads.

This patient has not returned to the clinic, but the social worker reports that he is well and able to work as a messenger boy.

10. *Paroxysmal auricular flutter. Chronic myocarditis, arteriosclerosis, hypertension, chronic bronchitis, bronchial asthma and emphysema.*

Mr. B., aged eighty-one, has been attending the Central Free Dispensary for various ailments, as chronic bronchitis, tonsillitis and rheumatism, for about ten years. During the last two to three years he has become more short of breath and was transferred to the cardiac clinic in October, 1919. At this time he was complaining of shortness of breath, cough, and wheezing in the chest.

Examination. The eyes were negative. The teeth were gone. The tonsils were small with no evidence of infection. The lungs were
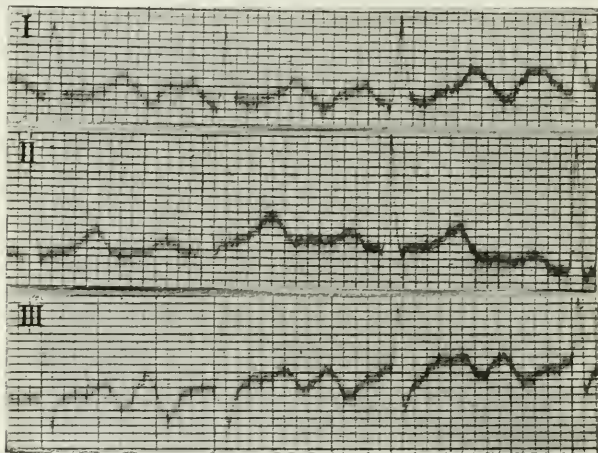
Fig. 4.—Case IX. Leads I and II are sinus rhythms. Lead III is apparently an auricular flutter with an auriculoventricular ratio of 3-1. The ventricular rate is 100 per minute and the auricular rate is 300 per minute.

emphysematous and sibilant rales were heard throughout. The left cardiac border extended to anterior axillary line. The tones were faint. A soft systolic murmur was heard at the apex and over the aortic area. The aortic second tone was accentuated. The rhythm was regular and the cardiac rate was 60 per minute. He had a bilateral inguinal hernia. There were no other abdominal findings.

The systolic blood-pressure was 180 and the diastolic 110 mm. Hg. The urine was negative.

On January 17 he was wheezing more than usual and was more dyspneic. The liver was palpable and tender. The cardiac rate was about 70 per minute and the rhythm was regular. The electrocardiogram (Fig. 5) showed auricular flutter. More rest was advised. The dose of tr. digitalis was increased from 15 to 20 m. three times a day.

At the next visit four days later his general condition had improved and a sinus rhythm had been established (Fig. 5), which has been maintained, according to our knowledge, ever since.

11. *Paroxysmal auricular flutter.   Chronic myocarditis and angina pectoris.*

Mr. H., aged sixty, complained of a feeling of constriction in the precordium on exertion. The pain extended into the arms at times. This distress was always relieved by nitroglycerin. He was also short of breath on exertion. These symptoms had been present about two months and were gradually growing more severe.

He had had typhoid at the age of sixteen and rheumatism several times, but not in the last thirty years.

Examination. The physical findings were negative except for the heart. The left cardiac border was 12 cm. from the mid-
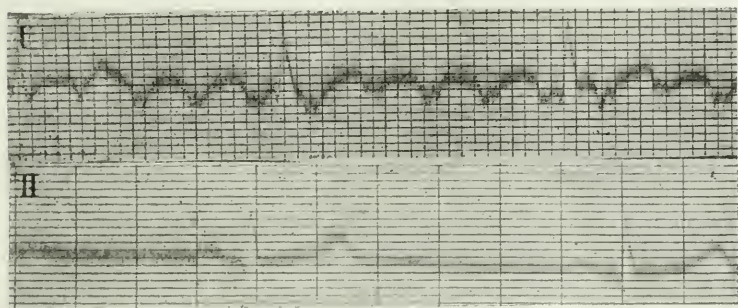
Fig. 5.—Case X. Top: Lead II shows an auricular flutter with an auriculo-ventricular ratio of 4-1. Bottom: Lead II, taken after the sinus rhythm had returned.

sternal line. A systolic murmur was heard at the apex. The aortic second tone was accentuated. There was an occasional premature contraction.

The systolic blood-pressure was 166 and the diastolic 85 mm. Hg. The urine and blood Wassermann were negative. The electrocardiogram (Fig. 6) showed an auricular activity suggestive of flutter in leads I and III. In lead II the auricular mechanism is different. The waves marked *P'* occur at regular intervals. If this is the *P* wave it differs from that in the same derivation shown at the bottom of Fig. 6, which is apparently a sinus rhythm. The electrocardiogram at the bottom of Fig. 6 was taken a few minutes later than the one shown at the top.

Summary of Cases. Brief histories of eleven cases are given in which paroxysms of an abnormal auricular action were discovered. In six instances it was auricular fibrillation and in five auricular flutter.

Those patients with auricular fibrillation were conscious of the onset of the attack. In three instances we observed the initial attack. In the other three the paroxysms had extended over periods of one, five and nine years respectively. Four had symptoms of
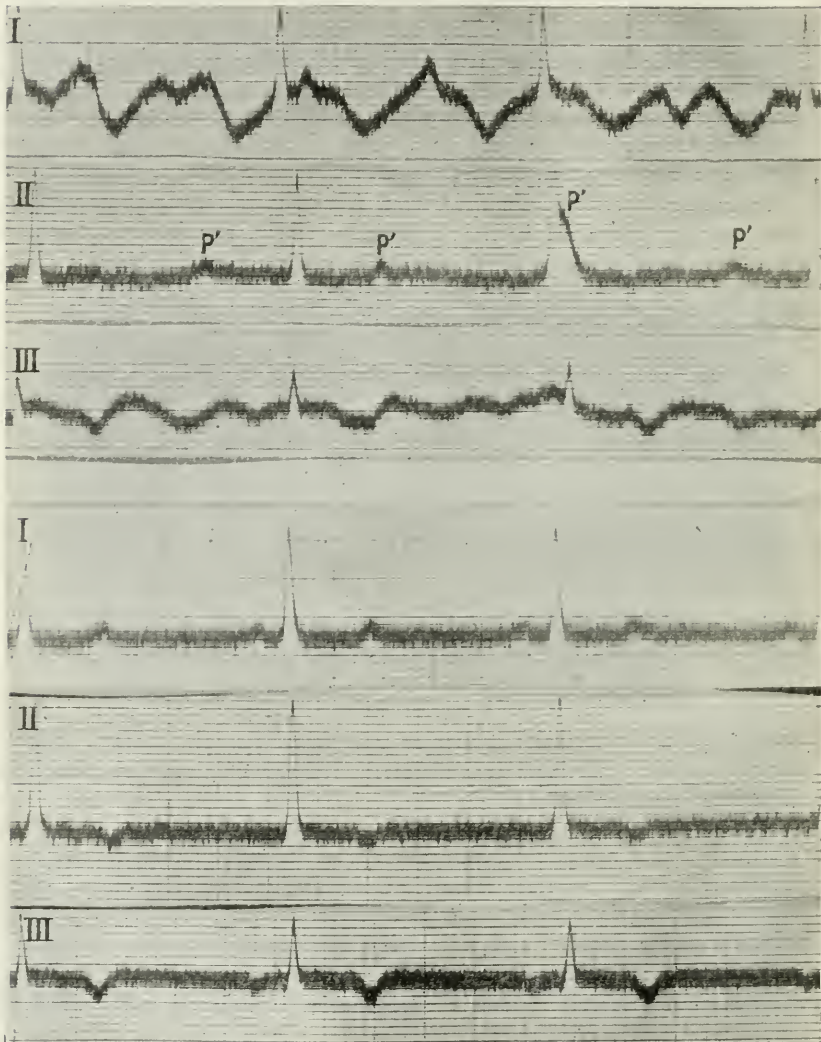
Fig. 6.—Case II. Top: Lead I is probably an auricular flutter. Lead III resembles lead I. Lead II is unlike the other derivations. The ventricular response has, however, remained regular. The wave marked *P'* occurs at regular intervals and may be a *P* wave. This wave, however, differs from the *P* wave in the same derivation in the electrocardiogram at the bottom of the figure, which is apparently a sinus rhythm. Bottom: Taken a few minutes following the electrocardiogram shown at the top.

myocardial failure. In one of these, however, the paroxysms antedated the appearance of other cardiac symptoms. In this case the attacks had been much more frequent since the onset of shortness of breath. Case No. 6 had two paroxysms of auricular fibrillation within a period of ten days in March, 1918. After this he was free from attacks until May, 1919. At this time gangrene of the right foot developed, the heart became decompensated and the auricles began fibrillating. The right foot was, however, amputated below the knee under gas anesthesia. Following the operation there was a period of more than two months during which the cardiac condition improved very slowly and stump did not heal. Later the cardiac compensation was restored, a sinus rhythm was established and the stump healed. The rhythm remained regular while the patient was quiet in bed. Upon slight exertion, however, the auricular fibrillation appeared again at times along with other signs of cardiac failure. Two had no cardiac symptoms other than the transient attacks of auricular fibrillation. In one of these the attacks had extended over a period of five years. The initial attack appeared at a time when he felt overworked. His general health later became improved and he was free for almost four years. During this time he worked very hard. He again began to feel tired and the attacks returned. In a recent communication he tells me that he rested for two months after seeing Dr. Herrick. During this time he felt better generally, was less nervous and was free from attacks. He began to work again and has since had a few attacks. The last patient had had attacks of rapid, irregular heart action for about one year. At the time she entered the hospital they appeared two or three times a week. While in the hospital some infected teeth were extracted and the diseased tonsils were removed. She has been free from attacks since this time. Her general health has improved and she feels better than she has in years.

The electrocardiograms of these patients were typically those of auricular fibrillation.

Five patients were observed during paroxysms of auricular flutter. One was conscious of the attack. In the remaining four the ventricular response was regular. In two of these the ventricular rate was 100, in one 75 and the remaining one 60 per minute. In each of these instances the auricular tachycardia was discovered accidentally. Each of the patients in this group had marked structural changes of the heart. One had in addition hyperthyroidism. All were short of breath. One had attacks of anginal pain.

The electrocardiograms of those cases considered as paroxysmal auricular flutter present some interesting features. The record of case No. 7 (Fig. 1) was taken during a cardiac attack in the fall of 1916. The ventricular response is irregular. In some cardiac cycles the auricular activity is suggestive of that of flutter, in others

that of fibrillation. The same patient had another attack in the winter of 1918. She felt faint and dizzy and at one time lost consciousness. The heart-rate was 40 per minute and the rhythm very irregular. An electrocardiogram taken the same morning showed auricular flutter. This record unfortunately was destroyed. The electrocardiogram in Fig. 2 was taken the following day. The ventricular rate was then about 96 per minute. Later when the sinus rhythm was established the PR interval was about 0.2 seconds (Fig. 2). Fig. 3 shows the onset of a short paroxysm of fine auricular flutter in Case No. 8. A normal ventricular rate and a regular rhythm were seemingly maintained during the attack. The top record in Fig. 5 is lead II of Case No. 10 taken during a paroxysm. At the bottom is the same derivation taken after the sinus rhythm had been established.

The electrocardiogram of Cases No. 9 and No. 11 are more difficult to interpret. In leads I and II of the electrocardiogram of Case No. 9 (Fig. 4) the ventricles are apparently responding to impulses formed at the sinus node. Lead III is apparently auricular flutter with an auriculoventricular ratio of 3 to 1. The same ventricular rate was maintained. Lead I of the electrocardiogram of Case No. 11 (Fig. 6) is seemingly a coarse auricular flutter. Lead III resembles lead I. In lead II, however, the auricular mechanism has changed, but the ventricular response remained regular. This derivation is unlike the corresponding one in the electrocardiogram at the bottom of Fig. 6 and is, therefore, probably not a sinus rhythm. The waves marked P' occur at regular intervals and may be P waves. If these are P waves, they are probably ectopic for they differ from those of the same lead after the sinus rhythm was apparently established. These changes in the auricular mechanisms were very fleeting. The two electrocardiograms in Fig. 12 were taken within ten minutes of each other.

Comment. *Clinical Significance of Paroxysmal Auricular Fibrillation and Flutter.* Paroxysmal auricular fibrillation and flutter occur in the same type of cardiac conditions. They are in the majority of instances discovered in individuals who have the clinical findings of a failing myocardium. These attacks frequently appear at the time of impending cardiac breakdown. They may subside as the cardiac reserve is improved or becomes permanent.

It is very probable that many cases of lasting auricular fibrillation and flutter are preceded by short paroxysms of these conditions. Three cases of mitral stenosis have recently been observed during the period of approaching cardiac failure, in whom the permanently established auricular fibrillation was preceded by one or more short attacks. One of these cases, No. 5, is included in this report.

In some instances paroxysmal auricular fibrillation and flutter are seemingly precipitated by extracardiac conditions, as focal infections about the mouth and hyperthyroidism. Case No. 3

has been free from auricular fibrillation since her infected teeth were extracted and the diseased tonsils removed.   Case No. 7 has had no further attacks since the thyroid symptoms subsided.   Case No. 6 was free from cardiac attacks for more than a year.   Later gangrene of the right foot developed.   Coincident with this auricular fibrillation appeared and continued until the leg was amputated and the stump healed.   Blackford and Willius[1] report cases that recovered from auricular flutter following thyroidectomy.   Willius[2] has observed patients with a sinus rhythm after thyroidectomy who had had, according to their history, an auricular fibrillation for more than a year.   Barker and Richardson[3] describe a case which seemingly recovered from attacks of simple paroxysmal tachycardia and auricular flutter after the clearing up of focal infection about the tonsils and teeth and the removal of a portion of the thyroid gland.

In some of those patients in whom there are demonstrable extracardiac factors there may or may not be much evidence of cardiac disease.   Even though the cardiac findings may be comparatively negative the appearance of these tachycardias should be considered as evidence in favor of structural changes in the heart. The longer these patients remain free from attacks after the removal of possible extracardiac factors, in the absence of other findings, the more certain we may feel that the cardiac changes are slight and not progressing.

The Relationship between Auricular Fibrillation and Flutter. Auricular fibrillation and flutter may occur in the same patient at different times.   Lewis[4] reported eight cases of flutter and reviewed eight more from the literature.   Thirteen of these patients had at some time had auricular fibrillation.   In six one condition passed directly into the other.   Some of these patients had been given digitalis.   Robinson[5] describes a case in which auricular fibrillation and flutter alternated with each other several times. He was able in the dog to produce experimental electrocardiograms that resembled those taken of his patient during the periods of auricular fibrillation and flutter and the transition between these conditions.   The electrocardiograms produced by faradization of the auricles resembled those of the transitional period in the patient. When, however, in addition the right vagus was stimulated the electrocardiogram was that of auricular fibrillation, whereas stimulation of the left vagus gave an electrocardiogram similar to that of auricular flutter.

Auricular flutter may in some instances be changed to auricular fibrillation by the administration of digitalis.   Before the latter stage is reached the electrocardiogram may show cardiac cycles in which the auricular activity suggests that of flutter, whereas the next few cycles may be that of auricular fibrillation.   The same type of electrocardiograms is occasionally produced by patients

who have not had digitalis (Fig. 1). Ritchie[6] believes that such electrocardiograms indicate a combination of auricular fibrillation and flutter. The same explanation has been more recently given by Schrumpf.[7] Lewis[8] emphasizes the close relation between the mechanism of these two conditions and publishes a curve from a dog in which auricular fibrillation was changed to flutter by vagus stimulation. He, however, does not believe in the simultaneous presence of the two disorders. This conception does not exclude the possibility of one mechanism changing to the other even at short intervals. That would possibly furnish a plausible explanation for some of the clinical electrocardiograms.

It is a pleasure to acknowledge my indebtedness to Dr. James B. Herrick for his suggestions and for the privilege of studying some of the cases covered in this report.

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THE RELATION OF THE ENDOCRINE SYSTEM TO THE GLYCEMIC REACTION FOLLOWING THE INJECTION OF HOMOLOGOUS PROTEIN.

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AND

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WE have previously shown[1] that variations in blood-sugar concentration follow the injection of a relatively large number of substances, and that when proteins from different sources are

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[1] Rohdenburg, Bernhard and Krehbiel: AM. JOUR MED. Sc., 1920, clix, 577.

injected into rabbits,[2] the variations observed in blood-sugar concentration follow a definite course and occur concomitantly with the development of antibodies. Variations in the blood-sugar content of normal rats and mice injected with homologous and heterologous protein were also observed,[3] and in a small series of spontaneous malignant tumor-bearing mice a large proportion of the animals showed, in contrast to normal animals, no variations in the blood-sugar concentration when injected with homologous protein.

With the intention of investigating the hypothesis that the occurrence of tumors is due to some endocrine disturbance, we have studied the effect of ablation of one or more of the glands of internal secretion upon the glycemic reaction following the injection of homologous protein. As has just been stated, tumor-bearing mice and rats differ from normal animals in their reaction to the injection of homologous protein as shown by the blood-sugar content. If the removal of one or more of the endocrine glands bring about a condition in which injections of homologous protein are not followed by a glycemic reaction, and if absence of a glycemic reaction under these conditions be considered as giving evidence of a predisposition to neoplasia, then the condition underlying predisposition to neoplasia might be subject to further experimental analysis. The term glycemic reaction in this paper has reference only to the variations in blood-sugar concentration which follow the injection of homologous protein.

Albino rats were employed, 0.05 c.c. of blood being obtained from the tail vein after the animal had fasted all night, and the blood-sugar concentration was determined by the method of Epstein.[4] The animal was then injected subcutaneously with 0.05 c.c. of an extract of homologous protein. This protein was prepared by cutting the tissues of another animal of the same species into small fragments and extracting it in approximately three times its bulk of normal saline for a period of about ten minutes. Sterile precautions are not essential. The opalescent, bloody, supernatant fluid was used. One hour after the injection of the protein extract the blood-sugar value was again determined. In the experiments recorded in this paper, spleen was used, but other tissues are equally effective. While it is true that all tissues contain glucose or glycogen the amount of either of these substances in the fluid injected was so minute that it could not be chemically estimated nor qualitatively identified.

After an injection of homologous protein one of three things may happen to the blood-sugar: It may rise, fall or remain relatively or actually stationary. No explanation can be offered for

[2] Rohdenburg and Pohlman: AM. JOUR. MED. SC., 1920, clix, 853.
[3] Rohdenburg: Jour. Cancer Research, 1920.
[4] Jour. Am. Med. Assn., 1914, lxiii, 1667.

the fact that in some instances the injection of homologous protein is followed by an increase in blood sugar while in other instances it is followed by a decrease. It is possible that the injection is always followed by an increase, but that this increase occurs with different degrees of rapidity in different animals; it may be that the time interval is so chosen that from some animals blood is drawn at a phase when the blood sugar, after having increased, falls below the normal before again returning to its preinjection level.

Thus in Fig. 1, A represents the preinjection level, B the maximum rise, C the fall below the normal and D the return to the normal. If this curve be either stretched out or compressed, as in Fig. 2, where the time intervals are shown by the upright lines, it is at once evident that in those animals in which the entire
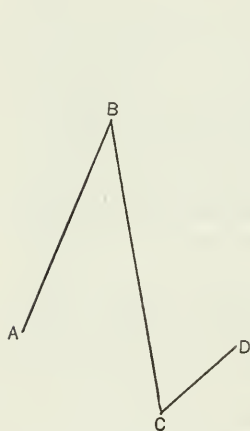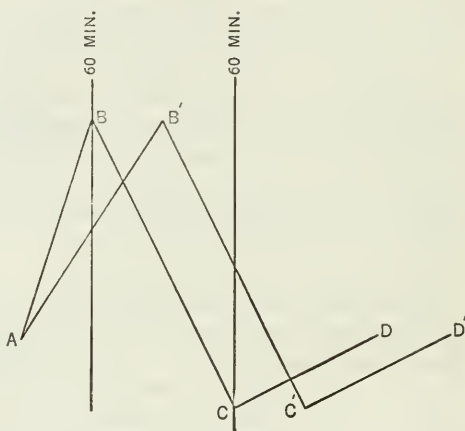
Fig. 1   Fig. 2

reaction is over quickly we might easily get a lower value one hour after injection than in those in which the reaction takes a longer period for completion.

A variation between the first and second estimations of blood sugar of 16 or more mgm. when the Epstein method is used, or of 10 or more mgm. when the Meyers-Bailey[5] modification of the Lewis-Benedict[6] method is employed, has arbitrarily been defined as a positive glycemic reaction. Reversely a negative reaction is one which shows less than these variations. It is immaterial to our present problem whether the values rise or fall.

In previous publications[2][3] we have shown that the alterations in blood-sugar concentration following protein injection are not

[5] Jour. Biol. Chem., 1916, xxiv, 147.
[6] Ibid., 1915, xx, 61.

due to the excitability of the animal, to the operative procedure, to the influence of a few seconds of anesthesia or to the injection of 0.5 c.c. of normal saline solution.

It is impossible to obtain from a rat twice within an hour the amount of blood necessary for the Meyers-Bailey modification of the Lewis-Benedict blood-sugar method, and it was for this reason that the Epstein method was chosen. We have previously commented upon the limitations of the Epstein method for determining sugar values and have pointed out the possible sources of error. Whatever the error may be, however, it is common to every determination made by that method and in comparative estimations may be disregarded if the results seem well correlated.

When 0.05 c.c. of blood is used the Epstein method gives values which are extremely high and which do not represent the actual blood-sugar content of the rat, as shown by other procedures; the figures are therefore merely relative.

A check experiment will prove the truth of this contention. Five guinea-pigs were tested according to the method outlined in a previous paragraph, the blood being obtained twice within an hour from the heart. On the specimens thus obtained blood-sugar determinations were made according to the Lewis-Benedict and the Epstein methods, 0.05 c.c. of blood being used for the Epstein method. If the assumption made be correct, then an equal percentage of positive reactions should occur, irrespective of the method employed, the double standard of comparison being kept in mind. The blood-sugar values, however, would be much higher with the Epstein than with the Lewis-Benedict method. The observations, as is shown in Table I, are in accord with our premise.

TABLE I.

Epstein method.			Lewis-Benedict method.		
Zero hour.	60-minute interval.	Variation.	Zero hour.	60-minute interval.	Variation.
No. 1 440	408	−32	No. 1 138	132	−6
No. 2 448	433	−15	No. 2 132	126	−6
No. 3 416	528	+112	No. 3 162	212	+50
No. 4 504	489	−15	No. 4 150	126	−24
No. 5 472	496	+24	No. 5 153	165	+12

Percentage giving positive reaction: Epstein method, 60; Lewis-Benedict method, 60. Averaged variation in mgm.: Epstein method, 40; Lewis-Benedict method, 20.

All figures indicate mgm. per 100 c.c. of blood.
    + = increase in blood sugar.
    − = decrease in blood sugar.

The glycemic reaction may be estimated in two ways: by the percentage of positive reactions in a given group, or by the averaged variation in sugar concentration. If we judge only by the per-

centage of positive reactions, then we have no means of estimating the degree of reaction, for with the standard as laid down a variation of 20 mgm., which is but 4 mgm. higher than what we designate a negative reaction, has the same significance as a variation of 64 mgm. It seems more accurate, therefore, to use the averaged variation as a standard of comparison.

In a series of seventy normal full-grown, healthy rats the blood-sugar values were determined before and after injection of homologous protein. As a result of these examinations it was found that 73 per cent. of the animals gave a positive reaction and that the averaged difference between the determinations at the zero hour and at the sixty-minute period was 29 mgm.; this figure has been adopted as the variation in normal animals.

In our first experiments the reaction was studied in animals from which one internal secretory gland had been removed. The glands removed individually were the spleen, thymus, both testes, both ovaries, both adrenals, all entire, approximately 90 per cent. of the thyroid and embedded parathyroids and approximately 90 per cent. of the pancreas. There were six full-grown normal animals in each group; and, with the exception of the adrenal-free group, in which owing to the short life of the animals the examinations were carried out after twenty-four hours; from fourteen to one hundred and twelve days elapsed after removal of the gland before tests were made. In a second series of animals double ablations were performed in such rotation that all possible combinations were obtained. For example: testes-spleen, testes-thymus, testes-thyroid, testes-adrenal, testes-pancreas. In each of these groups there were six animals and the averaged time of testing after gland ablation was fourteen days, again excepting the adrenal-free group, which was tested twenty-four hours after operation. A total of 162 animals were used in the experiment.

The effect of the various gland ablations upon the glycemic reaction is presented in chart form. The solid color indicates the averaged variation in milligrams for each group of 6 animals, the double vertical line the adopted normal variation of 29 mgm.

It is interesting to note that ablation of the sex glands alone influences the glycemic reaction in a different manner in each sex; thus, removal of the testes slightly inhibits, while ablation of the ovaries slightly stimulates the reaction. The removal of the spleen with either set of gonads markedly inhibits the reaction, while excision of the thymus and testes or of the thymus and ovaries causes no change from the normal. Ablation of the testes and pancreas causes a marked stimulation of the reaction; but removal of the ovaries and pancreas brings about a directly opposite result, that is, inhibition. An analogous difference in reaction is noted when the gonads are removed with the thyroid, for with this combination in the male inhibition follows, while in the female stimu-
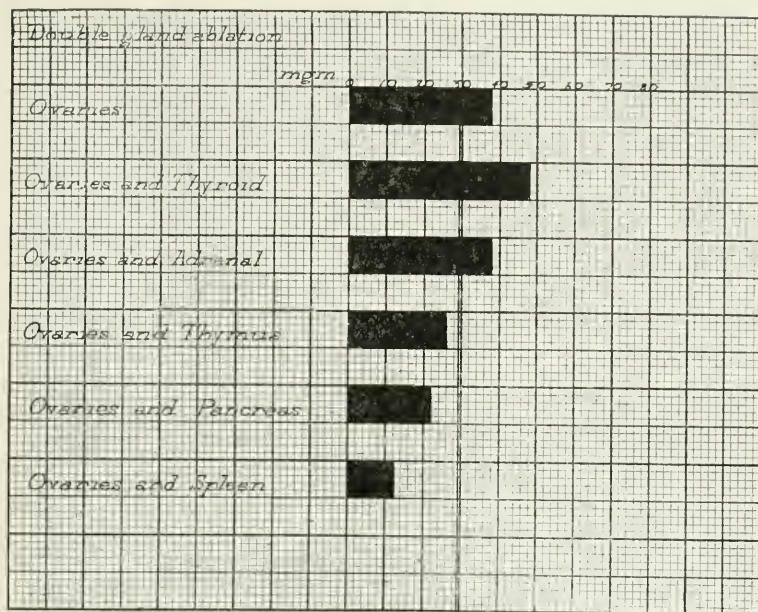
CHART I.
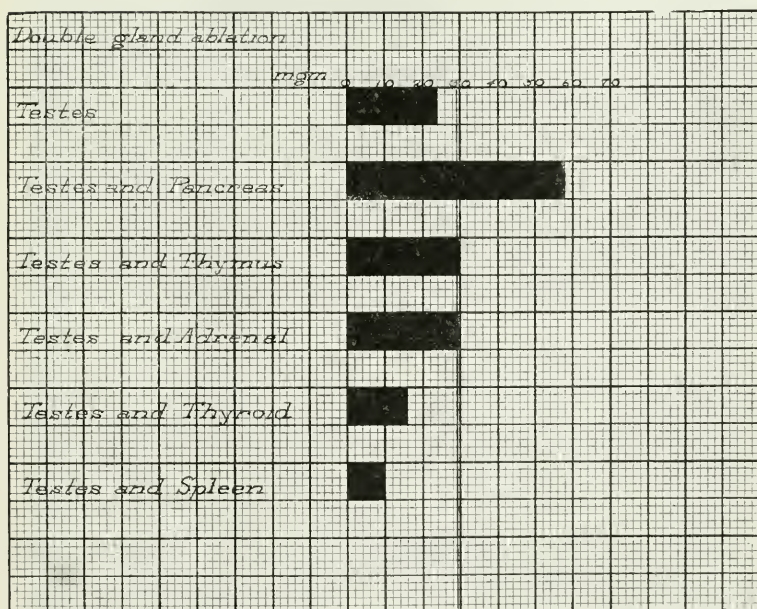
CHART II.

lation occurs. Extirpation of the adrenals in combination with the sex glands exerts little or no influence on the reaction (Charts I and II).

In rats almost complete removal of the pancreas has no effect upon the type of glycemic reaction under discussion (Chart III). However, when the thyroid, spleen or testes are removed in combination with the pancreas there is a very marked stimulation. In contrast to these results, removal of the ovaries or thymus and the pancreas shows a very slight inhibition of the reaction, while when the adrenals are ablated in combination with the pancreas there occurs the most marked inhibition encountered in the entire series of experiments.
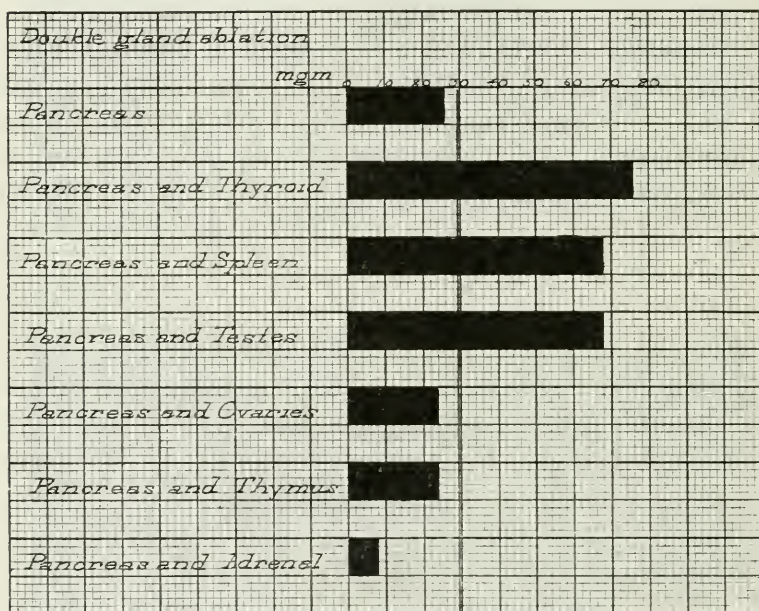
CHART III.

A very slight to moderate stimulation occurs when either the adrenals alone or a combination of adrenals with ovary, thyroid or spleen are removed. Ablation of either testes or thymus in combination with the adrenals shows practically no change from the normal, while, as previously stated, excision of adrenals and pancreas induces a most marked inhibition (Chart IV).

Excision of the thymus singly or in combination with either the testes or spleen exerts practically no influence upon the reaction. When the gland is ablated in combination with either the ovaries, adrenal, pancreas or thyroid there results a varying degree of inhibition, though it is not marked (Chart V).
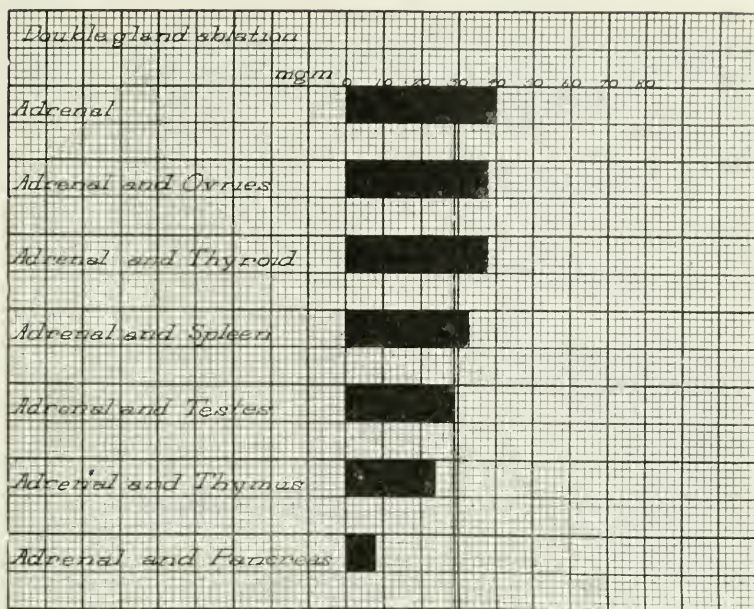
Chart IV.
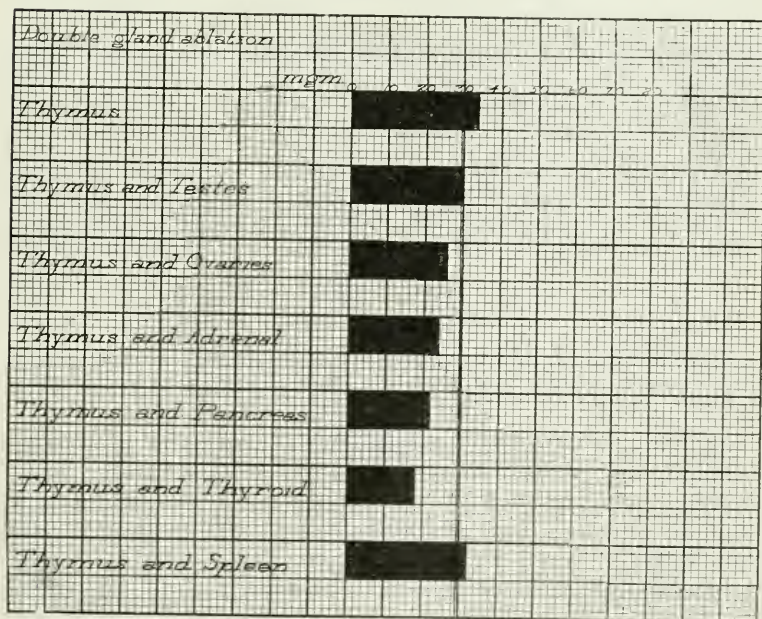
Chart V.

Removal of the spleen, alone or in combination with either gonad, induces a marked inhibition, while excision of the gland in combination with either thyroid or pancreas produces a marked stimulation. When either the adrenals or the thymus are removed in combination with the spleen there is no noteworthy variation from the normal (Chart VI).

Ablation of the thyroid, with such parathyroid tissue as may be embedded in it, results in a marked stimulation of the reaction and a similar condition prevails when the gland is removed in combination with the pancreas, spleen or ovary, and also, though to a
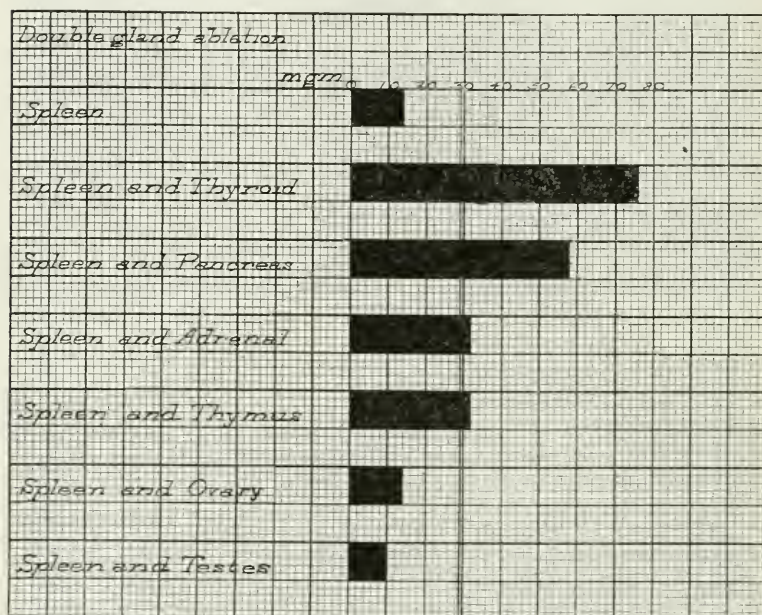
CHART VI.

lesser degree, when it is removed with the adrenals. The removal of the thymus or the testes with the thyroid gives rise to an inhibition (Chart VII).

The ablations, either of single glands or of combinations of glands which have thus far been described, result in one of three conditions: inhibition, stimulation or no change. Those which result in inhibition have, for easy reference, been collected in Chart VIII: the spleen with either set of gonads, and the pancreas and adrenals. Those which induce stimulation are shown in Chart IX: the spleen with either the pancreas or thyroid, the testes and pancreas, the thyroid and ovaries, and, finally, the pancreas and thyroid.
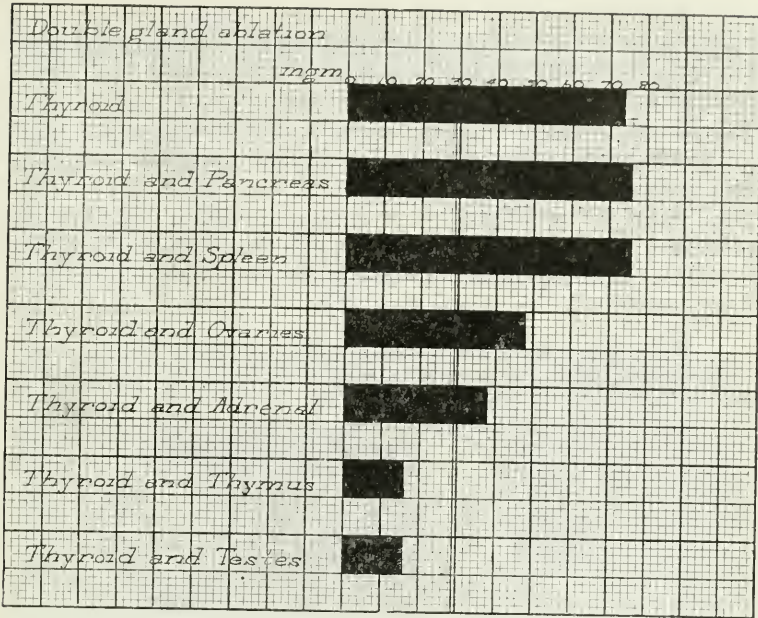
CHART VII.
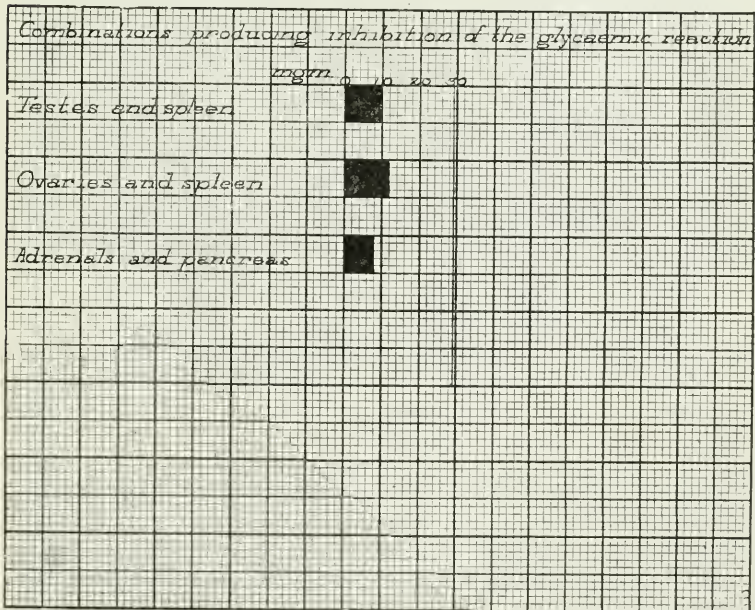
CHART VIII.

In order, if possible, to establish a correlation of glandular activity with respect to the glycemic reaction following the injection of homologous protein, further ablations were performed, three, four and five glands being removed from the same animal. Again, groups of six animals were used and the test was performed as previously described. From the results obtained it appears that the connection is as follows:

There are two combinations of endocrines which when ablated inhibit the reaction; these are (1) spleen and either gonad set, (2) adrenal and pancreas. If one gland from either system be ablated and with it one gland from the other system, there results

Combinations producing stimulation of the glycaemic reaction

Pancreas and Thyroid
Pancreas and Testes
Pancreas and Spleen
Ovary and Thyroid
Spleen and Thyroid
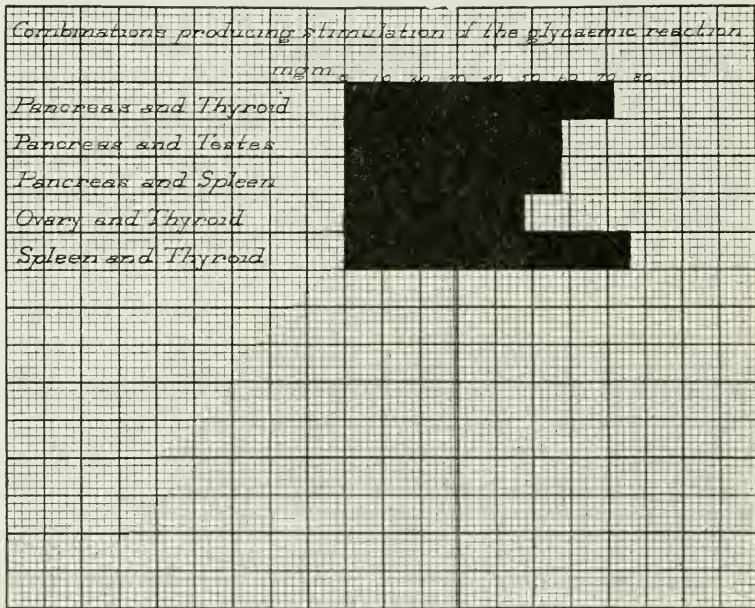
CHART IX.

little or no change from the normal reaction (see 1, 2 and 7, Chart X). If, however, one gland from one system be removed with one gland from the other system, and, in addition, either the thyroid or thymus, then marked inhibition occurs (see 5, 9, 10, 14, 15, Chart X). Removal of one gland from one system and of either the thyroid or the thymus results in practically no inhibition (see 4, Chart X). If both glands be removed from each system, then, in order to induce inhibition, both of the intermediate glands must also be removed, the removal of one intermediate gland is not sufficient (compare 3, 8, 11, 12, 13, Chart X). From this it would appear that there are two systems which control the reaction and

that these systems are connected through two apparently inter-changeable glands, the thyroid and the thymus.

We have still to consider how inhibition may occur when the various glands are *in situ*, the data so far presented having to do with conditions following their removal. It is probable that if the removal of a gland causes inhibition, then that gland when *in situ* acts as a stimulator, and that the same thing holds true for various combinations. Furthermore, it is possible that inhibition of the reaction may be due either to lack of action of the stimulators or to excessive action of the inhibitors.

Showing relation of Sex and Adrenal System

1. Ovaries and Pancreas
2. Ovaries, Spleen and Pancreas
3. Ovaries, Spleen, Pancreas and Thymus
4. Ovaries and Thymus
5. Ovaries, Pancreas and Thymus
6. Testes and Pancreas
7. Testes, Spleen and Pancreas
8. Testes, Spleen, Pancreas and Adrenal
9. Testes, Pancreas and Thymus
10. Testes, Adrenal and Thyroid
11. Testes, Spleen, Pancreas, Adrenal, Thyroid
12. Testes, Spleen, Pancreas, Adrenal, Thyroid, Thymus
13. Testes, Spleen, Pancreas, Adrenal, Thymus
14. Testes, Adrenal, Thyroid
15. Ovaries, Adrenal, Thyroid

CHART X.

The hypothesis that inhibition of the glycemic reaction following the injection of homologous protein may be an indicator of a state of predisposition to cancer, coupled with the demonstration that various combinations of gland removal bring about inhibition of the reaction, offers a wide field for speculation and suggests numerous other investigations. All that can, at the present time, be

stated as a result of the experiments here recorded is that the glycemic reaction, which follows the injection of homologous protein, appears to be under the control of the endocrine system and that inhibition of the reaction may be viewed as a disturbance of metabolism due either to hypoactivity or to hyperactivity of the endocrines. Whether this disturbance of metabolism is or is not of etiologic significance in neoplasia cannot be stated from the facts at present at our disposal.

THE LEUKOCYTES AFTER HEMORRHAGES.

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PHILADELPHIA.

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During the course of some experiments undertaken for the purpose of studying blood regeneration after simple anemia, an unusual opportunity was presented for studying the behavior of the leukocytes after hemorrhage. In this series of experiments the total number of white cells per cubic millimeter were enumerated in some cases before and in all cases immediately after bleeding and a differential count made at the same time. Other counts, both differential and total, were subsequently made at various intervals after the first count until the white cells had reached the level of the preliminary determination or had attained figures which were approximately normal for the dog. Coincidental blood-volume estimations by the dye method afforded a basis for interesting comparisons. In a previous series of forty-eight dogs these normal figures had been found to be as follows: Average count of white cells per cubic millimeter, 15,923; average number of polynuclear neutrophiles, 66.66 per cent.[1]

Before discussing the results that were attained in the present series the literature of the subject will be briefly reviewed. It seems to be a quite generally appreciated fact that a leukocytosis occurs after hemorrhage. However, in most hematologies or in books dealing with laboratory studies in general this fact either is omitted, or if mentioned but brief mention is made of this occurrence. For example, Simon[2] merely lists in a long column, among the other causes of leukocytosis, that which follows hemorrhage. Webster[3] discusses the matter more fully than do other authors of

[1] John H. Musser, Jr., and E. B. Krumbhaar: Studies of the Blood of Normal Dogs, Folia Haematologica, 1914, xviii, 576.
[2] Manual of Medical Diagnosis, 9th ed., Philadelphia, 1918, p. 55.
[3] Diagnostic Methods, 6th ed., Philadelphia, 1920, p. 572.

standard books. He says: "A well-marked leukocytosis which may begin in from ten to fifteen minutes and may reach as high as 20,000 within an hour has been observed following extensive acute hemorrhage. The leukocytosis in these cases bears a general relation to the extent and rapidity to the loss of blood and usually disappears or diminishes long before regeneration of the blood has occurred. The leukocytosis is of the polynuclear type." He further states that Stassano and Bellow, in a reference unattainable, assume from their work that a hypoleukocytosis is observed after the loss of small quantities of blood. Drinker,[4] in his admirable article on the pathological physiology of blood cells holds: "There are few biological reactions which may be so fully relied upon as the leukocytosis following hemorrhage." Camus and Pagniez[5] write that there is an immediate drop of leukocytes following hemorrhage to be followed by a leukocytosis which is merely relative, as there has not been during the hemorrhage an outpouring of white cells comparable to the loss of red cells and plasma. They quote Inagaki as achieving the same results in his studies. Levison[6] writes upon the subject from the standpoint of differential diagnosis and calls attention to the fact that a leukocytosis is valueless in differentiating intra-abdominal hemorrhage from acute inflammatory lesions. Hoessli,[7] studying the blood of rabbits after hemorrhage, showed that the white cells were decreased in the first six to eight hours and subsequently there was a temporary increase in the neutrophiles. Govaerts,[8] working under Dépage, studied the white count after hemorrhage and called attention to the fact that a leukocytosis is the most valuable sign of occult hemorrhage. He states that it showed itself before there is appreciable diminution in the number of red cells. The leukocytosis attains its greatest height several hours after the hemorrhage starts and reaches normal in from forty-eight to seventy-two hours. Krumbhaar[9] studying the leukocytosis that occurs after operation and after a relatively small hemorrhage found that the leukocyte count began to rise after four or five hours, almost doubling in the first thirty hours and then gradually declining to normal in several days to a week. He noted also that there was a greater tendency to leukocytosis after external hemorrhage than internal. Drinker[10] and his co-workers, in their work on the

[4] Diseases of the Blood, Oxford Medicine, 1920, ii, 563.

[5] Action immediate de la saignée sur le nombre des leucocytes, La rétention leucocytaire, Compt. rend. soc. de biol., 1908, lxiv, 1149.

[6] Leukocytosis a Deception Sign in Abdominal Hemorrhage, Jour. Am. Med. Assn., 1915, lxiv, 1294.

[7] Leukocytose bei Intraperitonealblutungen, Mitt. a. d. Grenzgeb. d. med. und Chir., 1914, xxvii, 630.

[8] Etude de l'anemie posthémorrhagique chez les blessés, Ambulance de l'ocean, 1917, 1, 355.

[9] Observations on the Nature of Postoperative Leukocytosis in the Dog, Ann. Surg., 1917, lxvi, 133.

[10] The Factors Concerned in the Appearance of Nucleated Red Blood Corpuscles in the Peripheral Blood, Jour. Exp. Med., 1918, xxvii, 383.

influence of certain procedures to increase the rate of blood-flow through the blood-forming organs, state that they have frequently seen the white blood count double within two hours. This they say is a real increase in the circulatory white cells and not a change in the distribution of the cells, emphasizing the fact that the marrow is a reservoir of leukocytes, which in an emergency has the power to discharge the cells independently and rapidly. Nanta[11] after a study of twenty-five cases of severe hemorrhage says that there occurs a well-marked leukocytosis, influenced by other factors than the gravity of lesion. Binet[12] claims that during the hemorrhage the white cells are diminished, but their fall does not parallel that of the red cells. From this brief review of the literature of recent years it may be noted that confusion exists not only as to the actual occurrence of a post-hemorrhage leukocytosis but also as to the duration of this leukocytosis. For this reason it seems worth while to report the results of the white cell counts made upon animals in whom the quantity of blood lost could be accurately controlled.

Experimental Data.—Eight dogs were used in all. Two dogs were used in each experiment. After the bleeding from the jugular vein the animals were given the standard diet and all the water they wished after the counts were made. The first counts were made approximately four hours after the bleeding and succeeding counts were all made in the early afternoon before feeding. A Thoma-Zeiss pipette was employed in collecting the blood and a Levy slide was used in making the count. In the estimation of the various types of cells, smears were made on cover-slips and stained with (Romanovsky's) modification of Wright's stain.

In the first experiment two long-time splenectomized dogs which had been bled small amounts repeatedly for some weeks were bled 430 c.c. and 400 c.c. respectively. Each dog showed a sharp rise in total cells and a rise as well in the percentage of polynuclear granular cells. In the case of dog 19-4 the cells of the end of four hours had risen from 10,200 to 24,700, with an increase in polynuclears from 81 per cent. to 90 per cent. Dog 19-6 had an increase from 12,200 to 24,100 total leukocytes and a percentage increase of polygranular cells from 58 to 90. Both animals showed a drop two days later and both had secondary rises. The full results of the counts can best be seen in Chart I.

In the one animal the count returned to normal by the eighth day and in the other by the twelfth day. In the second experiment (Chart II) each of the dogs a long time splenectomized were bled a total of 525 c.c. and 675 c.c. respectively in two succeeding days. Here one dog, 20–4, had an increase of cells to 18,100 to fall at

[11] Les modifications précoces de la formule leucocytaire après hémorrhagie, Compt. rend. soc. de biol., 1918, xxxi, 103.
[12] Presse méd., Paris, 1919, xxvii, 217.

the end of two days to 10,200, around which figure they remained until the eighteenth day. The other animal, 20–5, had a leuko-

PERCENT. POLYS.	W.B.C.	PRELIM-INARY	4 hours	2 days	4 days	6 days	8 days	10 days	12 days	16 days
90	25,000									
80	20,000									
70	15,000									
60	10,000									
50	5,000									

Dog 19-6 ●——= W.B.C. Both animals Splenectomized. Bled 100 c.c. for some weeks
●——= Polynuclears then 430 c.c. and 400 c.c. respectively Wt. = 13,450 gm. (19-6)
14,000 gm. (19-4)

Dog 19-4 ○——= W.B.C.
○——= Polynuclears
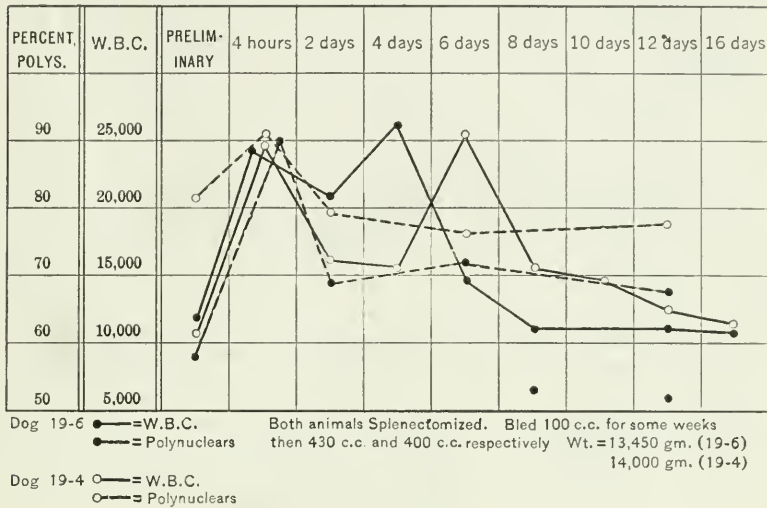
CHART I.

cytosis of 16,600 at the end of four hours, which increased to 23,600 in forty-eight hours and fell to normal by the twelfth day. Both animals had a polynuclear increase.

PERCENT. POLYS.	W.B.C.	4 hours	2 days	6 days	12 days	18 days
90	25,000					
80	20,000					
70	15,000					
60	10,000					
50	5,000					

Dog 20-4 ●——= W.B.C. Splenectomized Wt. = 12,550 gm. Bled 525 c.c. in 2 days
●——= Polynuclears
Dog 20-5 ○——= W.B.C. Splenectomized Wt. = 16,000 gm. Bled 675 c.c. in 2 days
○——= Polynuclears
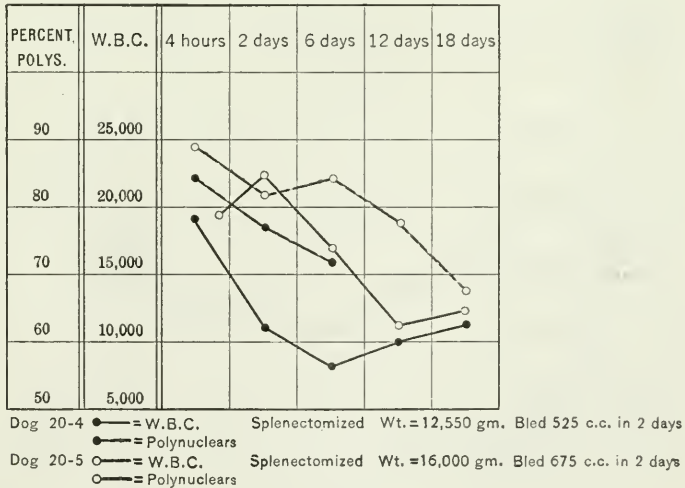
CHART II.

In the third experiment (CHART III) each dog was bled small amounts repeatedly and then several days before the first count 300

c.c., and on the day that counts were made 350 c.c. of blood were removed in the case of the larger dog and 250 c.c. from the smaller.

PERCENT, POLYS.	W.B.C.	4 hours	3 days	6 days	8 days	11 days	16 days	20 days	30 days
90	25,000								
80	20,000								
70	15,000								
60	10,000								
50	5,000								

Dog 20-11 ●——=W.B.C.   Bled 900 c.c. in 2 months   Wt. = 17,330 gm.
           ●‑‑‑=Polynuclears   300 c.c. 4 days before count
                               350 c.c. day of count
Dog 20-13 ○——=W.B.C.   Bled 800 c.c. in 2 months   Wt. = 15,600 gm.
           ○‑‑‑=Polynuclears   300 c.c. 5 days before count
                               250 c.c. day of count
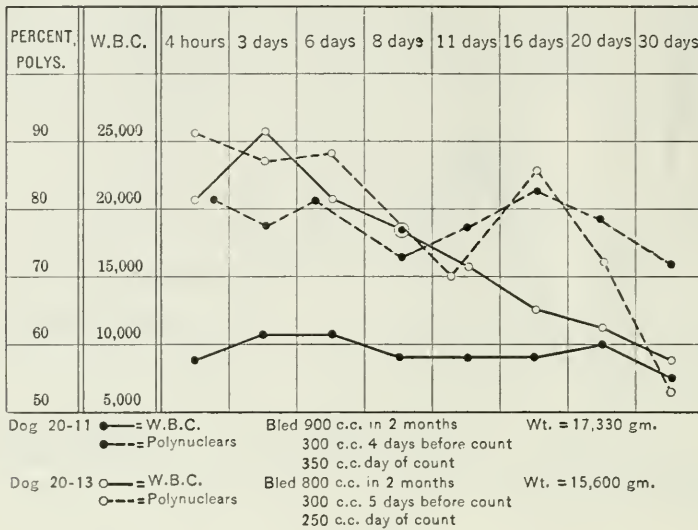
CHART III.

The large dog, 20–11, showed practically no change in his leukocyte count as the result of the hemorrhage. Eight counts made

PERCENT, POLYS.	W.B.C.	4 hours	8 days	12 days	16 days	23 days	30 days
90	25,000						
80	20,000						
70	15,000						
60	10,000						
50	5,000						

Dog 19-3 ●——=W.B.C.   Repeated bleeding 100 c.c. day of count Wt. = 15,730 gm.
          ●‑‑‑=Polynuclears
Dog 20-12 ○——=W.B.C.   Repeated bleeding 100 c.c. day of count Wt. = 9,510 gm.
          ○‑‑‑=Polynuclears
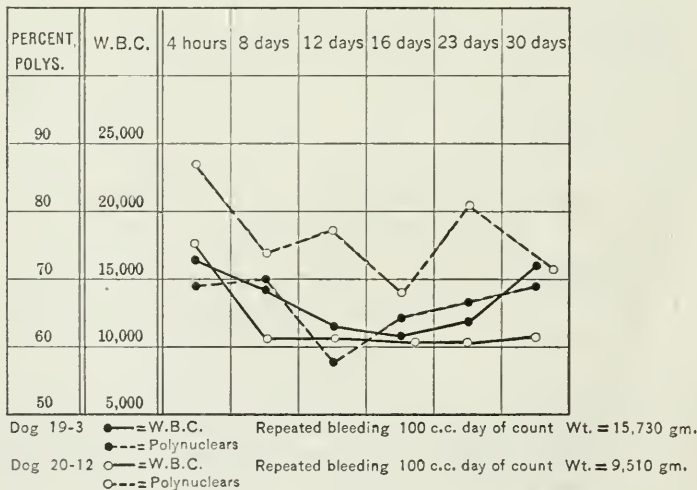
CHART IV.

over a period of thirty days showed a white count varying between 6400 and 10,800. The granular cells showed but a slight increase

after the hemorrhage. This dog showed no effect from the hemorrhage but was always active, ate well and seemed in the same good condition as the other animals. In the companion dog the leukocytes were 21,200 after the hemorrhage, three days later they were 25,900 and from this point gradually fell to 7800 at the end of thirty days. This dog showed a marked polynuclear increase, 94 per cent., which gradually fell to 73 per cent. by the twentieth day. In the last experiment (Chart IV) the effect of small loses of blood was studied. Two dogs that had been bled 100 to 150 c.c. weekly over a period of time were counted immediately after the withdrawal of 100 c.c. Dog 19–3 had a leukocyte count of 16,200 after the bleeding, twelve days later the count was 11,600, three counts in the next two weeks were about the same figures, but for some reason at the end of thirty days the count was 16,700, although no further bleeding had taken place. The polynuclear percentage closely followed the total count. Dog 20–12 had a leukocyte count of 16,600, which at the end of eight days was 11,200, approximately the same as in all subsequent counts of this animal. There was a considerable increase in the granular cells in this animal.

It is also of interest to note that at no time was there a disappearance of eosinophiles from the peripheral blood, as occurs in the leukocytosis of sepsis and which Simon calls the septic factor, as well as in various experimental conditions.

Discussion.—From the results of these experiments and from the review of the literature it may be seen that, as a very general rule, hemorrhage causes a leukocytosis. This is of importance not only in the diagnosis of internal hemorrhage, such, for example, as occurs after contusion of the abdomen, but also in the differentiation of various abdominal conditions.

It is of particular interest to consider the *pathogenesis* of this post-hemorrhagic leukocytosis. Other observers who have studied the condition advance various hypotheses: some as the result of experimental study, others from purely hypothetical reasoning. Levison[13] says that this phenomena is the result of temporary hydremia. This explanation does not seem adequate. Webster[14] writes that the condition is referable rather to the sudden outflow of lymph which occurs as a compensation for the loss of fluid than to the new production of cells, as this latter process does not take place for some time. This would seem to hold true if there was but one massive hemorrhage, but would not account for the rise in leukocytes that occurs even after repeated hemorrhage as shown by those present experiments. Drinker[15] assumes that the very rapid flow of tissue juice into the blood stream carries with it protein material foreign to the blood stream with a consequent

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[13] Loc. cit.   [14] Loc. cit.   [15] Loc. cit.

leukocytosis. Krumbhaar[16] believes that the post-hemorrhagic leukocytosis, which does not become apparent for four or five hours, is due chiefly to the summoning of new and younger forms of polymorphonuclear cells from the bone-marrow under the influence of an unknown stimulant. In one of his charts a distinct leukopenia during the first hour has been recorded. The French school, as reflected by the writings of Binet and of Camus and Pagniez,[17] would seem to have advanced only a questionable and a partial explanation for the leukocytosis that occurs after hemorrhage. They contend that the lowering of the blood-pressure incident to hemorrhage permits the more readily adaptable sticky white cells to adhere to the vessel walls and thus to remain in the system to a greater extent than the red cells. This relative increase in the number of circulating leukocytes must presuppose a marked diminution in the amount of circulating blood, because blood counts are absolute, not relative, and without a considerable diminution in the amount of plasma there would be little change in the count of cells in each cubic millimeter. In the present study confirmatory evidence of this theory may be presented. In all the dogs studied when blood-volume estimations were made the leukocytosis was found to be the most marked in those animals in whom there was the greatest proportional loss in blood volume. Yet even these factors of retention of white cells plus diminished blood volume do not seem sufficient to explain the very great increase of circulating cells that frequently occurs. It would seem likely that a third factor plays the most important part, namely, the response of the organism to an injury, in some respects analogous to an infection, and the consequent outpouring of preformed leukocytes into the circulating blood from the bone-marrow for the most part and to a lesser from the spleen and liver, where they lie in readiness to respond to any call for their services by the body tissue.

Conclusions.—1. A marked leukocytosis is the general but not constant rule after hemorrhage, and is of variable duration. The persistence of the leukocytosis would seem to bear a general relation to the severity of the hemorrhage.

2. This leukocytosis is made up largely of an increase in the polymorphonuclear neutrophiles.

3. Eosinophiles do not disappear from the circulating blood as they do in the leukocytosis of sepsis and other conditions.

4. The factors which seem to play a part in the pathogenesis of the condition are: Retention of the leukocytes in the blood stream during hemorrhage by adhesion to the vessel walls with diminution of blood volume, and, presumably, an outpouring of white cells from the bone-marrow after hemorrhage in response to an unknown stimulus.

[16] Loc. cit.   [17] Loc. cit.

POLARISCOPIC STUDY OF URINES OF A GROUP OF SYPHILITICS.

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Mettenheimer,[1] in 1858, first called attention to the existence of lipoid bodies seen under the polarizing microscope as globules showing a dark central cross separating four bright peripheral quadrants. Since that time many investigators have found these bodies in certain sputa, tuberculous pus and detritus undergoing advanced necrosis. It has been assumed that these bodies represent a more advanced stage than fatty degeneration and indicate an irreversible process. Considerable work has been done leading to some knowledge of the chemical and physical properties of these lipoid bodies. They are said to include cholesterin esters, fatty acids, sphingomyelin, cerebrosides and soaps of oleic acid. Lehmann has proposed the name of "fluid crystals" to designate these bodies intermediate between true fluids and true crystals.

Munk,[2] in 1913, found these bodies in certain urines studied in the appropriate method and first established a relationship of doubly refractile lipoids to syphilitic nephritis. He found them in cases judged clinically to be nephritis due to spirochetal infection. He also observed their less frequent occurrence in the urines of senile syphilitics without a true nephritis and also in tabetics and paretics.

Thus an impetus was given to closer study of syphilitic nephritis, as first reflected by the studies of Stengel and Austin,[3] the report of whose work appeared in 1915. These investigators studied a group of frank and severe nephritics. Their findings have been tabulated as follows:

	Total.	Lipoids in urine.
Nephritis with severe albuminuria:		
With syphilis	6	6
With syphilis doubtful	3	2
Without syphilis	14	5
Nephritis with little albumin:		
Some syphilitics	23	0

The conclusion reached was that the presence of doubly refractile lipoids in cases of severe nephritis does not imply syphilitic nephropathy, but that an abundance of them is highly suggestive thereof.

Cole[4] in a recent discussion of syphilitic nephritis did not take

[1] Am. Jour. Med. Sc., 1915, cxlix, 12.
[2] Ztschr. f. klin. Med., 1913, lxx, 1.
[3] Am. Jour. Med. Sc., 1915, cxlix, 12.
[4] Am. Jour. Syph., January, 1920.

into consideration the existence of these bodies in establishing the criteria for the diagnosis of this condition. This writer, quoting Fournier, claims that the following conditions must be met:

1. Proof of a recent luetic infection.
2. Symptoms of nephritis with lues.
3. Nephritis characterized by high albumin content in urine, rapid onset and tendency to early uremia.
4. Presence of spirochetes in catheterized urine.
5. Positive Wassermann.
6. Favorable influence of specific therapy.

Stokes,[5] of the Mayo Clinic, however, recently has reported a case of a syphilitic with nephritis, showing a heavy cloud of albumin and the presence in goodly numbers of these double refractile lipoid bodies. This patient failed to respond permanently to specific treatment. The nephritis was judged to be non-specific solely because of the failure of a therapeutic test. Response of a case to therapeusis he claims to be the court of last resort in determining whether the case is one of syphilitic nephritis.

The present study was instigated by the desire to determine whether the presence of albumin and casts in a large percentage of the urines of syphilitics might indicate a specific nephropathy. The urines of fifty syphilitics undergoing treatment in the genitourinary dispensary of the University of Pennsylvania Hospital were subjected to this special examination. All patients were males, ranging in age from seventeen to seventy-two years, and in injections of neoarsphenamin from none to twenty-two. None of these patients evidenced any clinical signs of nephritis; 72 per cent., however, showed albumin in varying amounts; 44 per cent. showed albumin with casts, 56 per cent. had an excessive number of epithelial cells of undetermined type, and it is of interest to note that of these, 86 per cent. were of patients who had undergone rather intensive arsphenaminization. The centrifugalized urine sediments were viewed under a microscope to which was attached two Nicol prisms set at right angles to each other. None of these showed the double refractile lipoids.

Conclusion. The study of fifty proved syphilitics without manifest true nephritis failed to reveal the double refractile lipoids.

[5] Jour. Am. Med. Assn., lxvi, 16, 1191; Am. Jour. Syph., July, 1920.

NEUROGENIC IRREGULARITIES OF THE HEART IN ADULTS.

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FLUCTUATION in the activity of the sino-atrial node in children is well known and is regarded as an expression of instability of the incompletely developed nervous mechanism of the heart, and hence is without significance. Concerning sinus irregularity in adults, clinical opinion varies. According to Mackenzie[1] its presence indicates that the heart is healthy; the individual showing it is never conscious of the irregularity; certain neurotic individuals may show it late in life. Norris and Landis[2] state that its recognition becomes important mainly for the purpose of excluding serious forms of arrhythmia. Eppinger and Hess[3] consider all sinus arrhythmia occurring after the age of fifteen years a symptom of vagotonia, that having been defined as a functional autonomic system disease. In 1912 Windle[4] asserted that this irregularity had not yet been shown to occur in degenerative heart lesions. However, two years before, Stokes[5] reported a case of sinus arrhythmia associated with anginal attacks occurring in a woman, aged thirty-six years, who had had rheumatic fever when ten years of age and who showed signs of heart involvement.

On the other hand, Thorne[6] after observing cases of sinus arrhythmia in soldiers concluded that the presence of sinus arrhythmia, "which indicates an irregular cardiac dilatation," is not an absolutely normal phenomenon and that most people in whom this irregularity is present are more liable to suffer from a cardiac breakdown under mental or physical strain than those who have a perfectly regular pulse. Danielopolu and Heitz[7] assert that many clinicians have established a relation between weakness of the circulation and the presence of sinus arrhythmia, and they report three cases of respiratory arrhythmia in association with high systolic blood-pressure. In a more recent paper Aalsmeer[8] has

[1] Principles of Diagnosis and Treatment in Heart Affections, London, Oxford Press, 1916.

[2] Diseases of the Chest, Philadelphia, W. B. Saunders Company, 1917.

[3] Vagotonia, New York, Nervous and Mental Disease Publishing Company, 1917.

[4] A Note on the Diagnosis of Sinus Arrhythmia, Quart. Jour. Med., 1911–12, v, 326.

[5] Sinus Arrhythmia Associated with Anginal Attacks, Heart, 1910, i, 297.

[6] The Clinical Significance of Sinus Arrhythmia, Practitioner, 1916, xcvii, 274.

[7] Sur La Présence d'Une Arythmie Sinusale Chez Quelques Hypertendus, Arch. Mal. du Cœur, 1914, vii, 449.

[8] Over Sinus Arrhythmie, Nederland. Tijdschrift voor Geneeskunde, 1919, lv, 825.

reviewed the cases of Laslett, Wenckeback and Vaquez and Esmein in which marked sinus arrhythmia was associated with symptoms of cerebral anemia, and he cites the case of a young soldier with an apparently normal heart in whom a sinus arrhythmia occurred in a simple tachycardia. As the vagus and accelerator systems seemed to be functioning perfectly, he concluded that the cause of the arrhythmia was to be sought in changes in the reacting organ. He likewise says that respiratory arrhythmia cannot be regarded as a sign of a good heart.

In the early clinical literature sinus arrhythmia has been attributed almost solely to variations in vagal inhibitory tone, usually dependent on phasic respiratory changes. Lewis, however, has shown sinus arrhythmia in a normal child not of respiratory origin. Aalsmeer has argued for the possibility of heightened accelerator tone as a cause of the arrhythmia. That the pacemaker is controlled by a dual nerve supply has long been known, and in 1897 Hunt[9] presented further evidence for the view that the inhibitory and accelerator nerves are mutually antagonistic. Later the work of Cohn showed that the right vagus was limited for the most part to the sinus node, and Rothberger and Winterberg showed a similar distribution for the right accelerator. Thus it is obvious that the sinus activity at any moment is a resultant of the two oppositely acting sources of innervation and that the cause of variation may be one of four possibilities: an increase or a diminution of vagal tone; an increase or diminution of sympathetic tone.

But in cases of variation of sinus activity in man there seems to be no way to show conclusively in which system fluctuation occurs. The conclusion of Aalsmeer that if with the faster rhythm following exertion the arrhythmia disappears the sympathetic system works well and the vagus falls short is open to criticism, for when the accelerator nerves are severed in dogs exercise promptly causes as great an increase in rate as in normal animals. Applying this knowledge to man the increase in heart-rate following exercise is to be attributed to diminution of inhibitory tonus. That in cases showing excessive activity in either the vagus or sympathetic system the overactive system might be in unstable equilibrium which would cause an arrhythmia seemed at first an attractive hypothesis, but sufficient facts were not found to support it, especially the behavior under atropin. Sinus arrhythmia is frequently seen in hyperthyroidism, in which condition excessive sympathetic activity is at present believed to occur. Fig. 1 is an example. The average pulse-rate was 90 and the R–R interval varied between 0.6 and 0.82 seconds. Fig. 2 is from a patient suffering from an acute toxic goiter; during the slower rate of 70 the R–R interval varied between

[9] Direct and Reflex Acceleration of the Mammalian Heart with Some Observations of the Inhibitory and Accelerator Nerves, Am. Jour. Physiol., 1899, ii, 395.
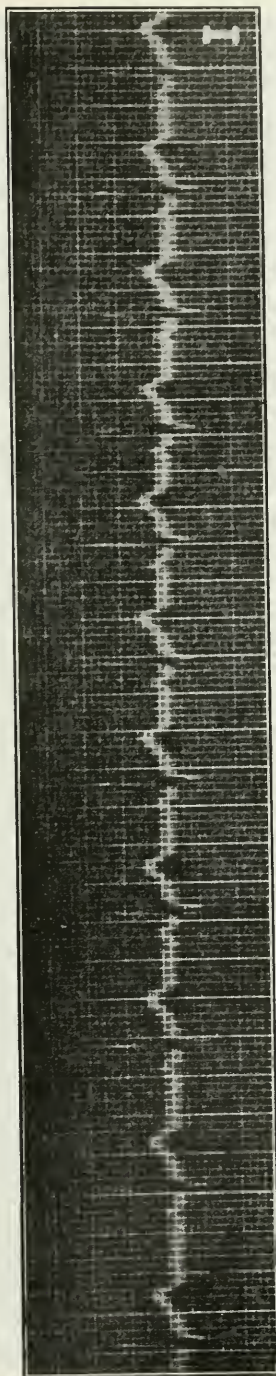
Fig. 1.—From a case of hyperthyroidism; average pulse-rate, 90.
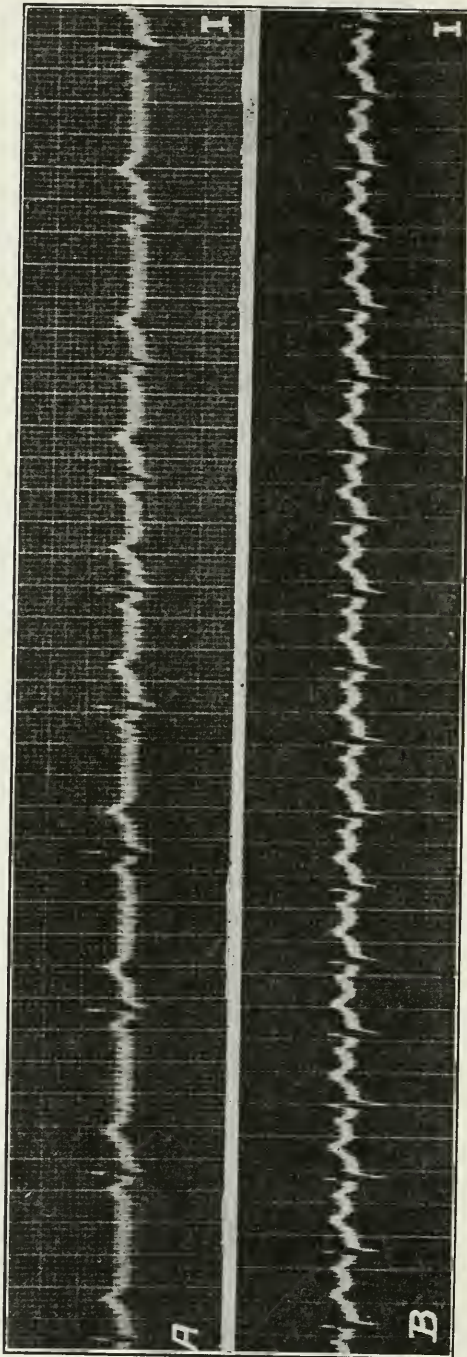
Fig. 2.—*A*, slow rate with sinus arrhythmia; *B*, simple tachycardia, rate 140; taken during an attack of palpitation.

0.6 and 1.04 seconds. Frequently attacks of palpitation occurred in which there was a simple tachycardia, with a rate of 140. Either as a result of diminution of vagus tone or an actual increase of sympathetic tone the accelerator system gained the upper hand, but no arrhythmia is present. Aalsmeer has also stated that sinus arrhythmia seen during a high rate after atropin is due to vagus influence. If such occurs after sufficient atropin to paralyze the vagi it would rather be due to fluctuation in accelerator tone. No example is available. It is customary to attribute the sinus arrhythmia seen in clinical conditions characterized by excessive vagal activity to fluctuation in inhibitory tone because the arrhythmia disappears after removal of vagus influence. However, one sees similar clinical pictures with vagus bradycardia but without arrhythmia. From the facts at hand the only tenable conclusion seems to be that sinus arrhythmia does not result directly from a preponderance of activity of either nervous system but is an expression of inequality of the antagonistic forces and is probably brought about by a periodic increase in the activity of the weaker system to restore, if possible, a more perfect balance. Such a concept is in a measure comparable to the familiar ventricular "escape" from prolonged vagus stimulation.

Knowledge of the factors which may modify accelerator tone is far from complete. Hunt regarded all cases of rapid heart action as due to diminution of activity of the cardio-inhibitory center and found no evidence that the accelerator nerves ever responded to reflex activity. But Hooker[10] has shown that when the heart is kept slowed by stimulation of the peripheral ends of the cut vagi various sensory stimuli would produce reflex acceleration. From the newer work of Cannon and others it would appear that in man reflex accelerator stimulation may be emotional or result from stimulation of sensory nerves.

Factors which may result in alteration of inhibitory tone are well known; the center may be acted upon by impulses from higher levels in the brain, impulses transmitted by various afferent nerves or by changes in the composition of the blood. All medullary centers are highly sensitive to changes in the H ion concentration; an increase causes stimulation of the inhibitory center. Reflex inhibition may result from stimulation of various sensory nerves or surfaces and the afferent fibers from the thoracic and abdominal viscera. The most important afferent nerves which affect reflexly the action of the heart, says Starling,[11] come from the heart and aorta itself. Einthoven[12] has shown electrical changes in the afferent fibers of

[10] May Reflex Cardiac Acceleration Occur Independently of the Cardio-inhibitory Centre? Am. Jour. Physiol., 1907, xix, 417.

[11] Human Physiology, Philadelphia, Lea & Febiger, 1915.

[12] On Vagus Currents Examined with the String Galvanometer, Quart. Jour. Exp. Physiol., 1908, i, 243.

the vagus due to each heart-beat.   Although the heart contains no true sensory nerves it is admitted by physiologists that in pathologic states impulses may arise in the heart which will result in sensations of pain, usually referred to the cutaneous areas supplied by the second and the third dorsal roots.   That under certain abnormal conditions of the myocardium afferent impulses arising in the heart might bring about disturbances of the cardiac mechanism by altering the inhibitory tone would seem to be well within the range of possibilities.

Sinus arrhythmia is seen in a variety of clinical conditions.   It frequently occurs following recovery from failure of the reserve force of the myocardium, and it is common after febrile diseases, especially those in which the heart may be affected, rheumatic fever, pneumonia, diphtheria.   For years Mackenzie has taught that the presence of this irregularity after a febrile illness indicates that the heart has escaped infection because, he argues, irritation within the myocardium and apparent vagus activity are incompatible, since during the febrile state when a rapid rate is maintained the vagus is unable to assert itself.   Such a theory assumes myocardial irritation as the sole cause for the rapid rate.   It is obvious that the more rapid the rate, the less will be the opportunity for the occurrence of an irregularity; a fibrillation under atropin at a rate of 200 will appear surprisingly regular.   On purely theoretical grounds sinus arrhythmia might be considered an expression of myocardial irritation, variations in the afferent impulses manifesting themselves in unstable inhibitory tone.   As far as rheumatic fever is concerned, when one considers the frequency of involvement of the heart, the incidence being about 55 per cent., and that the cardiac lesion is seldom if ever purely valvular, it may well be that sinus arrhythmia indicates not that the myocardium has escaped infection but that an irritation is present which is able to assert itself.

Reflex cardiac disturbances arising in the alimentary canal are common.   But even here there is the possibility that as a result of mechanical displacement by either distended or ptosed abdominal viscera the heart may be placed at a disadvantage or the coronary circulation embarrassed and thus become the seat of abnormal reflex activity.

Sinus arrhythmia due to vagotonia is usually associated with marked bradycardia, the pulse being from 60 to 40.   These patients suffer from hyperacidity and spastic constipation and show excessive moisture of palms and soles, dermographia and the varied nervous and mental reactions characteristic of that syndrome.   However, vagotonia will account for but a small part of the cases of sinus arrhythmia seen at this laboratory.

The occurrence of vagal irregularities in aortic disease is not

infrequent. Several illustrative cases will be cited later. Besides the usual sources of reflex vagal activity previously mentioned there remains the cardiac depressor nerve. This nerve was discovered by Ludwig and Cyon in 1866 and concerning its function in animals much is known. It is a purely afferent nerve which arises in the arch of the aorta. It contains two kinds of fibers, one of which causes reflex dilation of vessels and the other reflexly excites the cardio-inhibitory center. The fibers are carried in the vagus and the slowing is a vagus reflex which is abolished after division of those nerves. Arterial depression is a reflex by way of vasodilators. Bayliss,[13] using the string galvanometer, has shown that the nerve is excited at each heart-beat. Its function appears to be to protect the heart from too great a rise in blood-pressure. Sewall and Steiner[14] have shown that the depressors are highly sensitive to an increase of mechanical resistance to the action of the heart. Concerning abnormal functioning of the cardiac depressor in man in disease one can only speculate. But it is conceivable that in cases of pathologic changes in the aorta the endings of this afferent nerve may be the seat of abnormal impulse formation which will become manifest by disturbances usually regarded as purely vagal.

At the end of the paper may be found the histories of three adults, all past middle life, which present certain common features; each patient told of sinking spells or sensations of faintness or dizziness, and shortness of breath on exertion unaccounted for by any pulmonary condition; in each there was evidence of pathologic changes in the heart and aorta, and each showed a disturbance of cardiac mechanism due to abnormal vagal activity, the first, sinus arrhythmia, the second, partial atrioventricular block, the third, sinoatrial block. These irregularities are well known and all have been noted in hearts apparently free from disease and unassociated with any symptoms. It is not proved in these cases that the irregularity resulted in transient cerebral anemia which caused the sensation of faintness or loss of consciousness in one case, but in the search for the basis of symptoms such findings are worthy of consideration. The irregularities are regarded solely as manifestations of excessive inhibitory tonus, and it is the abnormal vagal activity which requires an explanation. To dismiss the question by saying that the affected individuals are "neurotic" is not justifiable in the presence of the physical findings. Neither psychic nor gastro-intestinal disturbances nor unusual sensory stimuli were present at the time the irregularities were recorded. The most apparent source for impulses that might result in abnormal vagal activity seemed to be in the heart or aorta in each case, and the afferent vagus fibers or the cardiac

13 Principles of General Physiology, London, Longmans, Green & Co., 1915.
14 A Study of the Action of the Depressor Nerve, Jour. Physiol., 1885, vi, 162.

depressor nerve provide the mechanism. The improvement following rest substantiates such a view.

The bearing of the irregularity on prognosis in such cases is problematical. The deciding factors would be the degree of dilation or relaxation of the aorta and the duration of the pause of the ventricle. The English cardiologists have called attention to the danger of premature beats in aortic disease and have found in the "compensatory pause" a possible explanation of sudden death. The same principle is involved in the cases described.

Summary. Certain facts concerning the regulation of the heart by the extrinsic nerves have been reviewed. The sinus node or "pacemaker" of the heart is under the control of the mutually antagonistic autonomic and sympathetic nervous systems, and its activity at any given moment is a resultant of these two forces. Sinus arrhythmia is an expression of imbalance between the two systems. Preponderance of either vagal or sympathetic tonus in itself such as is seen in vagotonia or hyperthyroidism does not necessarily cause arrhythmia. It appears that the irregularity results from periodic increases in the activity of the weaker system with the object of bringing about a more perfect balance.

In cases of vagal irregularities in adults it is important to determine the source of abnormal stimulation, and in considering the possibilities, it is to be remembered that the most important seat of formation of afferent impulses that may affect the cardio-inhibitory center is the heart and aorta. Just as in certain pathologic states impulses may arise in the heart which will result in sensations of pain, so it is believed that in other abnormal conditions impulses may form in the heart or aorta which, transmitted by the afferent fibers of the vagus or the cardiac depressor nerve to the inhibitory center, will become manifest as disturbances of the cardiac mechanism.

Three cases of vagal irregularities are cited, one each of sinus arrhythmia, partial atrioventricular block and sino-atrial block. In each there was evidence of pathologic changes in the heart or aorta, and the only apparent source of the excessive vagal activity was impulses which arose in those organs. Such irregularities occurring in aortic disease may be of prognostic significance as the combination of a prolonged ventricular pause and a relaxed or dilated aorta might result in a serious or even fatal cerebral anemia.

Reports of Cases.

Case I.—J. H., aged forty-eight years, formerly a cook in the navy, was admitted to the hospital on April 4, 1920, after suddenly having become unconscious and having fallen over while at work. He has had frequent attacks of what he calls giddiness. Shortness of
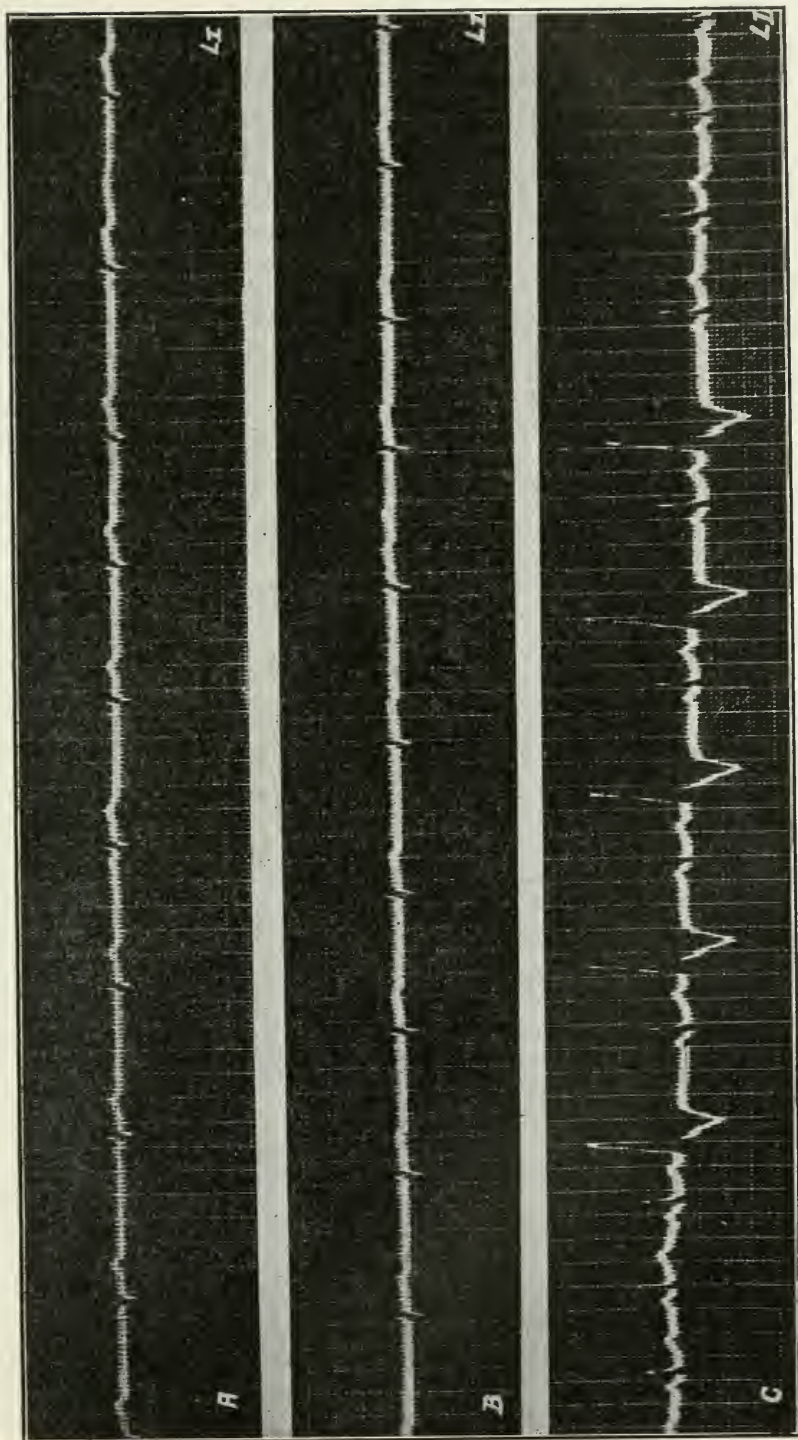
Fig. 3.—Illustrating Case I. *A*, first record; *B*, immediately after exercise; *C*, exercise three days later.

breath on exertion has been noticed for several years. He complained also of numbness in the arms and hands at times and of becoming easily fatigued.

The patient was a slender man of poor nutrition. The lips were cyanotic. Except for moderate emphysema the lungs were negative. The heart was not enlarged to percussion and the fluoroscopic examination showed a long, narrow heart; the aortic shadow was negative. At the apex the first sound was weak and the second sound was accentuated; at the aortic area a soft systolic murmur was heard and the second sound was accentuated and tympanitic. There was a marked sinus arrhythmia. Blood-pressure, 112-72. The palpable vessels were moderately thickened. The liver was palpable and tender. The extremities were cyanotic; the interossei and hypothenar eminences of both hands showed definite atrophy. The knee-jerks were hyperactive; the plantar response was normal.

The Wassermann reaction was negative and the spinal fluid negative, except the globulin test, which was reported two plus.

When first examined the heart-rate was 50 and the R–R intervals varied between 1.06 and 1.4 seconds. Exercise did not increase the rate and the arrhythmia remained unchanged. The almost complete disappearance of the "P" wave was doubtless also the result of vagal stimulation (Fig. 3, A and B). Following pressure on the right vagus a few right ventricular ectopic beats appeared, but there was no marked slowing, the longest pause recorded was 1.46 seconds. Left vagus pressure was without effect. The heart-rate increased to 78 and the irregularity disappeared following 0.02 gr. of atropin. After a few days of rest in bed the heart-rate increased to 70. The exercise test was repeated; this time there was a slight increase in rate, the sinus arrhythmia diminished and many ectopic beats appeared with several short periods of "coupled" rhythm (Fig. 3, C). The patient later resumed work in the hospital. The sinus arrhythmia persisted with an average of 80, and although the respiratory rate was 24, polygraphic records seemed to show that the irregularity was independent of respiration.

CASE II.—Mrs. L., a woman, aged fifty-three years, first seen on January 21, 1920, described frequent attacks of sudden onset characterized by weakness, exhaustion, blurring of vision and a sense of sinking away; loss of consciousness, however, never occurred. At such times the pulse was said to be slow and irregular, and shortness of breath on relatively slight exertion marked. These attacks began two years ago, but during the past three months have been more frequent and the period of exhaustion lasts longer, necessitating rest in bed. There is occasionally slight "nagging" pain referred to the heart. Two years ago shortness of breath when walking up hill was first noticed. Four months ago swelling of the lower
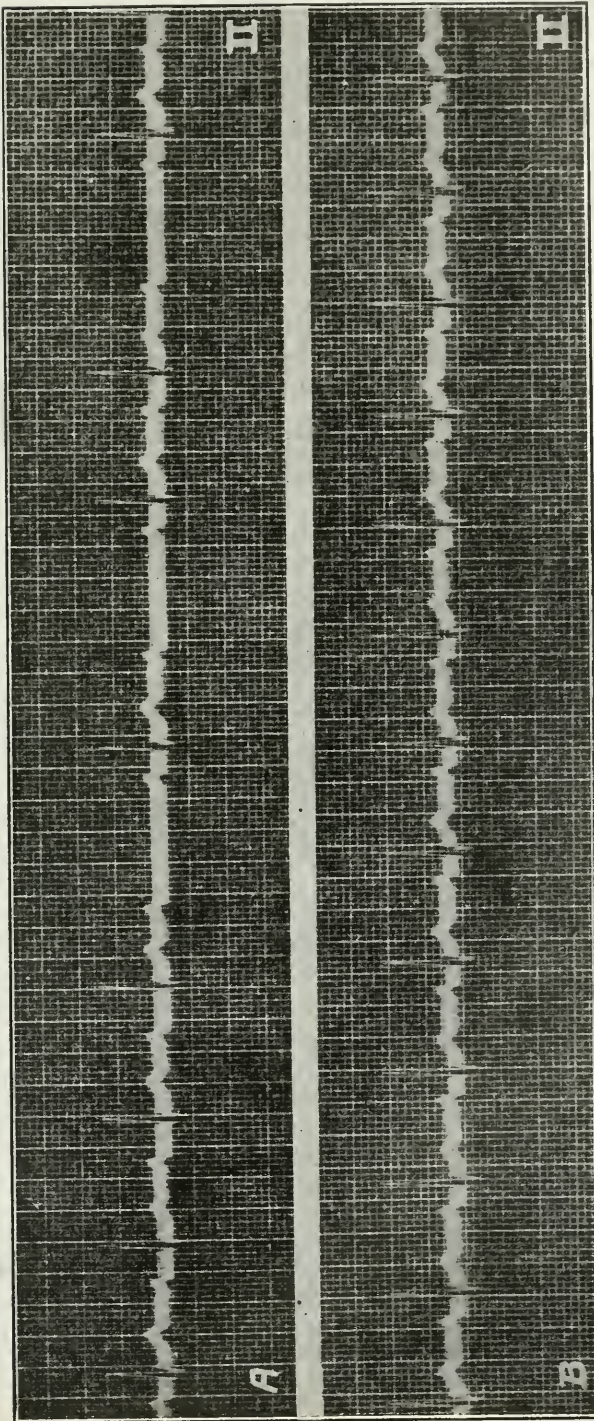
Fig. 4.—Illustrating Case II.   A, first record; B, after atropin.

extremities at the end of day first occurred. Two months later she suffered from a severe attack of "bronchitis followed by congestion of the lungs."

History prior to two years is negative. In early life she had measles and scarlet fever. She has born seven children, and except for migraine attacks at the menstrual period her general health has been good. There is no evidence of syphilis.

The following are the salient facts in the physical examination: The patient was an obese woman of phlegmatic temperament. The lips were slightly cyanotic. There was no edema. The eyes were negative, except for sclerosis of the retinal arteries. The lungs and abdomen were negative. The reflexes were normal. The heart was not enlarged to percussion. The first sound at the apex was rather weak and was accompanied by a systolic murmur, not transmitted to the axilla. Over the aortic area and manubrium was heard a low-pitched, systolic murmur which was transmitted into the neck. The aortic second sound was accentuated and of a definitely tympanitic quality. The rhythm was irregular. Blood-pressure, 145–85. The peripheral vessels were moderately thickened.

The report of the roentgenologist stated: Slight degree of general cardiac hypertrophy. Aortic shadow broadened laterally. Aortitis of descending portion.

Electrocardiogram: Showed the irregularity to be due to partial heart block. There was usually progressive lengthening of the $P–R$ interval through three or four successive cycles and then the impulses failed of passage and a ventricular beat was missed. Following 0.03 gr. of atropin the mechanism became normal, rate 86, $P–R$ interval 0.2 seconds (Fig. 4, A and B).

After two days at rest in bed in the hospital the mechanism was normal and remained so during the period of observation.

CASE III.—Mrs. Y., aged sixty-one years, was first seen on November 3, 1919. For the past two years following "ptomain poisoning" she has noticed that her heart missed beats, and during the past year after an attack of influenza she has been subject to sinking spells which often came on after eating or after exertion. Loss of consciousness has not occurred. For some time she has suffered from agorophobia and avoided assemblies and even shopping, apparently because of a fear of fainting. She has palpitation at times and shortness of breath on exertion and indefinite pain which she said suggested the presence of glass in the heart.

Examination showed a very large heart, the apex being beyond the anterior axillary line. The aorta was somewhat broadened. At the apex the first sound was of a dull character and accompanied by a short murmur. At the aortic area was a short rough systolic murmur and the aortic second was accentuated and definitely tympanitic. The blood-pressure was 125–70.
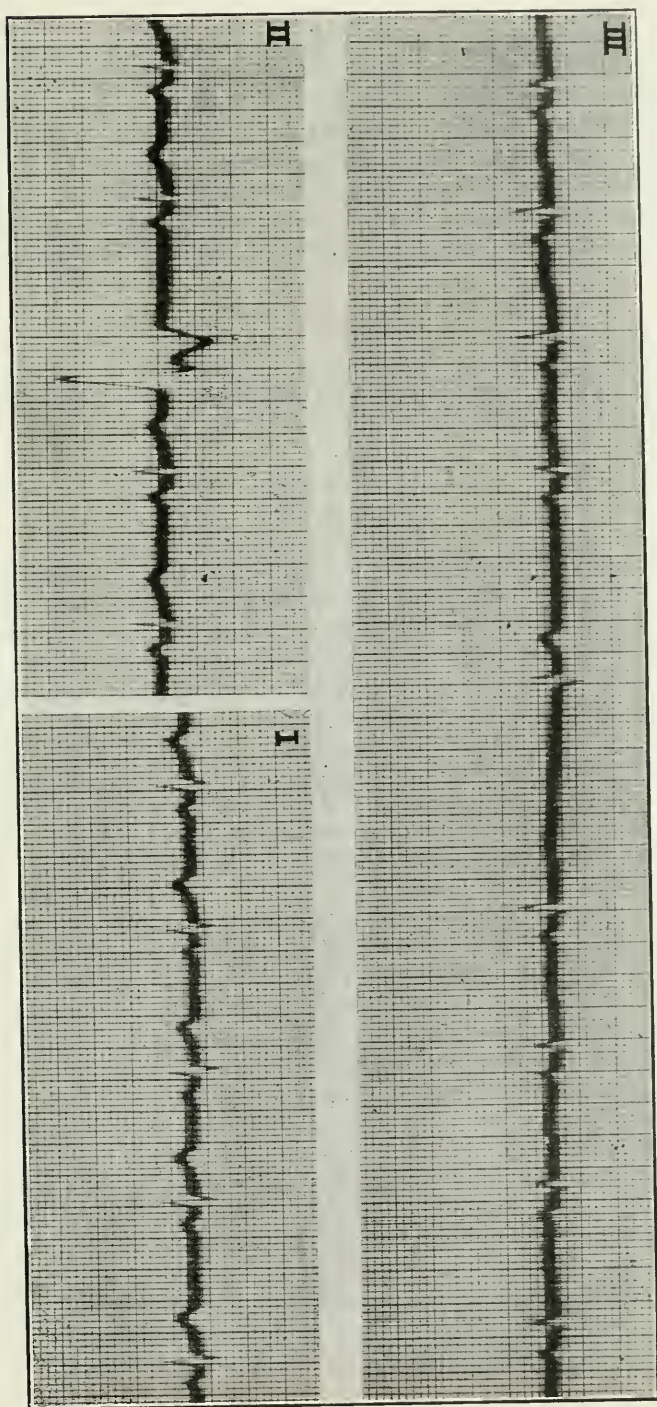
Fig. 5.—Illustrating Case III

The electrocardiogram showed sinus arrhythmia; sino-atrial block, with a pause of 1.36 seconds from which there was an escape by an impulse originating in the upper junctional tissues, and occasional ectopic beats which arose in the right ventricle. The block occurred at irregular intervals and neither it nor the sinus arrhythmia appeared to be related respiration (Fig. 5).

This patient has been seen several times during the year. Each subsequent visit was after a rest and she was clinically improved. The sino-atrial block was observed only at the first examination.

AN EVALUATION OF THE ALLEN METHOD OF TREATMENT OF DIABETES MELLITUS.[1]

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BEFORE the year 1915 a quite different method of treating diabetes mellitus prevailed than has since been employed. This change in method, which must be looked upon as an improvement, owes its inception to the experimental work done on dogs by Frederick M. Allen, and since confirmed by studies on humans by Allen and a number of independent workers. Among other things, Allen showed that diabetic patients could be rendered urine sugar- and ketone-free by the withdrawal of food, by fast days, and periods of underfeeding. Previous to this, other workers including Geulpa, had combined fasting with various dietary procedures, but all such work lacks the basis of scientific study. Their observations were largely clinical and uncontrolled.

Prior to 1915 the treatment of diabetes consisted chiefly in restricting the intake of carbohydrate foods, substituting for the loss occasioned thereby, additional fat and proteins. Methods were largely conjectural. Particular curative virtues were ascribed to certain foods which later investigations do not warrant. Oatmeal, skimmed milk, potato, sour milk, maple sugar and other special food cures are still in our memories. A host of drugs, ferments, animal extracts and mineral waters have similarly been exploited and have been found wanting.

Furthermore, clinical observations and statistics on diabetes made prior to 1915 are unquestionably grossly inaccurate. It has been commonly assumed by physicians that an individual whose

urine would reduce a copper solution under certain conditions had diabetes. It is now well known that reducing substances other than sugar are found in the urine and that the presence of sugar in the urine is not conclusive proof of diabetes. At least 10 per cent. of the cases referred to my clinic as having diabetes are found not to have this malady. When reducing substances other than glucose are found in the urine in considerable amount, they lead to confusion in diagnosis. During the past year I have carefully examined 480 new cases presenting various medical problems with the following result:

Of 480 cases examined, 250 patients, or 55 per cent., had no urine sugar. 106 patients, or 23.2 per cent., were diabetics. 100 patients, or 21.8 per cent., had sugar or other reducing substance in the urine.

Of these 100 patients who had a reducing substance in the urine, 8 had blood sugars of 0.15 per cent. or higher; 8 had blood sugars between 0.12 per cent. and 0.15 per cent.; 84 had blood sugars between 0.07 per cent. and 0.12 per cent.

Of the 100 cases which had reducing substances in the urine, several were excreting glycuronic acid, others were eliminating animal sugars, a number of cases have renal diabetes and a fourth group are patients affected with low-grade chronic infections in which traces of sugar are often found in the urine. This entire question is reserved for a separate study and will not here be further discussed. Reference to it is made because unquestionably many of the alleged cures from diabetes attributed to medicines, ferments, pseudo-scientific mechanotherapy and religiopsychologic methods, are effected on patients who belong in this group and who have not true diabetes. Furthermore the statistics of the older scientific workers are undoubtedly diluted and vitiated by the inclusion of such cases.

Since 1915 the older clinical methods of studying the metabolism of the diabetic have been supplemented by blood chemistry and studies of the respired air. Moreover the necessity for accurate control of food intake has been realized. Accordingly the clinical observations of workers in this field during the past five years are much more accurate and trustworthy.

What is now known as the Allen treatment really represents the composite ideas of a number of workers. As first employed, patients were fasted until the urine was free from sugar. Food was then cautiously added until glycosuria reappeared. This was followed by a fast and the process repeated more cautiously until a point was found where, if possible, the patient would remain urine sugar- and ketone-free. The next step in the evolution of the treatment was the discovery that the incautious use of fat was responsible for many of the failures. The most recent and important improvement, in

my judgment, was the discovery that to really improve the food tolerance of a patient, one must restrict the diet to the point where the blood becomes and remains approximately normal as to its sugar content.

To summarize the principles involved in the present method, it is assumed that every diabetic—

1. Has a limited total food tolerance.

2. He has a limited carbohydrate tolerance.

3. He may in addition have a special intolerance for fat and protein.

The method of study employed in my clinic has been along the following lines: On admission, in addition to a physical examination, a careful routine chemical study of the blood is made, supplemented by a Wassermann test and cell examination. In this study the blood sugar, urea, creatinin, cholesterol and blood bicarbonate are determined. Whenever any of these elements are found in abnormal amount the blood test is repeated at intervals of two or three days. In actual practice this means that, as a rule, the blood sugar only is determined every second or third day during the patient's average three weeks' stay in the hospital. The urine is examined daily, but patients rarely show sugar after the third or fourth day. The food intake is regulated with great care on the basis of the blood-sugar level. The diet is kept low until the blood-sugar level becomes normal. Food is added cautiously while the blood-sugar level remains within normal limits and is reduced in amount when the level becomes high. Fast days are rarely used. Rest days in which the diet is reduced one-half or one-third are employed instead. Supplementing these scientific observations the patients are taught by various means and devices the elements of food chemistry, so that they may know without reference to books or charts the foods that are safe for them to use. They are also taught the approximate weights or quantities which are permissible.

Instruction is also given in the preparation of food and in matters of personal hygiene. In the diet kitchen we are experimenting with special dishes and foods. For example, we have developed a method of making a good soy-bean flour and also a flour from casein at a great saving to the patient. Ordinary pork and beans are proscribed in the diet of the diabetic, but we have developed a method of preparing pork and beans, with tomato sauce, which is perfectly safe and which compares favorably in flavor with the well-known commercial preparations of navy beans.

Our unit for the study and treatment of diabetes consists of scientific laboratories, a special diet kitchen, a room for the instruction and entertainment of patients and a group of eleven bedrooms. The unit has been in operation since 1915. From the very first

we have made an effort, by follow-up letters and by having them return for examination, to keep in touch with patients after they have left the hospital.

All kinds of patients have been treated, the courageous and the cowardly, the enterprising and the slothful, the attentive and interested, and the indifferent. These types are mentioned because the character of the individual has much to do with the outcome. To successfully contend with diabetes a patient must not only be wisely advised, but he must also possess courage and a willingness to learn and assist, to create new dietary habits and eliminate old ones.

All of the foregoing is what we now call the Allen treatment. The question which first presents itself to the new diabetic is, "Is it worth the sacrifice and effort?" This must be the question uppermost in the minds of physicians in general practice who see only an occasional case. There is not the slightest doubt about the immediate value of the treatment. No procedure in medicine of which I have knowledge gives more spectacular relief than does the institution of this method in the acute stages of untreated diabetes. I have witnessed many patients, practically moribund, temporarily saved from impending coma and death by its use. The ultimate value of the treatment has yet to be determined. Since I have had the good fortune to treat patients along the most approved lines since it was first proposed and have had a large number of cases constantly under observation, I shall try to answer the following questions:

1. Does the method ever restore the diabetic to health with power to use unlimited quantities of food?

2. Can severe cases always be kept from failing by rigorously following the method?

3. Does the method of undernourishment improve the physical condition of the diabetics enough to make the sacrifice and expense worth while, or does it merely increase or prolong the misery occasioned by the disease?

4. Does the use of the Allen treatment add materially to the expectancy of life of the diabetic?

To the first question as to the possibility of a complete cure and the use of an unlimited diet the answer is that it is highly improbable. I have seen several mild cases apparently become able to eat temperately of all kinds of food, even cane sugar. One case in particular was that of a physician who on admission had a blood-sugar level of 0.25 per cent. on a slightly restricted diet. At the present time, and after a lapse of three years, his blood sugar is normal and he is eating a general diet, including cane sugar, although it should be admitted that his eating habits are temperate. Many mild cases, particularly adults, have gained so much in tolerance that they are able to eat with discretion all kinds of ordinary foods

except cane sugar. I have never seen severe cases make such notable gains.

In answer to the second question as to whether or not severe cases can be kept from failing, it may be said that many can be kept alive, although it may be necessary to constantly readjust and maintain the diet at levels exceedingly low. For example, I have had such a case in a young man whom I am treating jointly with Dr. Allen. His diet is rarely permitted to go above 650 calories. I have had bad cases live for more than two years on diets averaging below 700 calories. A certain number of cases will succumb in spite of all fasting and underfeeding, as will be seen in tables exhibited later.

The third question as to whether or not the condition of severe patients is improved sufficiently to make the undernutrition ordeal worth while, I think can truthfully be answered in the affirmative. If patients properly regulate their daily activities so as not to exhaust themselves they can live with a fair degree of comfort and with greater freedom from symptoms for a much longer time than if treated by any other method of which I have knowledge.

The fourth question as to the gain in expectancy of life is a very difficult one to answer in terms of precision, and for several reasons. In the first place one must compare a given set of cases treated by the method with a similar group treated by older or former practices. To do this with any assurance of accuracy is quite impossible. (a) Included in all former studies on diabetes as before mentioned, because of inefficient methods of investigation, there must be many cases, particularly those of mild or uncertain form, which were not true diabetes; (b) there is great variation in the severity of diabetes in different individuals and a corresponding variation in prognosis; therefore, only cases of similar degrees of severity can be fairly compared; (c) a large proportion of diabetics have complications or associated diseases which are frequently the cause of death; obviously only groups of cases of uncomplicated diabetes can be compared.

Secondly, a large proportion of those who succumb to diabetes under the Allen treatment are not faithful to the method, as shown by the appended tables. Most of them are unwilling to continue under limitations and privations which it imposes and rarely follow it for more than a few weeks.

In spite of all these disconcerting factors, from careful observation one gains a distinct clinical impression that life is materially lengthened by the treatment. Curves plotted so as to show the average duration of life of fatal cases arranged according to age of onset and duration of disease between 408 fatal cases treated by Joslin[2] prior to December 1, 1915, and 103 fatal cases treated by me since 1915,

2 Joslin, E. P.: Treatment of Diabetes Mellitus, Lea and Febiger, 1917, p. 36.

show that life has been prolonged from one to two years in most of the age groups.

Children when seen at the onset of diabetes, even when severely ill, may be greatly relieved for several months, oftentimes for upwards of two years. There may be noted, however, a gradual decline in the ability to use food. If the diet be constantly reduced to keep the blood sugar within normal limits, the child will get along fairly comfortably for several months more, provided it does not succumb to some other disease or until trophic disturbances and evidences of malnutrition become distressing. Even under these conditions, children may live for four or five years. It is my judgment that the length of life of the average diabetic child is doubled by the Allen treatment.

Young adults do somewhat better than children. In many cases the tolerance for food slowly declines in spite of the most rigid restrictions; others do fairly well; but I have seen very few cases which justify the hope that anything approaching a normal tenure or life or physical well-being will ever be attained by this unaided treatment.

Older adults, as would be expected, do correspondingly better. A large proportion of my living cases are in good health and many of them undoubtedly will live out a normal expectancy.

My conclusions from this study are as follows:

1. Statistics as to the prevalence of diabetes, cures obtained and other data, based on former and inaccurate and incomplete methods of study, are untrustworthy. It is quite impossible therefore to compare with fairness results obtained by the use of the Allen method and results obtained by methods formerly in use.

2. In spite of these difficulties an extended clinical experience covering the use of all known forms of diabetic treatment justifies the conclusion that the Allen treatment is a distinct clinical advance. While permanent cures are not attained, nevertheless patients for a considerable time are much benefited.

3. It is difficult to say how much is added to the expectancy of life of the diabetic by this treatment. In young people in whom the disease is most serious it would appear that it is at least doubled. Middle-aged and elderly diabetics who are not too seriously afflicted with complications and when faithful to the treatment can probably survive the life-expectancy of the average normal individual.

4. The Allen method is of the greatest service when instituted early in the disease. Like tuberculosis and cancer, diabetes should be recognized and thoroughly treated in its incipiency. Most of the failures in its use are due either to serious complicating disease, or more frequently to unfaithfulness on the part of the patient. In the majority of cases its value is in inverse proportion to the seriousness of the failure of metabolism.

TABLE 1.—TOTAL NUMBER OF CASES OF DIABETES TREATED BY
ALLEN METHOD—304.

	Cases.	Per cent.
Total:		
Adults	266	87.5
Children	38	12.5
Living	201	66.0
Adults	186	61.0
Children	15	5.0
Dead	103	34.0
Adults	80	26.0
Children	23	8.0

COMMENT. The foregoing represents only cases studied in the metabolic ward and does not include cases seen in consultation or in office practice.

TABLE 2.—SHOWING SEVERITY OF DISEASE AT BEGINNING OF
TREATMENT IN 103 CASES OF DIABETES OF ALL AGES
WHICH HAVE ENDED FATALLY.

Cases.	Per cent.	Severity.
11	10.5	Mild.
19	18.5	Moderately severe.
73	71.0	Severe.

COMMENT. The greatest hope and safety for the victim of diabetes depends upon the early recognition of the disease and its intelligent and faithful treatment. In this respect it resembles tuberculosis.

TABLE 3.—SHOWING SEVERITY OF DISEASE AT BEGINNING OF
TREATMENT IN 80 CASES OF DIABETES IN ADULTS
WHICH HAVE ENDED FATALLY

Cases.	Per cent.	Severity.
11	13.5	Mild.
19	24.0	Moderately severe.
50	62.5	Severe.

COMMENT. In this series of fatal cases in adults more than 80 per cent. were seriously ill before treatment was undertaken.

TABLE 4.—SHOWING SEVERITY OF DISEASE AT BEGINNING OF
TREATMENT IN 23 CASES OF DIABETES IN CHILDREN
WHICH HAVE ENDED FATALLY.

Cases.	Per cent.	Severity.
23	100	Severe.

COMMENT.   Diabetes in a child rapidly becomes serious, often it is in an advanced stage before a physician is consulted.

TABLE 5.—IMMEDIATE AND CONTRIBUTING CAUSES OF DEATH IN 103 CASES OF DIABETES OF ALL AGES.

Cases.	Diseases.
71	Diabetes, no evident serious complication.
4	Pneumonia, lobar.
2	Influenza.
2	Tuberculosis, pulmonary.
1	Whooping-cough.
11	Cardiovascular renal.
5	Gangrene
3	Miscellaneous surgical diseases.
2	Cancer.
1	Syphilis.
1	General sepsis.

COMMENT.   The foregoing table means that in 71 cases of fatal diabetes there were no serious complications while 32 cases were seriously afflicted with some other disease.

TABLE 6.—IMMEDIATE CAUSE OF DEATH IN 11 CASES OF DIABETES WHICH WERE MILD AT BEGINNING OF ALLEN TREATMENT.

Cases.	Disease.
3	Diabetes, treatment abandoned.
1	Gangrene.
1	General arteriosclerosis.
1	Apoplexy.
1	Pneumonia.
1	Heart.
1	Cholecystitis.
2	Surgical disease.

COMMENT.   The Allen treatment of diabetes is of little avail when serious infections are present or when the patient is afflicted with the degenerative processes of old age.

TABLE 7.—IMMEDIATE CAUSES OF DEATH IN 19 CASES OF DIABETES WHICH WERE MODERATELY SEVERE AT BEGINNING OF ALLEN TREATMENT.

Cases.	Disease.
3	Diabetes, uncomplicated.
5	Diabetes, treatment abandoned
2	Gangrene.
3	Apoplexy.
2	General arteriosclerosis.
1	Pneumonia.
1	Tuberculosis.
1	Nephritis.
1	Heart.

TABLE 8.—IMMEDIATE CAUSES OF DEATH IN 73 CASES OF DIABETES
WHICH WERE SEVERE AT BEGINNING OF ALLEN TREATMENT.

Cases.		Diseases.
14	. . . .	Diabetes.
46	. . . .	Diabetes, treatment abandoned.
2	. . . .	Gangrene.
2	. . . .	Pneumonia.
2	. . . .	Influenza.
1	. . . .	Syphilis.
1	. . . .	Heart.
1	. . . .	Sepsis.
1	. . . .	Tuberculosis.
2	. . . .	Cancer.
1	. . . .	Whooping-cough.

COMMENT. The foregoing table shows that many cases find the
Allen treatment too exacting and rigorous. A very considerable
proportion of those who die from pure diabetes are severe cases who
wilfully violate their diets and then rapidly succumb to the malady.

TABLE 9.—SHOWING FAITHFULNESS TO ALLEN TREATMENT IN
103 CASES OF FATAL DIABETES, ALL AGES.

Cases.		Per cent.	Allen treatment.
22	. . . .	21.5	Treatment had nothing to do with death.
17	. . . .	16.5	Treatment abandoned after preliminary observations.
28	. . . .	27.0	Treatment carried on for a very short period, then abandoned.
22	. . . .	21.5	Treatment carried on for a longer period, then abandoned.
14	. . . .	13.5	Treatment faithfully carried on until death.

COMMENT. It will be observed that in the above series comparatively few of the fatal cases, less than 14 per cent., were persistently
faithful to the treatment. Many cases unquestionably die because
of lack of courage. Cases with serious or hopeless complications
frequently abdomen dietary treatment.

TABLE 10.—SHOWING FAITHFULNESS TO ALLEN TREATMENT
IN 80 CASES OF FATAL DIABETES IN ADULTS.

Cases.		Per cent.	Allen treatment.
18	. . . .	22.5	Treatment had nothing to do with death.
14	. . . .	17.5	Treatment abandoned after preliminary observations.
19	. . . .	23.8	Treatment carried on for a very short period, then abandoned.
19	. . . .	23.8	Treatment carried on for a longer period, then abandoned.
10	. . . .	12.5	Treatment faithfully carried on until death.

COMMENT. In many of the foregoing cases in adults death resulted because of the inability of the patients to provide suitable care. It will be noted that comparatively few were faithful to the treatment.

TABLE 11.—SHOWING FAITHFULNESS TO ALLEN TREATMENT IN 23 CASES OF FATAL DIABETES IN CHILDREN.

Cases.	Per cent.	Allen treatment.
4	17.5	Treatment had nothing to do with death.
3	13.0	Treatment abandoned after preliminary observations.
9	39.0	Treatment carried on for a very short period, then abandoned.
3	13.0	Treatment carried on for a longer period, then abandoned.
4	17.5	Treatment faithfully carried on until death.

COMMENT. Neglected diabetes is more rapidly and certainly fatal in a child than in an adult. Persistent and careful treatment imposes on the parents a task requiring much fortitude and intelligence.

TABLE 12.—SHOWING FAITHFULNESS TO ALLEN TREATMENT IN 201 LIVING CASES OF DIABETES.

Allen treatment.	Cases.	Per cent.
Abandoned after preliminary observations	9	4.5
Carried on for short period, then abandoned	9	4.5
Carried on for a longer period, then abandoned	44	21.5
Faithfully carried on up to present date	128	63.5
Unknown	11	5.0

COMMENT. There is little question but that many failures ascribed to the treatment are due to lack of faithfulness on the part of the patient.

TABLE 13.—SHOWING PRESENT CONDITION OF 89 CASES OF DIABETES TREATED BY THE ALLEN METHOD WHICH WERE MILD AT BEGINNING OF TREATMENT.

Cases.	Per cent.	Present condition.
49	55.0	Good.
6	7.0	Fair.
7	8.0	Poor.
3	3.0	Very poor.
11	12.0	Dead.
13	15.0	Unknown.

COMMENT. The majority of cases who live within their food tolerance gain in physical vigor; furthermore the distressing symptoms incident to the disease noticeably lessen.

TABLE 14.—SHOWING PRESENT CONDITION OF 67 CASES OF DIABETES
TREATED BY THE ALLEN METHOD WHICH WERE MODER-
ATELY SEVERE AT BEGINNING OF TREATMENT.

Cases.		Per cent.	Present condition.
33	. . . .	49.0	Good.
7	. . . .	10.5	Fair.
4	. . . .	6.0	Poor.
3	. . . .	4.5	Very poor.
19	. . . .	28.5	Dead.
1	. . . .	1.5	Unknown.

COMMENT. Moderately severe cases do surprisingly well, as
evidenced by the foregoing table.

TABLE 15.—SHOWING PRESENT CONDITION OF 148 CASES OF
DIABETES TREATED BY THE ALLEN METHOD WHICH
WERE SEVERE AT BEGINNING OF TREATMENT.

Cases.		Per cent.	Present condition.
30	. . . .	20.0	Good.
6	. . . .	4.0	Fair.
18	. . . .	12.0	Poor.
7	. . . .	4.5	Very poor.
73	. . . .	50.0	Dead.
14	. . . .	9.5	Unknown.

COMMENT. Severe cases which have not been rigidly dieted are
markedly benefited by the institution of the Allen treatment.
Cases which have been dieted carefully for long periods do less well.

TABLE 16.—SHOWING TIME WHICH HAS ELAPSED SINCE ALLEN
TREATMENT WAS BEGUN IN A SERIES OF 66 LIVING CASES
WHICH WERE SEVERE AT BEGINNING OF TREATMENT.

Cases.		Per cent.	Time.
18	. . . .	27.5	Less than 1 year.
11	. . . .	16.5	1 to 2 years.
14	. . . .	25.0	2 to 3 "
5	. . . .	7.5	3 to 4 "
18	. . . .	27.5	4 to 5 "

COMMENT. The time element is a most important factor in the
evaluation of any treatment. The Allen method has been in use
approximately five years, hence eighteen of the foregoing severe
cases have been treated by the method since it was first made public.
Under ordinary methods of treatment it is probable that few if
any of these cases would be alive today.

THE APPLICATION OF OCCUPATIONAL THERAPY IN CIVIL LIFE TO CASES PRESENTING PARALYSIS, CONTRACTURE, FIBROSIS, OR LACK OF COÖRDINATION.

By JOHN H. ARNETT, M.D.,

PHILADELPHIA.

Introduction. The men who worked with Dr. Charles H. Frazier on the neurosurgical staffs of our army hospitals in Cape May and Staten Island had the opportunity to observe under favorable conditions over 1200 cases of peripheral nerve injury. We were able to compare the effect of rest and exercise of the injured part; to observe the relative value of active and passive motion; and finally to study the curative value of various types of active movement. Although toward the beginning there were conflicting ideas regarding the best method of treating extremities, paralyzed by peripheral nerve lesions, after observing these cases over months we concluded, practically unanimously, that the men who used their paralyzed limbs did better than those where rest was practised and that those who engaged in good hard work at home on the farm or in the occupational workshop of the hospital did better than those who only received massage and used their injured limbs but little. In consequence of these observations, occupational therapy was developed along certain new lines. Instead of looking upon it as a means of amusing and diverting the patients, a study was made to determine just which muscles and joints were brought into play by each occupation. An attempt was then made to assign each patient to the type of work best adapted to the treatment of his particular disability. In watching these developments we have been impressed with the possibilities for utilizing certain branches of occupational therapy in our civil hospitals in the treatment of peripheral nerve cases. What applies to the treatment of nerve injuries may also be true of many other groups of cases showing one or more of the phenomena which the former present, namely, paralysis, contracture, fibrosis or lack of coördination. This paper will deal with those phases of occupational therapy which were found to be of most value in our army experience and which seem most readily applicable to the treatment of the various forms of disability found in civil life.

The Application of Occupational Therapy. *Conditions under which it is Indicated.* The examiner should first assure himself of the presence of a lesion of such a character that improvement under occupational therapy might be expected. Next, that no condition exists which would contra-indicate the use of the disabled part.

Finally a decision should be reached as to which aspect of the patient's case should receive the first consideration.

Is pain a marked feature? If so, only one type of work is available until this condition improves, this being clay modelling.

Are fibrosis or undesirable contractures present? If so, treatment should next aim to correct these and wood-polishing would be indicated in the average case. It should be borne in mind, however, that some contractures are of benefit. In musculospiral paralysis, for example, treatment should not aim to overcome moderate contractures in the extensors, as this condition is desirable, since it assists in holding up the wrist and makes possible for the patient many compensatory movements.

Does paralysis alone exist? If complete paralysis in certain groups of muscles is present, work should be prescribed which would by the alternate contraction and relaxation of the muscles lying nearest to the paralyzed ones have the mechanical effect of increasing the flow of blood and lymph about the paralyzed muscles. This might be likened to massage of a diseased muscle by its healthy neighbor, and for this action, carpentry is probably of the greatest value.

Is recovery of function commencing? If so the work should aim to produce well-coördinated action in the newly innervated muscles. Typewriting was found to be quite valuable in this respect.

If recovery of function in certain muscle groups is improbable, treatment should be directed toward the development of compensatory movements. The mechanism of these substituted movements has been discussed in a previous paper.[1]

Directions to the Patient. 1. Length and Character of Treatments. The character of the work, the length and time of the working period and the number of such periods during the day should be specifically stated in the directions to the patient. The length of the periods should not exceed five minutes at first. After a few days this can be gradually increased, but should never exceed an hour. The number of working periods prescribed in a day must depend upon the time the patient is willing to give to his work and the time given to other forms of treatment. About one-third of the patient's treatment time should be spent in occupational therapy.

2. Appliances. The patient should be instructed which tools and appliances are to be used and whether or not a splint is to be worn. Generally speaking, such appliances as the wrist-drop and the foot-drop splints, which are used to prevent overstretching, should be worn while working. Splints used to overcome deformity from contractures should be removed just before work is begun and reapplied the instant the work is finished, so that any gain which is made in overcoming the deformity may be held by the splint.

[1] Ingham and Arnett: Arch. Neurol. and Psych., February, 1920.

3. Position of the Patient. The exact position of the patient while at work should be specified. Here the general rule is to immobilize, as far as possible, all parts of the body proximal to the structures which are being treated. For example, in prescribing work to increase the mobility of the radio-ulnar joint the upper arm should be immobilized by grasping it from behind with the other hand. Furthermore, some positions tend to overstretch the paralyzed muscles and should be avoided.
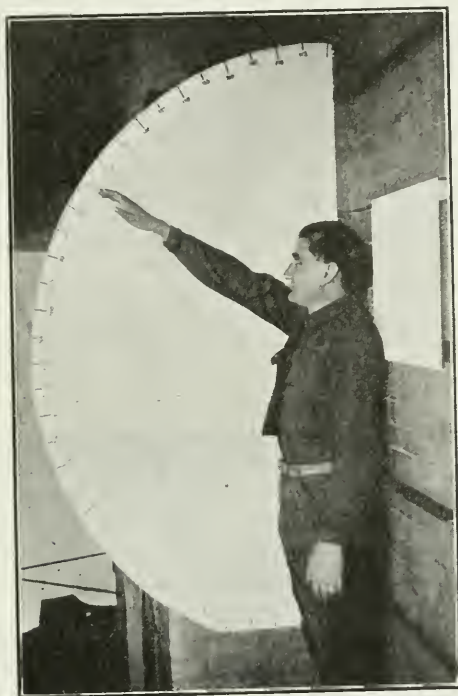
Fig. 1.—Shoulder extension is being measured. Modifications of this simple metrotherapy device may be used for other joints. Each week the reading is graphically charted and furnishes a quantitative record of the degree of motion attained.

4. Cautions. Patients with sensory loss are very liable to the occurrence of traumatic ulcers which are slow to heal and may interfere with all forms of treatment for weeks. In wood-polishing such patients should wear a suitable device to prevent blister formation, and whenever at work they should be under constant supervision.

5. Metrotherapy. Before treatment is begun the degree of both active and passive movement should be measured in one or more of the joints under treatment, and each week this measurement should be repeated. Simple measuring devices which are very satisfactory

can readily be constructed (Fig. 1). A graph showing the curve of recovery should be made, as this is of value in maintaining the patient's interest and showing how well the work is accomplishing its purpose. When the curve ceases to rise it means either that full mobilization has been secured or that this form of treatment is unsuccessful. In either case the therapy should be changed.

Contra-indications to Occupational Therapy. Where an unhealed wound or infection exists, obviously rest is required. Likewise, following nerve suture, ample time must be allowed for the down-growing axis-cylinders to bridge the gap and become firmly implanted in the distal nerve segment, before the part can be used. Finally in patients with sensory lesions, certain occupations, such as tin work are contra-indicated because of the danger of cutting or burning the hands.

Forms of Occupational Therapy. *For Pain.* In painful lesions involving the upper extremity, clay modelling is the occupation *par excellence.* The clay should be kept at about 100° F., and should be of mushy consistency where pain is great. Movements during the very painful stage should be largely passive in nature, the painful hand being immersed in clay and moved by the other hand. Later, clay of harder consistency may be moulded by rolling and twisting movements. Finally monolith beads may be rolled or pottery made. Clay modelling is valuable not only where pain is the chief factor in the case but also where extensive paralysis is present without fibrosis. Here this form of occupational therapy is resorted to simply because the patient is unable to move his fingers sufficiently to do anything else.

For Fibrosis. Where fibrosis or contractures exist without marked pain, oft-repeated movements of the affected joints are indicated.

1. Wrist or Finger-joints Involved. Where the finger- or wrist-joints are deformed, wood-polishing is most satisfactory. Where the deformity is one of flexion the holder shown in Figs. 2 and 3 should be worn upon the palmar surface of the hand. By wearing the same appliance upon the dorsal surface of the hand, deformities of extension may likewise be treated. After a few hours' work upon ordinary wood a beautiful polish will reward the patient while the constant pressure and repeated movements increase the circulation and are of demonstrable benefit in overcoming the average deformity.

2. Radio-ulnar Joint. Where fibrosis exists which interferes with the movements of pronation and supination, work requiring rotation of the radius upon the ulna is indicated. This motion may be secured by the use of the screw-driver, the gimlet, or the awl. It is well to immobilize the upper arm by grasping it from behind, otherwise the humerus will rotate instead of the radius. If the

patient shows a tendency to rotate the entire body, this may be overcome by having him work in the sitting position.
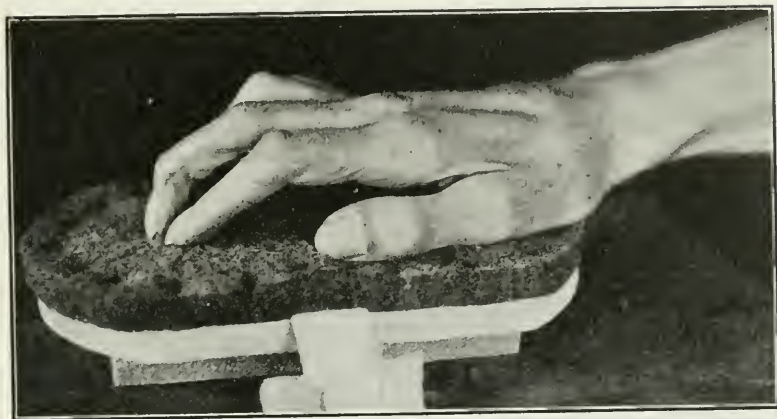
FIG. 2.—Hand with marked contractures due to brachial plexus injury, ready to be fastened into the wood polishing appliance. The thick felt back protects the palm and fingers. The block beneath, holding the sandpaper, can readily be removed, and fresh sandpaper inserted.
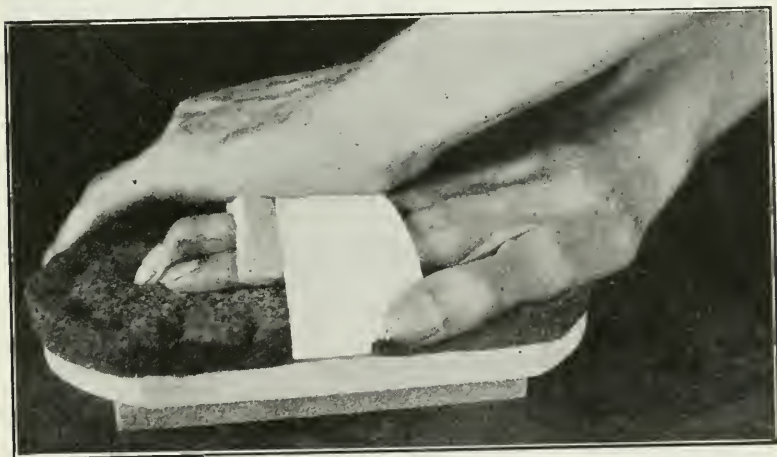
FIG. 3.—The same patient shown engaged in wood polishing. The tight strap over the back of the hand assists in straightening out the deformed fingers, and pressure with the other hand, aided by the to-and-fro motion of polishing, tends to work out the fibrosis and to increase nutrition.

3. Elbow. For limitation of flexion and extension of the elbow, planing and sawing are very satisfactory. Here again the sitting position is best (Fig. 4).

4. Shoulder. For limitation of shoulder movement, wood-chopping or swinging a heavy sledge is valuable. Where the disability prevents this, sweeping movements may be of benefit, and are produced in polishing large surfaces, such as windows or table-tops.

5. Ankle. For fibrosis limiting ankle motion, any apparatus with a treadle like that of the common sewing machine is valuable. Most jig-saws are propelled in this way. To prevent stretching of the anterior tibial muscles, the patient should sit or stand in such a position that the ankle at no time extends beyond 90 degrees. If this cannot be attained by a regulation of the patient's position a thick pad may be inserted beneath the sole as far as the instep. If
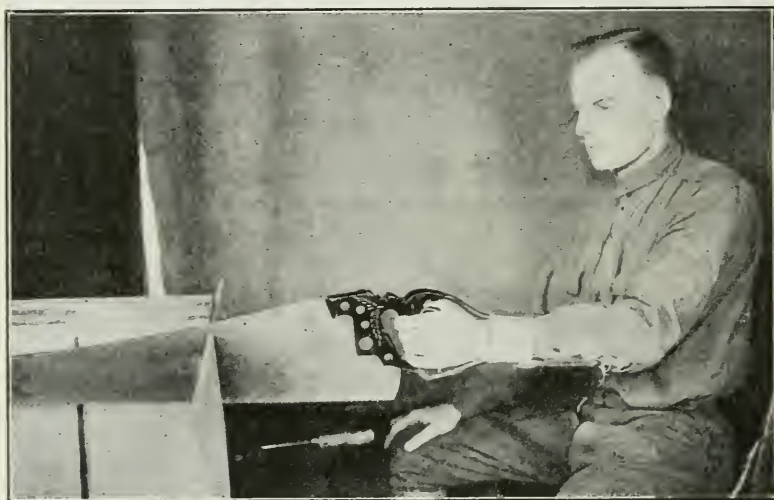
Fig. 4.—Sawing is valuable in mobilizing the stiff elbow, and bringing the shoulder muscles into play. The patient, a case of musculospiral paralysis, is shown wearing his wrist-drop splint as he works. The sitting position immobilizes the trunk, so that the work is done entirely with the upper extremity.

there is danger of stretching the muscles supplied by the internal popliteal nerve the heel may be raised by a block and a position assumed which will prevent flexion of the ankle beyond 90 degrees.

6. Knee or Hip. Where fibrosis limits the knee or hip movements a lathe, jig-saw or other machine propelled with pedals, like a bicycle, is valuable. In this case as soon as the knee becomes straighter the seat should be raised higher, so that finally the seat should be so high that the knee must be fully extended to permit the foot to touch the pedal.

For Uncomplicated Paralysis. Here we have the problem of maintaining the nutrition of paralyzed muscles, developing compensatory movements and preventing fibrosis. Carpentry, metal-

work, book-binding, weaving and toy-making have been found particularly useful for accomplishing these objects. Considerable latitude may be exercised in the selection of the occupation, yet the best results will be obtained by choosing work which will call into action such movements as are most like those produced by the paralyzed muscles. Thus compensatory movements will best be developed, the joints most liable to fibrosis will be brought into play and the muscles nearest those which are paralyzed will be exercised.

For Muscles which are Recovering. Finally we are met with the problem of reëducating and recoördinating muscles which are recovering. The best results are here attained by laying stress
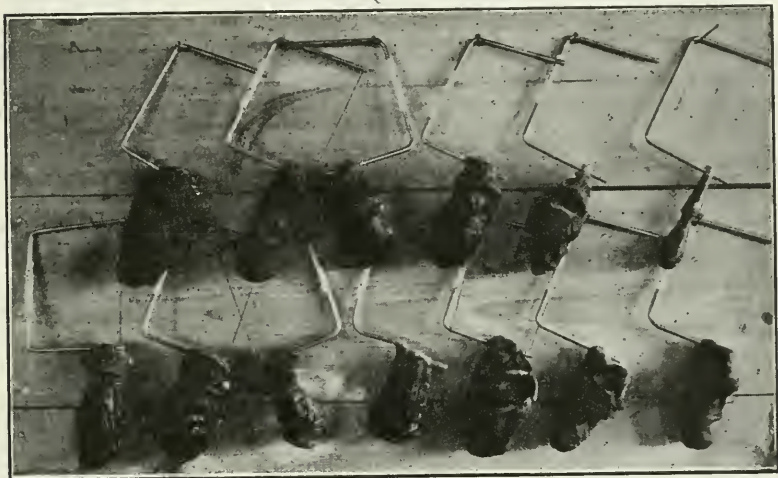
FIG. 5.—Coping saws, used in making toys and puzzles. Each handle is covered with modelling compound containing the impression of a patient's hand. Such saws can be used by patients with deformities and paralyses so severe that they would be unable to hold the ordinary saw.

upon the accuracy of the work done. Musculospiral cases, for instance, who have been doing simple beaten work which requires merely repeated strokes of the hammer upon metal may be given fine beaten work or they may use the carpenter's mallet and chisel.

For pronation and supination, engraving and certain types of wood-carving are valuable.

For flexion and extension of the elbow the coping saw may be substituted for the carpenter's saw and thin material cut into the shape of toys or puzzles (Fig. 5).

For intrinsic hand muscles, type-setting, type-writing, beadwork knitting and penmanship are very valuable.

Conclusions. The advantage which occupational therapy possesses over other forms of mechanical treatment lies in the fact

that interesting work secures repetition of movements without undue fatigue. Not only must the physician take into consideration, therefore, the type of movements produced by the work which he is about to prescribe, but also the desires and interests of the patient.

We found that the soldiers in the hospital took kindly to occupational therapy, and often in spite of their disabilities produced work which from an artistic and technical point of view was of a high order. From a study of these cases over a period of more than a year it became evident that the results of this form of treatment entitle it to an important place among the therapeutic agents at our disposal in the treatment of injuries presenting paralysis, contracture, fibrosis or lack of coördination. In view of the fact that occupational therapy has been proved to be of definite value in the treatment of various other conditions, possibly the day is not far distant when an occupational therapy department, under a trained supervisor, will be recognized as a necessary part of the equipment of every up-to-date hospital.

SOME OBSERVATIONS ON THE USE OF ARSPHENAMIN: ITS EFFECT ON THE KIDNEYS AND ITS THERAPEUTIC RESULTS.

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Recent medical literature is pregnant with articles either extolling the virtues of salvarsan and arsphenamin by reporting series of cases in which observations on the clinical manifestations and serologic reactions have indicated the therapeutic value of the drug or abusing and condemning the use of it by reporting all manner of reactions varying from the mild vasomotor disturbances to fatalities. It is the purpose of this paper to do neither the one thing nor the other, but rather to take the opposite ground; to submit some evidence, after studying 39 cases which have had twenty or more doses of arsphenamin, to show the non-toxic effect of the drug on the kidneys when administered in therapeutic doses over a comparatively long period of time and at the same time to give some data concerning its value as a therapeutic agent.

Concerning the gross and histopathologic changes of acute arsphenamin poisoning we have already acquired considerable information from the studies and reports of Kolmer[1] and others, but concerning the chronic poisoning we have less information largely because of the comparatively recent use of the drug. In the future, no doubt,

[1] Am. Jour. Med. Sc., 1920, clx. 188.

we will have a more accurate knowledge of the pathologic effects of its prolonged use and can come more nearly answering the important question, "What changes are produced in the kidneys by the prolonged use of arsphenamin?" One only appreciates the importance of such a question when he reflects on the fact that thousands of doses of arsphenamin are being administered every day to patients throughout the country and by the energetic application of their plans to eradicate syphilis the U. S. P. H. Service and the State boards of health are increasing daily the number of patients treated.

In this clinic prior to 1918 it was the policy to give weekly injections continuously as long as the patients would submit to it and the Wassermann reaction was positive. Since that date the policy has been to administer a course of arsphenamin consisting of six weekly injections, the dose being, unless contra-indicated, 1 decigram per thirty pounds body weight followed by a ten weeks' course of mercury in the form of the inunctions, the protoiodides or injections of the salicylate of mercury and after this a rest of one month without treatment. During the second and third year the same plan of treatment is used, but the duration of the course is modified somewhat to meet the clinical aspect of the case, the serologic findings and the mental attitude of the patient.

Wassermann tests are taken every second week while arsphenamin is being given and at the end of each course of mercury. Acetone insoluble and alcoholic extract reinforced by cholesterin antigens are used in all tests.

It was possible to study the kidney function of 39 patients who had had over twenty doses of arsphenamin. The phenolsulphonephthalein tests were performed after the method of Rowntree and Geraghty,[2] the urea nitrogen, non-protein nitrogen and creatinin after the method of Folin and Wu[3] and those cases that showed albumin in the urine by the heat and nitric acid tests were further tested for globulin by the use of ammonium sulphate, etc., as described by Hawk.[4] The data of kidney function tests is given in Table I.

The average number of treatments for these 39 cases is approximately 30 doses, consisting of 4.6 decigrams each distributed over a period of a little over two years. To state it another way these patients have had an average of 14 treatments of arsphenamin per year for about twenty-six months. The preparations used have varied but in the main consisted of arsenobenzol, "Billion" arsphenamin, Metz and all later treatments have been of arsphenamin made by the Dermatological Research Laboratory of Philadelphia.

[2] Jour. Pharm. and Exper. Therap., 1910, i, 579.
[3] Jour. Biol. Chem., 1919, xxxviii, 81.
[4] Pract. Phys. Chem., 1918, 6 ed., p. 454.

TABLE I.

Case No.	History No.	No. of doses.	No. of gms.	Duration treatment.		Present phenolphthalein output.		Qualitative urine exam. after last treatment.				Present blood examination.		
				Year.	Months.	First hour.	Second hour.	Specific gravity.	Albumin.	Casts.	Sugar.	Non-protein N.	Urea N.	Creatinin.
1	245	32	12.0	1	7	50	18	1020	0	0	0	33	12	1.6
2	254	24	17.5	1	4	60	13	1020	0	0	0	32	15	1.8
3	281	50	20.8	4	9	55	18	1018	0	0	0	27	17	2.2
4	566	27	13.0	6	2	60	23	1020	0	0	0	33	12	1.7
5	660	52	20.0	1	7	55	18	1020	0	0	0	30	13	2.2
6	634	42	15.4	3	2	55	18	1012	Faint tr.	0	0	28	13	1.6
7	647	29	13.8	4	5	30	15	1015	0	0	0	46	14	2.0
8	432	26	12.9	..	9	70	15	1025	0	0	0	34	17.5	2.4
9	419	28	14.2	1	6	55	Lost	1020	0	0	0	33	16	2.0
10	370	38	15.0	2	11	65	13	1023	0	0	0	25	10	1.5
11	667	35	11.7	1	8	25	20	1025	0	0	0	31	17	1.8
12	810	44	20.0	3	9	50	20	1025	0	0	0	34	15	1.5
13	68	38	13.0	5	3	65	12	1010	0	0	0	28	12	2.3
14	431	36	15.6	3	6	60	13	1021	0	0	0	37	17	2.0
15	360	25	8.0	2	2	60	18	1025	0	0	0	32	12	1.7
16	444	20	7.7	2	5	60	13	1005	0	0	0	34	13	2.2
17	33	39	21.0	2	6	60	23	1012	0	0	0	30	14	2.8
18	37	21	12.0	1	2	60	15	1025	0	0	0	28	20	1.9
19	63	25	7.25	1	5	30	20	1004	0	0	0	27	14	1.7
20	64	32	13.4	4	2	50	10	1010	0	0	0	28	12	2.3
21	109	25	10.0	1	11	60	15	1015	Tr., none 2d exam.	0	0	31	20	2.0
22	158	45	20.0	4	5	50	20	1025	0	0	0	32	12	1.6
23	215	35	15.7	2	11	70	10	1015	0	0	0	35	13	2.0
24	220	22	9.35	..	11	55	20	1025	Very faint tr., none 2d exam.	0	0	37	20	1.3
25	123	33	13.2	1	9	25	15	1018	Dis. tr.; no glob.	Li. gr.	0	37	17	1.6
26	758	34	15.6	2	..	60	15	1024	0	0	0	33	12	1.6
27	582	31	12.8	1	8	60	10	1021	0	0	0	35	17	1.5
28	295	21	11.5	1	..	55	15	1020	0	0	0	35	17	1.7
29	595	22	11.0	2	4	30	15	1012	Cloudy, alb. and glob.	0	0	29	14	1.6
30	585	32	15.1	1	6	30	15	1015	0	0	0	29	14	1.7
31	246	34	15.5	1	11	60	15	1025	0	0	0	31	13	1.7
32	275	20	7.9	2	1	60	10	1015	0	0	0	42	15	1.6
33	232	20	9.9	1	4	60	15	1020	0	0	0	46	20	1.6
34	166	28	13.8	1	11	55	20	1024	0	0	0	40	18	1.7
35	18	23	11.5	1	..	55	10	1024	0	0	0	34	17	1.7
36	597	26	12.1	2	2	65	20	1020	0	0	0	29	13	1.7
37	656	20	10.0	1	1	55	15	1018	0	0	0	33	14	1.6
38	217	21	10.4	2	1	60	15	1010	0	0	0	37	16	1.6
39	258	29	13.4	1	3	65	10	1020	0	0	0	33	13	1.8

A table giving the arsphenamin received, the duration of treatment, the phenolsulphonephthalein output of the kidneys and the urine and blood examination of patients having had twenty or more doses of arsphenamin.

With the exception of patient No. 25, who was transferred from the medical clinic, where he was first seen and diagnosticated tabes and nephritis, there is no conclusive p oof of an existing nephritis in any of these cases. At that time and at all subsequent examinations the urine of patient No. 25 showed some casts and albumin.

His condition apparently is no worse now than when treatment was first instituted. Judging from the phenolsulphonephthalein output and he albumin and casts in the urine this patient has some nephropathy, but the evidence is in favor of its having been acquired prior to treatment. Patients Nos. 6, 21, 24 respectively show a trace of albumin at one examination, but there is no other evidence of a nephritis. Patient No. 29 shows a cloud of albumin, but when appropriate tests were used it was discerned that more than 50 per cent. of the protein precipitate was globulin. This case is well clinically, shows no other evidence of nephritis in the other examinations and therefore might be a case of non-nephritic proteinuria.

The data of table No. 1 lead in general to the conclusion that no demonstrable kidney damage has been done. There is, of course, nothing to show whether or not there has been any limitation of the wide factor of safety which the kidney naturally possesses. Several of the patients show a decreased phthalein output which one may interpret as one will.

The efficiency of any new system of treatment must be determined ultimately by the Wassermann reaction, for it has long been known that negative clinical manifestations are no guide to the patient's potential syphilitic state.

The technic employed in our laboratory for doing Wassermann tests has been modeled after that described by H. K. Detweiler.[5] We use, however, only 0.1 c.c. of patient's serum and use the water-bath instead of dry heat for incubation. Detweiler's method of daily titrations of the complement as well as the amboceptor has proved very satisfactory. The antisheep hemolytic system is employed.

Two antigens are used, the acetone insoluble and the cholesterin reinforced alcoholic extract, made after the method described by Kolmer.[6] These antigens are titrated every six weeks for their antigenetic and anticomplementary values. The former is tested on the pooled sera of patients who both clinically and serologically are luetic.

In our experience with cholesterized antigen it is the more sensitive and the last to become negative. The acetone insoluble is far more liable to be a correct index to the true condition when positive, but often fails to give a positive reaction in the early and late stages and also after a limited amount of treatment. This fact is demonstrated in Tables III, IV and V. Although it is true that a cholesterinized antigen will not infrequently give a false positive reaction, we believe it is the most valuable antigen that can be employed as a guide to treatment.

[5] Am. Jour. Syph., 1918, ii, 120–137.
[6] Inf. Immunity and Spec. Ther., 1917, 2d ed., p. 446.

TABLE II.

Case No.	Age.	Chief lesion on admission.	Duration of disease. Yrs.	Mos.	Stage.	No. of doses.	Courses of mercury. Ung.	Pro-toid.	Wassermann on admission.	No. of doses before first persistent neg. Wass.	Present condition. Clinically.	Serologically.	No. of consecutive neg. Wass.	Time since first neg. Wass., months.	Total arsphenamin, decigrams.	Duration of treatment, weeks.
1	45	To be cured	9		Third	32	3	4	St. pos.	21	Well	Negative	3	4	124	82
2	36	To be cured		4	Latent	24	4		St. pos.	9	Well	Negative	8	16	175	68
*3	45	Dizzy spells; negative Wass.; spinal fluid	10		Third	50		3	St. pos.	Wass. pos.	Very much improved	Wk. pos.			208	247
4	37	Maxillary sinusitis	12–13		Third	27	11	1	Positive	26	Well	Negative	3	3	130	319
*5	35	To be cured	3		Latent	52	1	1	St. pos.	43	Well	Negative	4	16	222	84
*6	39	Gumma of throat	3		Third	42	1	4	St. pos.	Wass. pos.	Well	Wk. pos.	0		151	166
*7	40	Ozena	3–4		Third	29	3	2	Positive	20	Well	Negative	4	8	138	228
8	32	General adenitis	5		Late	26	1	8	Positive	Wass. pos.	Well; small glands	Positive	0		129	41
9	32	General weakness	?		second	28	3	3	Wk. pos.	7	Well	Negative	3	2	142	80
*10	27	Cervical adenitis		2	Second	38	1	2	St. pos.	34	Well; small glands	Negative	3	10	154	156
11	50	Abdominal aneurysm	23		Third	35	2	4	St. pos.	Wass. pos.	No change	Wk. pos.	0		117	87
*12	32	Keratitis rash		3	Second	44	10		St. pos.	4	Well	Negative	4	2	200	196
13	13	None	Congenital		Congenital	38	Continuous inunctions		St. pos.	23	Well	Negative	2	10	130	273
*14	50	Headache; dizziness	10		Third	36	4		Positive	29	Well	Negative	3	14	156	180
*15	26	Chancre		2	First	25	2	3	St. pos.	7	Well	Negative	3	28	113	111

No.		Diagnosis			Stage				Before treatment		Condition after treatment	Present Wassermann				
16	36	Diabetes insipidus			Third	20	4		St. pos.	19	Strong; improved	Negative	2	12	77	74
*17	37	Ulcer of penis	9		Third	39	5	4	St. pos.	35	Well	Negative	2	12	210	75
18	35	Pharyngitis			Second	21	2		St. pos.	Wass. pos.	Well	Wk. pos.			120	61
19	9	Interstitial keratitis	Congenital		Congenital	25	4	1	St. pos.	Wass. pos.	Well	St. pos.	6		72	74
20	43	Optic atrophy			Third	32	5	1	St. pos.	20	Improved	Negative		12	134	215
21	42	Leg ulcers			Third	25	3	2	St. pos.	Wass. pos.	Well?	Wk. pos.			85	102
22	32	Mucous patches in mouth	14		Third	45	1	1	St. pos.	15	Well	Negative	12	24	207	228
23	34	Pain in heels?	12		?	35	4		St. pos.	Wass. pos.	Well	Wk. pos.			157	154
24	30	?			?	22		1	St. pos.	16	Well	Negative	7	3	93	48
25	44	Tabes			Third	33	2	7	Neg. +++ after first treatment	9	Very much improved	Negative; blood and spinal fluid	5	6	132	192
26	37	Luetic sore-throat	1		Second	34	1	4	St. pos.	21	Well	Negative	5	12	156	106
*27		Headache; weakness	4	2	Third	31	1		St. pos.	30	Well	Negative	1	18	128	87
*28	32	Chancre		1	Late primary	21		4	Wk. pos.	17	Well	Negative	2	14	115	54
29	33	Leg ulcers	9		Third	22	1	3	Wk. pos.	17	Well	Negative	5	12	110	120
30	40	Myocarditis			Third	32	3	4	Positive	14	Well	Negative	4	30	151	177
31	26	Myocarditis; aortitis			Third?	34	2		Positive	Wass. pos.	Somewhat improved	Positive			155	98
32	30	Rash	1		Second	20	3		St. pos.	12	Well	Negative	5	12	79	105
33	38	To be cured		4	Late primary	20	3		St. pos.	Wass. pos.	Well	Wk. pos.			99	70
34	34	Ozena			Third	28	3		St. pos.	13	Well	Negative	9	14	138	98
35	33	Rash; mucous patch		2	Second	23	1	2	St. pos.	7	Well	Negative	8	12	115	53
36	31	Chancre		1	Primary	26	5	3	Positive	Wass. pos.	Well	Wk. pos.			121	108
37	35	Body pains			Second	20	1	2	St. pos.	18	Well	Negative	1	2	100	155
38	27	To be cured			Latent	21	3		St. pos.	7	Well	Positive			104	105
39	37	Macular eruption		2	Second	29			St. pos.	11	Well	Negative	8	12	134	65

A table giving a summary of the history, treatment and present condition of the patients of Table I.

TABLE III.—IN THESE TEN CASES THE CHOLESTERINIZED ANTIGEN IS APPARENTLY MORE SENSITIVE THAN THE ACETONE INSOLUBLE ANTIGEN.

Case No.	1		2		3		4		5		6		7		8		9		10	
History No.	899		P.P.		960		1059		1063		1086		1043		986		1067		1049	
Lesion	Chancre.		Chancre.		Chancre.		Early secondaries.		Chancre.		Chancre.		Early secondaries.		Chancre.		Chancre.		Erup. macular.	
Weekly injec. arsphenamin — Wass.	C.	A.	C.	A.	C.	A.	C.	A.	C.	A.	C.	A.	C.	A.	C.	A.	C.	A.	C.	A.
1	2	1	2	—	1	—	4	—	4	3	4	1	4	2	4	—	3	—	3	—
2																				
3	—	—	1	—	—	—	4	4	4	3	1	—	4	1	—	—	1	—	4	2
4	4	—	..	..	..	..	1	—	..	..	..	..	..	..	2	—				
5	..	..	—	—	—	—	2	—	3	3	..	..	—	—	—	..	1	—	1	1
6	1	—	..	..	..	..	..	..												
								Two months of mercury												
15	—	—	—	—	..	..	..	..	—	—	..	..	..	..	..	..			—	—
16	—	—																		
17																				
18																				

TABLE IV.—IN LATE STAGES OF SYPHILIS THE CHOLESTERINIZED ANTIGEN SEEMS TO BE MORE SENSITIVE IN SOME CASES.

Case No.	1		2		3		4		5		6		7		8		9		10	
History No.	1021		1048		1019		1027		966		963		1078		951		976		1	
Lesion	Latent.		Body pains.		Ulcer.		Vascular.		Latent.		Latent.		Ulcer.		Body pains.		Ulcer.		Latent.	
Weekly injec. arsphenamin — Wass.	C.	A.	C.	A.	C.	A.	C.	A.	C.	A.	C.	A.	C.	A.	C.	A.	C.	A.	C.	A
1	3	—	4	—	4	—	3	—	4	2	4	—	4	—	4	—	4	3	4	1
2																				
3	1	—	3	1	1	1	2	1	3	—	4	1	4	1	4	—	4	3	4	2
4																				
5	3	1	..	..	..	..	4	—	1	—	2	2	2	—	4	—	4	1	4	—
6	..	..	3	1	4	1														
								Two months mercury												
15	2	1	..	..	4	1	..	..	..	..	1	—	1	—	—	—	2	—	3	—
16	..	..	..	..	..	..	..	..	—	—	3	—	..	..	..	..	4	1		
17	..	..	..	..	..	..	..	..	..	..	..	..	..	..					—	—
18	..	..	..	..	..	..	..	..	—	—									—	—
19	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..		
20	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..		

Tables giving the Wassermann reactions with acetone insoluble antigen (A) and cholesterinized alcoholic extract antigen (C). The figures 1 to 4 mean Wassermann 1 to 4 plus, — implies a negative Wassermann. The specimens of blood were taken at the time of the weekly injection of arsphenamin.

TABLE V.—UNDER TREATMENT THE CHOLESTERINIZED ANTIGEN OFTEN REMAINS POSITIVE AFTER THE ACETONE INSOLUBLE ANTIGEN HAS BECOME NEGATIVE.

Case No.	1		2		3		4		5		6		7		8		9		10	
History No.	886		222		891		8		102		880		427		442		567		976	
Lesion	Chancre.		Secondaries.		Spondylitis.		Secondaries.		Mucous patches.		Gumma of sternum.		Rash.		Aneurysm.		Mucous patches.		Ulcer of septum.	
Weekly injec. arsphenamin	Wass.		Wass.		Wass.		Wass.		Wass.		Wass.		Wass.		Wass.		Wass.		Wass.	
	C.	A.	C.	A.	C.	A.	C.	A.	C.	A.	C.	A.	C.	A.	C.	A.	C.	A.	C.	A.
1	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4
2																				
3	4	4	4	4	4	4	4	4	.	..	4	3	4	4	4	4	4	4	4	3
4	4	4	4	3	..	..	..	..	4	4	4	4	4	2	4	4	..	..	4	1
5	..	..	2	0	4	1	4	—	..	..	4	1	4	2	4	2	..	..	4	1
6	3	1	..	..	..	..	3		—		4	1	2	—	4	2	..	..	2	1
									Two months of mercury											
15	1	—	..	..	..	..	..	..	2	—	..	..	..	..	..	..	4	—		
16	—	—	..	..	4	1	—	—	4	—	..	..	4	1	2	3	4	—		
17	..	..	..	..	..	..	..	..	..	..	3	—	..	..	..	..	4	—		
18	—	—	..	..	3	1	..	..	4	—	..	..	—	—	4	4				
19	..	..	..	..	..	..	..	..	..	..	—	—	..	..	..	..	1	—	4	—
20	..	..	..	..	4	1	..	..	..	..	..	..	4	2	4	—	—	—		
									Two months of mercury											
29	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1	—				
30	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	—	—		
31	..	..	..	..	..	..	..	..	..	..	..	..	..	..	2	—				
32																				
33	..	..	..	..	..	..	..	..	..	..	..	..	..	..	2	—	—	—		

Tables giving the Wassermann reactions with acetone insoluble antigen (A) and cholesterinized alcoholic extract antigen (C). The figures 1 to 4 mean Wassermann 1 to 4 plus, — implies a negative Wassermann. The specimens of blood were taken at the time of the weekly injection of arsphenamin.

When we make a study of Table II we find 17 of the 39 cases have now had a negative Wassermann reaction for a year or more. Nine of the group have had a negative reaction for less than one year and 13 of the 39 cases continue to have weakly positive and strongly positive reactions. Of those with persistently negative reactions for a year or more 2 were in the primary stage, 4 were in the secondary and 11 in the tertiary and latent stages. The average number of doses to produce persistently negative Wassermann reactions in this group was 18.7, for those in the primary stage 12, for those in the secondary stage 12.7 and in the tertiary and latent stages 21.3 doses.

For the 39 patients the average salvarsan per patient has been 136 decigrams and the average time of treatment one hundred and seventeen weeks. This treatment has resulted in making 17 out of the 39, or 43 per cent. of the patients clinically and serologically negative for a year or more. Seven more patients, 18 per cent., have had more than two persistently negative Wassermanns, so

that, on the whole, more than half of these 39 patients already have a very favorable outlook as far as the ultimate outcome of their treatment is concerned.   This 61 per cent. of the patients has had an average of 4.9 courses of six weeks of mercury in some form or other.

TABLE VI.—SECONDARY STAGE.

Case No.	History No.	Number of positive Wassermanns	Decigrams arsphenamin to first persistent negative Wassermann.	Weeks to first persistent negative Wassermann.	Total arsphenamin.	Total weeks.	Number of persistent negative Wassermanns
1	1	1	53	29	68	52	3
2	172	2	40	20	80	44	4
3	315	2	45	18	61	21	2
4	247	2	49	32	73	79	5
5	257	2	35	19	92	82	5
6	324	3	38	28	48	56	3
7	920	4	30	18	70	28	4
8	399	3	51	20	78	24	2
9	914	3	20	4	56	39	4
10	412	4	67	56	67	56	6
11	567	4	55	30	90	52	3
12	843	3	45	5	60	36	6
13	635	2	50	32	60	38	1
14	855	5	57	30	65	44	3
15	685	2	47	52	47	52	1
16	738	2	142	44	142	44	1
17	879	4	65	39	85	42	2

A table giving the arsphenamin and Wassermann records of patients starting treatment in the secondary stage.   The time under observation for these patients is short and their ultimate status is still uncertain.

TABLE VII.—TERTIARY STAGE.

Case No.	History No.	Number of positive Wassermanns	Decigrams arsphenamin to first persistent negative Wassermann.	Weeks to first persistent negative Wassermann.	Total arsphenamin.	Total weeks.	Number of persistent negative Wassermanns
1	4	4	95	237	95	237	1
2	183	1	57	102	57	102	1
3	290	2	60	40	90	48	3
4	260	3	96	116	96	178	2
5	880	4	40	20	45	20	1
6	416	4	34	48	59	80	2
7	452	4	72	72	96	92	3
8	553	1	77	48	109	76	5
9	867	4	40	34	94	42	5
10	713	3	59	34	69	45	1
11	807	2	55	34	65	38	2

A table giving the arsphenamin and Wassermann records of patients starting treatment in the tertiary stage.   These   patients are to be classed with those of Table VI in respect to observation time.

In Tables 6 and 7, which are composed of cases now negative that presented secondary and tertiary lesions on admission, and in the majority of cases more than one positive Wassermann reaction, I believe we get a fair index as to the efficiency or inefficiency, as you may choose to call it, of our present method of treatment. The average amount of treatment necessary to produce the first persisting negative Wassermann reaction in the group of secondary

cases was 52 decigrams and the average time twenty-eight weeks. That is to say, they received 10.2 doses of arsphenamin consisting of 5 decigrams each. The average case, therefore, in this group did not give a persisting negative reaction until near the end of the second course of treatment.

It took an average of 62 decigrams to produce a persisting negative Wassermann reaction in the tertiary group. The time averaged seventy-two weeks. This means that it was during the third course of arsphenamin that they began to show a negative reaction. This at first seems better than the situation with the patients of Table II, but it is to be understood that for the patients of these latter tables more relapses may be expected. We frequently see patients who having received six to twelve doses of arsphenamin have been discharged with a negative Wassermann only to return within about a year both clinically and serologically positive.

Summary. 1. Because of its extensive use at present it is highly important that we know more perfectly the effects of the prolonged use of arsphenamin on the kidneys.

2. Kidney functional tests on 39 cases after they have received thirty does of arsphenamin, each dose consisting of 4.6 decigrams, and distributed over a two-year period, fail to give any conclusive evidence of injury to the kidneys.

3. The efficiency of any method of treatment must ultimately be determined by the Wassermann reaction. It is more trustworthy to use at least two antigens; the acetone insoluble antigen is a safe guide to diagnosis and the alcoholic extract reinforced by cholesterin is an excellent guide to treatment.

4. It is impossible to say how much arsphenamin and how many courses of mercury may be necessary to produce a negative Wassermann reaction in any given case.

5. Six injections of arsphenamin and one course of mercury, the amount too often prescribed by certain groups of physicians, may produce one negative Wassermann reaction, but the average case of secondary or tertiary syphilis will require twelve or more doses of arsphenamin and a corresponding amount of treatment with mercury to produce a negative Wassermann reaction, and one which only with further treatment may reasonably be expected to persist.

THE TREATMENT OF TUBERCULOUS ADENITIS BY ROENTGEN RAYS AND RADIUM.[1]

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FORMERLY radiotherapy was used in the treatment of tuberculous adenitis to avoid deformity and unsightly scars; today this treatment is advised because more permanent cures are obtained than by any other method. At present surgeons of experience are not operating primarily for tuberculous adenitis. If they operate it is only to remove fibrous nodes after the tuberculous foci have been destroyed by roentgen rays or radium. Then a dissection of the cervical glands is always contra-indicated. Radiotherapy alone will cure over 90 per cent. of the cases.

Experience has proved that tuberculous adenitis is not primarily a surgical disease. The reason that it took years to prove that cervical adenitis was better treated by radiotherapy was really our fault in being too slow in reporting the cases, and a surgeon would see only a few cases, in the most of which the treatment was inefficient and incomplete. As before stated, in only a small percentage of cases, 5 to 10 per cent., is it advisable to remove fibrous nodules after radiation. If such nodules are removed and examined, little or no tuberculous material would be found, the fibrous stroma of the glands remaining.

In the treatment of tuberculous adenitis the first and most important consideration is that it is a local manifestation of a constitutional disease.

Most of the laryngologists are referring tuberculous adenitis for radiation as a routine procedure, and many will not remove diseased tonsils if the cervical glands are enlarged until the glands have been given a thorough course of treatment, either by roentgen rays or radium. Radiation of the enlarged cervical glands is important before removing the tonsils of children under fifteen years of age, and particularly so if under the age of five or six, as the lymphatic vessels are wide open, and in the removal of the tonsils before radiation there is danger of producing a general infection if tuberculosis is present.

In the past the treatment of tuberculous glands depended largely upon the physician first consulted. The treatment given has been the hygienic, medical, roentgen ray and radium and light therapy, vaccine and surgical. Tuberculin has given unsatisfactory results, and since radiation produces a systemic effect similar to successful

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[1] Read before the Westmoreland County Medical Society, Greensburg, Pa., November 9, 1920.

tuberculin treatment and the results are more dependable, vaccines are seldom ever indicated, or at least not until we are able to obtain a more stable vaccine. The local application of iodin, ichthyol and other drugs is useless. Prophylactic treatment is important and should receive more attention. Until recently very little attention was paid to the source of infection. An effort should always be made to find the channels of infection, although it is often difficult to find the primary focus. The importance of removing unhealthy tonsils, bad teeth, etc., should not be overlooked.

The surgical treatment has not comprised any single method. Some would drain abscesses; others would inject antiseptics; others would excise the enlarged glands unless suppuration had occurred; others would do a complete dissection of the superficial glands. Some have hesitated to operate until Nature had partially walled off a sinus, while others disregarded that entirely. As a rule, nothing was done until suppuration had taken place.

Injudicious surgery has been very detrimental. Inefficient surgical treatment is followed by recurrence in the adjacent glands so frequently that when there is an operation performed it is looked upon as the beginning of a series of operations. The contra-indications of treatment by surgery are: (1) Children get well without it; (2) we have no certain method of diagnosis in early cases; (3) all the affected glands cannot be removed; (4) scars; (5) recurrences. Since the disease can be removed more successfully by roentgen rays or radium, with no danger of spreading the disease without scarring and without sacrificing tissue, complete extirpation of the tuberculous glands should never be performed until the disease is well localized. Past experience and present results should make everyone advise radiotherapy, for at least the localized effect.

In many clinics more than a thousand cases have been treated by radiotherapy, and operation was required in less than 10 per cent. of the cases, even for the removal of fibrous nodules. Over 90 per cent. were cured by radiation alone.

Different authorities call attention to the fact that when the older methods are employed a certain percentage of the patients acquire pulmonary tuberculosis. This possibility never occurs when radiation is given before any lung involvement takes place. For this reason the medical treatment should not be persisted in too long without radiotherapy.

· Large glands due to an inflammatory process are frequently secondary to a septic condition elsewhere and a search should be made for the primary lesion. When this is found and treated, if the glands remain large, and particularly if they show a tendency to suppurate, radiotherapy should be employed at once. If they are given treatment promptly and properly, suppuration can nearly always be avoided. I do not favor opening a tuberculous mass as soon as it begins to soften, as many advocate. Radiation given first

greatly facilitates repair of the parts and the sinus which frequently follows will not be so deep and will heal more readily. Certainly nothing is slower to heal than a sinus leading into a gland which has been opened just as suppuration was beginning. There is no better treatment than radiotherapy for carbuncles, boils or any other of the localized pus infections. Then why be in such haste to open a tuberculous abscess before it begins to bulge? Radiation of abscesses is never painful. This brings up the question—Do the rays produce an immunity both to tuberculosis and mixed infections?

I am sure that the susceptibility to the development of tuberculosis is always greatly lessened after a few radiations, and that the patient, at least in some cases, is rendered immune.

Recent investigations regarding tuberculosis and the various processes of tuberculous infection lead to the conclusion that tuberculosis has three stages: (1) The infection of the glands, usually coming in childhood; (2) the infection of the bones and joints; (3) the infection of the lungs.

There is no longer any doubt that the lymphatic glands form the first line of defence against tuberculosis. Nowhere is this so well demonstrated as when the glands of the neck are invaded, because almost invariably the virulence of the bacillus is greatly lessened after its entrance into the glands. In many cases the disease does not become general, so that many patients recover in a way that shows truly this infection is arrested. These tumors may spontaneously subside without suppuration, while in other patients the disease progresses until fluctuation shows that suppuration has taken place in the glands. Constitutional infection is not uncommon when tuberculous glands are neglected. Therefore a patient with chronic enlarged glands in the neck should have treatment before the constitutional symptoms develop. In the past this did not receive sufficient attention. We see too many cases coming too late where the glands have been enlarging a year or more. Such neglect often necessitates longer treatment and may even endanger the life of the patient.

Untreated tuberculosis of the glands is often followed by tuberculosis of the bones and joints, and finally there is an extension into the glands. In some individuals the process is checked in the bones or the joints. The process becomes very chronic, the resistance of the patient being sufficient to end the infection. Therefore it should be our aim to destroy the disease while it is a primary infection of the glands.

By raying the local infection in the glands its hypersusceptibility is reduced, which prevents the spreading of the disease. Tuberculin has been given for this purpose, but experience has shown that unless we are able to give the proper dosage, with the proper intervals, it may even increase the hypersusceptibility of the patient.

We must remember the responsibility of checking the disease in

the primary stage and treat the glands by radiotherapy as soon as discovered. It should be apparent to everyone that the removal by radical operation is contra-indicated, and when a recurrence takes place, not on account of the lack of surgical skill but because of the presence of the tubercle bacilli which are beyond the reach of the knife, the organism is rendered more susceptible, giving the disease a greater chance to spread than before the operation. The hypersusceptibility to tuberculosis is greatly increased by anything which tends to lower the vitality of the patient.

Tuberculous glands have been classified with regard to the pathologic involvement. Closed glands are found in two varieties, the hyperplastic and the fibrous. In the hyperplastic type the glandular substance increases, together with the stroma. If this variety is left untreated the glands soon liquefy and form an abscess known as soft glands. These may remain a long time, but if left untreated a tryptic ferment will digest the capsules, finally reaching the surface and producing unsightly scars. Fibrous glands occur in those who have a greater resistance, the tuberculous process is slower and the glandular material is not increased in the same ratio as the fibrous tissue. In the fibrous variety Nature is almost curing the patient. If the fibrous tissue does not entirely absorb it will frequently leave a hard nodule, the size of which is determined by the number of glands.

Cicatrized glands are enlarged glands in which the tuberculous process has been healed by the formation of scar tissue. If the glands have attained great size before radiotherapy has been employed a palpable nodule will usually be left. The patient may then think there is still a tuberculous process, and even the physician may not realize that a fibrous healing takes place in the cervical glands the same as it does in the lungs. Particular attention should be directed to this end, and the rays cannot be expected to absorb all the scar tissue which has been formed by the tuberculous process, when the glands have attained great size or when large amounts of fibrous tissue have been formed by Nature's cure before radiotherapy has been employed.

Then when operations are performed for such cicatrized glands radical procedures are never necessary and large, unsightly scars are avoided because the operation is performed for a different purpose. The healed nodules can be removed through a small incision and closed by sutures so that no deformity is left.

Open glands are those that have suppurated and opened to the surface. There are two varieties: those that break down as a result of tryptic ferment, the discharge of which is sterile, and those which break down, due to a mixed infection.

Recurrent glands, after a radical operation consisting mainly of mixed infections, are those recurrent immediately after the operation and those coming on slowly and some time after the operation, which

are usually of a purely tuberculous character.   The increased hyper-susceptibility of the patient after the operation is often a factor in the recurrence.   Glandular enlargements on the opposite side of the neck or in any part of the body shows the increase of suscepti-bility after a radical operation.   In these cases it is important to begin radiotherapy at once and not attempt a second operation, as has been the custom in the past.

It has been known for a long time that contagious diseases increase the hypersusceptibility to a marked degree.   We have different grades of susceptibility in tuberculous adenitis.   The small closed glands naturally represent the lowest grade of susceptibility, which is explained by the fact that the glands act as filters and contain the tubercle bacilli on their route to other organs.

As long as the glands do not suppurate they are usually check-ing the tubercle bacilli, although they are undergoing pathologic changes.   When the glands have broken down they will not per-form their full function as filters and the extension of tuberculosis is more likely.   The result obtained by the treatment of tuberculous adenitis with radiotherapy leaves no doubt that this method is the treatment *par excellence* for this condition.

Radiologists are often called upon to treat other glandular en-largements (such as sarcoma, Hodgkin's disease, lymphatic leukemia) and the more rare tumors, such as yaws, glanders and actinomycosis.   A few years ago nearly all the glandular enlarge-ments except carcinoma were considered a form of tuberculosis, but at present each has a characteristic picture when studied by the microscope, together with the clinical history.   From a clinical standpoint Hodgkin's disease is closely analogous to lymphosarcoma, and in a large majority of cases they resemble each other in the man-ner in which they react to roentgen rays or radium.   Both of these diseases have a malignant tendency to invade adjacent glands and to recur.

It is rather striking how all of these glandular tumors respond to radiotherapy.   Either radium or roentgen rays is the best treatment we possess for all these glandular tumors except syphilis, for which we have a specific.

Radiotherapy in its development to date offers a number of problems, a solution of which means a great advancement in the treatment of diseases described as multiple glandular tumors. There is no other treatment which adds so much to the comfort of the patient and prolongs life to the same extent in lymphatic leukemia, Hodgkin's disease and lymphosarcoma.

Conclusions.   1. Radium and roentgen rays will cure more cases of tuberculous adenitis than any other method.   Radiotherapy alone will cure over 90 per cent. of these cases.

2. Surgical treatment is always contra-indicated primarily in every case of tuberculous adenitis.

3. Those who still hold to radical operation will find the responsibility harder to shoulder with the ever-increasing recognition of the fact that tuberculous adenitis can be cured without it.

4. Hard, fibrous nodules following radiotherapy seldom ever contain any tuberculous foci, but it may be advisable to remove these nodules through a small incision the same as a foreign body.

5. It is to be remembered that large cervical glands may be due to sarcoma, Hodgkin's disease, leukemia, etc., and that radiotherapy is still the best form of treatment for multiple glandular tumors, but the end-results are not the same as when the enlargement is due to tuberculosis.

6. In the treatment of tuberculous adenitis in the future, when a more systematic raying is employed and when the cases are referred earlier, this method of treatment will be universally accepted.

SOME CONSIDERATIONS IN CONNECTION WITH GALL-BLADDER DISEASE.[1]

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Someone has styled the left border of the sternum in its cardiologic relationship as the romantic area. If one might apply this phrase to the abdomen, few would disagree that the right upper quadrant is deserving of the same characterization. It is quite true that many times the diagnostic story in the right hypochondrium is told in a very real manner, but all too often little respect is shown for the truth and much is left to the imagination.

In this comparatively small area, easily covered by the outstretched hand, are found the antral portion of the stomach with the pylorus, the duodenum, the biliary system, including the gall-bladder, the head of the pancreas, the right kidney, the ascending colon and the hepatic flexure, to say nothing of the appendix. This close anatomic relationship alone is sufficient to explain the problems in differential diagnosis encountered in this region. Besides this the more or less common nerve supply going to all of these structures, sympathetic and vagal in origin, increases the diagnostic troubles many times. A lesion in any one has its reference in one or all of the other organs. This alliance seems to be especially close between the gall-bladder and the stomach. The relationship of the intercostal nerve supply to the abdominal wall and the splanchnic innervation to the underlying viscera explains the upper right rectus rigidity when it spreads its protective cover over each one of these

[1] Read at a meeting of the Northampton County Medical Society, Easton, Pa.

structures as it becomes involved in some inflammatory process. Further diagnostic difficulty is met with by the presence of an abdominal reference which supradiaphragmatic lesions have in the right upper quadrant, and we need not be reminded that the reverse is also true. How convinced is many a cardiac that his trouble is subdiaphragmatic and how often does the victim of a gall-bladder or gastric attack believe that his lesion is in or about the heart. A common embryologic origin with a similar blood supply also offers an excuse for additional diagnostic puzzles that arise in the gastro-duodeno-hepatico-pancreatic system as it has been styled by McCarty.

As we are prepared in our medical schools we hear at least two or three times more about chest diagnosis than about abdominal methods of investigation. The new house doctor too often makes the physical examination note "abdomen negative," which usually means that he is more or less at sea in abdominal diagnosis. Of course it is more sensational and at the same time easier to demonstrate a good presystolic rumble than it is to palpate a spastic colon, and it is more impressive to hear a metallic tinkle than it is to outline an air-distended stomach. All of which means that an especially difficult field of diagnosis is rendered more so by a failure to stress the abdomen in our undergraduate teaching.

We said that the gall-bladder is in this complex upper right abdomen, and it is superfluous to say to you who have had your baptism of fire that its lesions, their etiology, pathology, symptomatology, diagnosis and treatment, furnish some of the most baffling and at the same time most interesting of medical problems. It is not our purpose to make a formal presentation in the matter of gall-bladder diseases but rather to point the way to a profitable mutual discussion of the subject.

The most interesting diseases of the gall-bladder are cholecystitis and cholelithiasis. Other lesions are comparatively rare and almost impossible of clear-cut diagnosis. That these two conditions are usually present at the same time needs little emphasis, and that either can exist alone is difficult of refutation. We still believe that the leading etiological rôle in these diseases is an infectious one, and that stones are consequent upon the precipitation of cholesterin, bile salts, lime salts and other substances around some nidus, usually desquamated epithelium or bacteria. Just how this precipitation is accomplished is uncertain. The inflammatory lesion is always, we believe, bacterial in origin, and as Rosenow and others have shown, the streptococcal and colon group are the chief offenders. The typhoid bacillus no longer assumes the important rôle of earlier days as Chauffard and others have shown. There are those who champion an inflammatory lesion of the gall-bladder due to some chemical change in the bile; and there are those who speak very knowingly of biliary stasis and gall-stone formation. Another

group adhere strongly to the belief that a hypercholesterinemia of chronic or acute variety is responsible for stone-production. There is no good evidence, however, to show that an increased blood cholesterol, *per se*, is constantly associated with or responsible for cholelithiasis. Indeed, the testimony in the matter of this monatomic alcohol and its relationship in the animal economy, whether normal or pathologic, is very uncertain and conflicting. It is quite true that single stones, usually pure cholesterin, are found with no inflammatory lesion in the biliary tract; but then too, there is every reason to believe that inflammation and its bacterial origin may be completely erased in these structures as it can be in others. The factors of abdominal trauma, ptotic viscera and pregnancy make for interesting etiologic discussion. The increased incidence of gall-stones in women, of course, lends support to the correctness of these theories. All must know of the phrase "fair, fat and forty." It is quite true that a thin wiry type, especially in the male, seldom yields a gall-bladder diagnosis, and it is equally true that these lesions are emphasized with advancing age and increasing inactivity, but we can fairly assume that their origin goes back to an earlier day. There is then, we believe, no single etiologic theory that holds for all cases of gall-bladder disease. Each case, in all probability, has its own particular history.

It is largely artifice that leads to a distinction between cholangitis and cholecystitis. Usually the whole biliary tract is involved in an infectious process and it is difficult to conceive how the ducts may be affected and the gall-bladder remain free, or *vice versa*. The very close relationship between the integral parts of the biliary system makes it doubtful whether clinically a differential diagnosis can be made between a duodenitis, choledochitis, cholecystitis and a hepatitis; and, furthermore, this close interrelationship would seem to demonstrate the futility of taking out a gall-bladder in some cases if the ducts too are involved in the infectious process.

We shall not tarry in the matter of the pathology of gall-bladder disease nor with the stereotyped discussion of the composition of gall-stones. We might do the same for symptomatology, still there are some points deserving emphasis in this direction. These include the fact that the clinical picture varies in wide degree with the extent and severity of the lesion and the presence or absence of infection in combination with lithiasis. Initial nausea and vomiting, fever, pain and tenderness over Murphy's point, tenderness at the tip of the right eleventh rib, muscular rigidity and a large and tender gall-bladder constitute the story for vesical inflammation. With subsiding gall-bladder attacks there may only be tenderness in the right costovertebral angle as pointed out by Sailer. Jaundice may be present and a leukocytosis is a rather constant finding. Adding colic to this picture may make for a stone diagnosis, but such colicky pain may be attributable at times to cholecystitis alone. The pres-

ence of stones usually is productive of a picture of chronic inflammation manifested by long-continued or recurring attacks of indigestion. The symptoms are usually paroxysmal in type and may be most severe.

Gall-stone colic is variable in character. The history of a sudden, severe, agonizing pain in the right hypochondrium or epigastrium, and rarely in the left hypochondrium radiating to the chest or to either scapula, nausea, vomiting, prostration, weak rapid pulse, sweating, etc., generally labels such an attack as stone.

Colicky pains usually have their origin in one of these ways:

1. Adhesions of a gall-bladder no longer containing stones.

2. Adhesions when large stones are present in the gall-bladder and the cystic duct is patent.

3. Inflammatory processes in a gall-bladder distended by fluid or stones when the cystic duct is occluded by inflammation or by the presence of a stone in the neck of the gall-bladder.

4. The transit of a stone through the bile passages.

5. Inflammation of a dilated calculous common duct or its tributaries without impaction by stone. Jaundice in these conditions always is a variable feature dependent, in fact and degree, upon the relative completeness of bile obstruction.

Whether or not gall-stones can be latent occupies much discussion in the literature. Probably a careful anamnesis would always develop in the postmortem quiescent stone patient the story of "stomach trouble," "indigestion," "dyspepsia," etc. On the other hand there is evidence to show that innocent stones are not a myth, and that, too, in well-observed cases. Clark reported 86 incidental gall-stone cases in connection with pelvic operations including 19 cases absolutely free of symptoms referable to the biliary tree.

A thickened cicatrized gall-bladder manifestly is not palpable and must be interpreted in the light of Courvoisier's law as being due to stone impaction. The other half of the law implies that a chronic palpable gall-bladder is consequent upon some extra duct obstruction, such as carcinoma of the head of the pancreas, etc. We need not dwell upon the Charcot type of intermittent fever in connection with these cases. Common duct, and cystic duct obstruction by stones are followed by many interesting conditions.

It is an easy matter to draw pictures for didactic purposes, but unfortunately disease does not always run true to type. All that may be said about diagnosis fails in certain cases. Volumes might be written on the various differential possibilities over against gall-bladder disease. I shall be content with merely mentioning some of them: gastroduodenal ulcer, appendicitis, renal calculus, intestinal obstruction, dilated duodenum due to ligamentous adhesions at the duodenojejunal junction, crises of tabes, cardiac lesions, especially with decompensation and angina pectoris; pneumonia, aortic aneurysm, Pott's disease, visceroptosis, abdominal adhesions,

pancreatitis, peritonitis, lead colic, twisted ovarian pedicle, etc. The picture of gall-bladder disease is much altered by neighborhood adhesions of the thick variety or even by actual adhesions of the gall-bladder to the duodenum, pylorus, pancreas and colon.

Can we expect any diagnostic assistance from the roentgen ray? In a variable percentage of cases gall-stone shadows are obtained. Some roentgenologists claim this percentage as high as 50 while a conservative estimate must be placed at 20 per cent. The demonstration of diseased gall-bladders is likewise a procedure of uncertainty and great difficulty. Some roentgenologists claim 25 per cent. accuracy in this direction while others are not as sanguine. It is the calcium salts, of course, that cast the stone shadows.

We have suggested that there is no good evidence to show that gall-stone formation results from a hypercholesterinemia, *per se*, and that the evidence in the literature is contradictory on this point. Our own experience leads us to believe that blood cholesterol estimations confuse rather than clear up a gall-bladder diagnosis. Hypercholesterinemic figures are obtained in lesions other than biliary ones and the results obtained for a given disease are inconstant in individual cases and variable in a group of identical cases. It is quite likely that hypercholesterinemia and an increase in bile cholesterol are factors in gall-stone formation, but we have not as yet solved the pathologic physiology.

The examination of the duodenal contents offers a promising means of arriving nearer the truth in gall-bladder disease than many things thus far suggested. The technic is rather long and tedious, requiring extensive experience in the matter of interpretation. The best results are obtained by passing an approximately sterile duodenal tube into the fasting stomach; 75 to 80 cm. of the tube are swallowed and the patient lies on the right side. Sometimes elevation of the pelvis facilitates the passage of the capsule into the duodenum. This procedure is preceded by an attempt at sterilization of the upper respiratory tract by Dobell's solution or spraying and gargling with some antiseptic solution, *e. g.*, a potassium permanganate solution, 1 gr. to the ounce. The stomach, too, is washed out by a liquor antisepticus alkalinus solution in the continual secretion cases and weak hydrochloric acid solutions are used in the subacid cases. A variable amount of time is required for the tube to pass over into the duodenum, but when it does so a bile-tinged return may or may not be obtained. The tap should be alkaline. This technic accords with that utilized by Lyon, who recently gave the investigation of the duodenal contents an added stimulus and emphasized the contentions made by Einhorn and others a number of years ago.

In 1916, at the meeting of the American Gastro-enterological Society, Meltzer promulgated his theory of contrary innervation as applied to the biliary apparatus. In a footnote attached to this

report he says: "I make, therefore, the suggestion to test in jaundiced and biliary colic a local application of a 25 per cent. solution of magnesium sulphate by means of the duodenal tube. It may relax the sphincter of the common duct and permit the ejection of bile and perhaps even the removal of a calculus of moderate size, wedged in the duct in front of the papilla of Vater." Lyon took advantage of this footnote and now douches the duodenum with a 25 per cent. magnesium sulphate solution, which is followed frequently by a richly colored return flow of bile through the duodenal tube. The examination of this bile chemically, bacteriologically and cytologically affords a possible means for better diagnosis in a limited number of cases. These include the extensive inflammatory lesions along the biliary tract as well as the common and cystic duct obstruction cases. In the former cases the presence of an excessive amount of degenerated epithelium, leukocytes and an unusually rich bacteriology serves as a criterion for a positive infection diagnosis. If no bile whatever is obtained when the duodenal capsule is properly placed we may assume common duct obstruction, and if no dark colored bile is returned after Epsom salts douching a blocked cystic duct or a functionless gall-bladder may be inferred.

This procedure of tapping and douching the duodenum affords a diagnostic aid and may be a means of treating infectious processes along the biliary tract. The use of other substances than magnesium sulphate, such as olive oil, calomel solutions, a 2 per cent. solution of hydrochloric acid and a cup of bouillon, serves to call forth an abundant bile drainage. This drainage method becomes a seemingly rational means of treating, e. g., acute catarrhal jaundice. Weak antiseptic solutions of argyrol or ichthyol, as suggested by Einhorn, may be utilized daily in a therapeutic way through the duodenal tube.

We find that little stress can be laid upon the gross appearance of duodenal tube bile as indicating normality or pathology. A turbid bile may be found in continuous gastric secretion cases when there is no gall-bladder lesion. A weak hydrochloric acid solution serves to render a bile solution cloudy. In our experience bile of all colors, viscosity and transparency may be obtained in normal cases. We do not subscribe to the possibility of diagnosing differentially by this means a duodenitis, cholecystitis, choledochitis or a hepatitis. The duodenum receives the gastric, biliary, pancreatic and duodenal secretions and to segregate them seems well-nigh impossible. The bacteriology of duodenal taps require careful study and involves a most difficult and uncertain field of study. Many organisms are reported as being obtained normally and pathologically. We have principally found members of the colon group. The pneumococcus is reported by some men. Just how this fact can be reconciled with the general bile solubility of this organism is difficult for a non-bacteriologist to explain.

The rôle of the gall-bladder as a focus of infection in extrabiliary pathology is deserving of much thought. In our experience we have noted very little influence derived from excision of a diseased gall-bladder in such cases as multiple arthritis. Generally these cases are well advanced when this is tried and naturally very little can be done. As a matter of fact the subject of focal infection is a many-sided and complex one, so that it is dangerous to draw conclusions even on an extensive experience in this field.

It has been both unfortunate and fortunate at the same time that in recent years there has been a domination of our ideas by surgical conceptions. In the matter of gall-bladder disease, as well as in other conditions, the viewpoints of the family doctor, the gastro-enterologist and the surgeon are different, and therefore their conclusions do not harmonize. The general practitioner sees the first attack of cholecystitis and sees many such bladders yield to ordinary medical procedures never again to cause trouble. The gastro-enterologist sees the chronic dyspeptic and the surgeon in his turn sees well-advanced pathology. We know of nothing that will influence the fate of gall-stones other than surgery, but we do not believe that primary attacks of cholangitis or cholecystitis belong to this therapeutic field. We do assign to the surgeon gall-bladder disease of early chronicity because of the frequent tenacious persistence of infection in the gall-bladder wall and surrounding lymphatic system. This affords the possibility of a focus of infection for other parts of the body as well as fresh outbreaks in the biliary tract itself. Drainage by way of the duodenal tube and even by cholecystostomy can offer no hope in the chronic case with gall-bladder wall infection; indeed, duodenal tube installations in any event can offer little advantage over the time-honored method of taking Epsom salts by mouth.

Whether or not the operation is to be one of cholecystostomy or cholecystectomy offers a fine opportunity for sound judgment on the part of the operator. Both procedures are followed by successes, by failures and by reformed or overlooked stones. Routine chole-cystectomies are to be condemned as all routine treatment should be. A badly inflamed bladder with impacted stones in the cystic duct; an old, thickened gall-bladder; a bladder distended with clear fluid; suspicious bladder malignancy; a strawberry gall-bladder with no stones and extensive pericholecystic adhesions should indicate a cholecystectomy. To take out the gall-bladder is not exactly comparable to an appendectomy. The former has a distinct function in accomplishing the concentration of hepatic bile and pancreatitic juice. Continual bathing of the duodenum may serve in a reflex way to be responsible for the frequency of anacidity or even an achylia gastrica in these postoperative cases, to say nothing of other sequelæ. In common-duct strictures and pancreatitis it is often of distinct value to retain the bladder for future cholecyst-

duodenostomy or cholecystenterostomy purposes. The controversy in the matter of cholecystostomy *versus* cholecystectomy is not for us to decide, but we wish to put in a plea for the careful non-routine gall-bladder surgery. Such surgery is indicated in any case of early chronicity and stones. With the finding of one or more gall-stones in a relatively normal gall-bladder, further search should always be made for other abdominal pathology. A duodenal ulcer, for example, may be the real cause of trouble in such a patient. Sometimes in primary gall-bladder attacks operative interference may be required for gangrene, empyema and rarely perforation. Gall-bladder disease is seldom immediately dangerous, always remotely so. The appendix nearly always threatens life. An operation on the acute appendix nearly always relieves. In the case of the gall-bladder this is not always the case.

The surgeon always claims to prefer gall-bladder surgery only after a thorough medical treatment has failed. Such medical treatment at times is very successful while at other times it seems to be of little avail. The early institution of proper diet to control the gastric symptoms and to offset the intestinal stasis is often of prophylactic help in the purely inflammatory gall-bladder cases. Most of these patients are badly constipated and experience their worst attacks if intestinal peristalsis is cut down. We question the value of hexamethylenamin and salicylic acid as antiseptics in these cases. The cholagogues may have their therapeutic place here, but we believe what most of these agents accomplish is the release of gall-bladder bile into the duodenum, and that they do not especially influence bile formation. An active outdoor life seems to help many gall-bladder patients; on the other hand, there are times when exercise seems to aggravate acute attacks. In the light of Meltzer's theory infrequent and insufficient feeding may be conducive to biliary stasis and stone formation, so that frequent feeding perhaps promotes biliary drainage and helps infected cases. For the acute attack we know of nothing better than hot-packs, rest in bed and the judicious use of salines. In stone colic usually we, of course, need morphin and atropin. Experimentally, it is said that urotropin and iridin influence gall-stones. The same is said to be true of "Harrowgate old sulphur water," and barium chloride is supposed to stimulate the gall-bladder.

That gall-stones predispose to cancer is a point for much argument. It is true that a high percentage (70 to 90) of operated primary carcinoma cases of the gall-bladder is accompanied by stone. This is not true for primary duct carcinoma. Whether the stones do not frequently follow rather than precede the carcinomatous change in the gall-bladder is also a matter for dispute. Primary bladder malignancy is sometimes accompanied by stone formation, and there are cases which develop bladder cancer some years after stones have been removed or it may develop at the old cholecystos-

tomy site. Secondary carcinoma of the gall-bladder seldom is accompanied by stones because of the comparatively short duration of the disease and also because the invasion is by way of the serous coat of the bladder. It would seem rather that cancer of the gall-bladder is more prone to follow ulcerative processes and their consequent cicatrices than upon the mere presence of stones, just as we believe to be the case in gastroduodenal carcinoma.

In conclusion, we wish to emphasize the great difficulties of gall-bladder disease diagnosis in many cases. We have indicated some of the reasons why there is such difficulty. Frequently one must depend upon clinical intuition, and often William Mayo's dictum is realized upon "that where there is trouble in the right upper quadrant only a laparotomy will reveal the exact cause of the trouble." This should be true in fewer instances if we combine the evidence obtained by good, careful history-taking, physical examination, laboratory and roentgen-ray study. The case of long-standing indigestion, gas, eructation, etc., with perhaps interpolated acute abdominal attacks, is more or less typical, although the picture of gall-bladder disease is a variable one. The possibility of latent stones and some theories for gall-stone formation are mentioned. The relationship of cancer and gall-stones is indicated and some points are made in the controversy between those who practice cholecystotomy or cholecystectomy as an operation of choice. The study of duodenal contents is mentioned as a diagnostic aid and the practice of duodenal lavage in catarrhal jaundice and primary acute gall-bladder attacks is mentioned as a possible therapeutic measure. After any degree of gall-bladder chronicity is attained such lavage or medical measures are of little avail, and, indeed, frequently the problem is not met by surgery.

PHYSICAL EXERCISE IN HEART DISEASE.

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One of the important things which physicians have learned from their war experience is that physical exercise plays a dominant role in the hygiene of normal men and that certain circulatory disorders, variously termed *effort syndrome*, *neurocirculatory asthenia*, etc., may be benefited by the same measure. With no more than this experience it would seem reasonable to believe that a therapeutic measure as valuable as exercise has proved itself to be might be useful in circulatory disorders of a more serious nature.

The great drawback even to experimenting with exercise in disease of the heart has been the difficulty of determining just when a patient's heart was overtaxed by physical work and a lively fear of the results of such an overtaxing. Physicians have been extremely cautious about advising these patients to exercise. Generally the advice has been to be careful not to overdo and a very potent therapeutic measure in circulatory disease has been gradually discarded.

The term *exercise tolerance* has been frequently used of late and the implication has been that the above-mentioned difficulty has been solved. Actually the same dilemma confronts us. This term simply puts before us the conception that we can best judge of the heart's reserve power by the way a person tolerates exercise rather than by various other procedures. This conception is undoubtedly valid, for the best way to judge of an organ's capability is to set it doing its own particular work and base our judgment upon the result of such experiments. A person's ability to tolerate physical work depends essentially upon his heart's reserve power provided his lungs and body muscles are functioning in a normal way. Inability to tolerate a given amount of work means that the heart's reserve power has been overtaxed,[1] and the problem of deciding when this occurs is no different from what it has always been.

The fact that the term *exercise tolerance* expresses the correct method of ascertaining the amount of cardiac reserve power, would seem enough justification for its adoption. It has, however, a certain drawback. We have no form or amount of physical work which will serve as a standard capable of being translated into other forms of physical activity. A patient's heart may easily tolerate the exercise of walking on a level and be decidedly overtaxed by climbing a short flight of stairs. To speak of a person's *exercise tolerance*, therefore, without qualifying the word *exercise* means but little.

A brief summary of what we know about the circulatory physiology of physical work and of some experiments on patients with different amounts of cardiac reserve power will give us an insight into the principles to be followed in prescribing exercise in heart disease.

Circulatory Physiology of Physical Work. The salient phenomena accompanying muscular work are a rise in arterial pressure, a larger output from the heart and an increased flow of blood through the heart and working muscles.

The rise of blood-pressure is due to the increased output of the heart into a stream bed which has been narrowed by constriction of the splanchnic vessels. The rise implies, therefore, that the heart is able to increase its output and that the vasomotor center is acting upon the splanchnic vessels. Chiefly by means of the

[1] Bainbridge, F. A.: The Physiology of Muscular Exercise, 1919, p. 138.

increased blood-pressure are the heart muscle and working muscles provided with more blood—that is, with oxygen sufficient to satisfy the increased metabolism incident to work.[2]   A subsidiary factor in producing the increased blood supply is relaxation of the arterioles and capillaries in the working muscles and of the coronary vessels in the heart.   The rise of systolic blood-pressure during work is the most significant fact in the circulatory physiology of muscular exercise.   It means that the heart is acting more energetically, that it is increasing its output and that the heart muscle is being supplied with more blood.

The course of the blood-pressure during work has been determined by a number of observers, and the course after work has been even more carefully investigated because of the easier technic.   The relation between the pressure during work and that after work has received little attention.

In 1916 I published a record of experiments upon three normal people and upon two patients suffering from cardiac disease in whom the systolic blood-pressure curve was plotted during and after the performance of work.[3]   In the three normal persons it was shown that the pressure rose *during* work and the degree of rise was proportional to the intensity of this work; also, that the height of blood-pressure during the first sixty seconds *after* work approximated the height reached during work.   The records then published of the experiments on two patients with cardiac disease were incomplete because of the infrequent readings made during work.   These latter experiments have been repeated.

Three patients were selected having different degrees of cardiac reserve power.   The first patient was confined to bed and suffered from aortic regurgitation and a marked cardiac failure.   His legs were much swollen, there was some fluid in the abdomen and he was dyspneic.

The second patient had a chronic myocarditis and auricular fibrillation.   He was able to be up and about, but his ankles showed almost constantly some edema and his heart's reserve power was very slight.

The third patient had a double mitral lesion and a moderate reserve power.   She could walk about and do light household work.

Twenty-five experiments were carried out on these three patients. Work was furnished for the bed patient by alternately flexing the thighs on the abdomen and for the walking patients by the same maneuver, the patients standing during the work.   Each working period lasted from thirty seconds to two minutes.   Naturally the rate at which they worked varied considerably.   The longest period of work always resulted in overtaxing the patients' hearts, earlier or later in the working period, as was shown by their marked dyspnea

[2] Bainbridge, F. A.:   The Physiology of Muscular Exercise, 1919, p. 86.
[3] Barringer, T. B., Jr.:   Arch. Int. Med., 1916, xvii, 363-381.

and fatigue. The blood-pressure was read every ten seconds by auscultation *during* and *after* work. The following charts depict a typical series of experiments in each patient and also the same experiments in a control with normal heart.

These experiments show the following facts: *During work* the pressure rose and reached its highest figure during the greatest
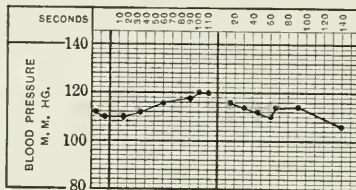

CHART I.—Curve of systolic blood-pressure during and after work in a normal person. Space between the two heavy perpendicular lines represents working period. Work furnished by flexing the thighs alternately on the abdomen at a rapid rate.

amount of work. *After work* the rise noted was, in the majority of instances, greater than that observed during work, and from its height we gained an idea of the height which had been reached during work. A "delayed rise" and prolonged fall were noted whenever the work overtaxed the heart. The rise in pressure both during and after work was much more marked than was noted in the normal control. Very small amounts of work produced very marked rises in blood-pressure in these patients with damaged
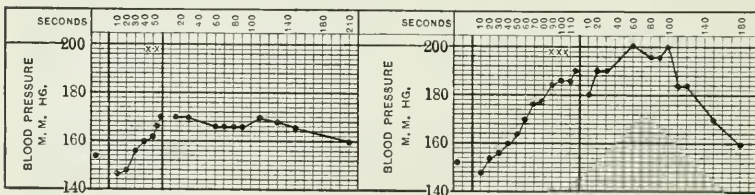
CHART II.—Curve of systolic blood-pressure during and after work in patient C. R., confined to bed, suffering from aortic regurgitation and extreme cardiac failure. Legs swollen; free fluid in abdominal cavity. Space between the two heavy perpendicular lines represents working periods of sixty and one hundred and twenty seconds respectively. At x^2 patient was dyspneic. At x^3 patient was very dyspneic (respirations 43 per minute) and fatigued, and it was apparent that he could work but a few seconds longer.

hearts. It would require very much larger amounts of work to produce as great rises in normal persons. We have seen that the increased cardiac output is the chief factor in producing the rise in blood-pressure in normal hearts. It seems very improbable that a damaged heart could increase its output enough to cause such high blood-pressures, as we have noted in our experiments, particularly

since the work was very small in amount.   It is caused much more probably by an exaggerated activity of the vasomotor center.[4] This high pressure makes it increasingly difficult for the ventricle to empty itself, thus tending to produce an insufficiency.
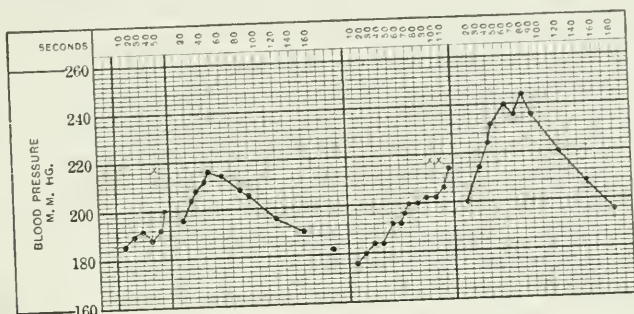

CHART III.—Curve of systolic blood-pressure during and after work in patient J., suffering from chronic myocarditis, cardiac hypertrophy, auricular fibrillation and moderate cardiac failure.   Patient was up and about but showed almost constantly some pretibial edema and could not climb a short flight of stairs without distress.   Space between the two heavy perpendicular lines represents working periods of sixty and one hundred and twenty seconds respectively.   At x^1 patient dyspneic; at x^2 decidedly dyspneic and exhausted.   In reading the blood-pressure the height at which the first strong beats came through was recorded.   It is interesting to note that the heart in this patient with auricular fibrillation reacted to exercise in the same manner as did the other patients with rhythmical heart action.

Up to a certain limit exercise must act upon a damaged heart exactly as it does upon a normal heart; that is, increase the cardiac output, increase the blood supply of the heart muscle and raise the blood-pressure.   As soon as this limit is exceeded the patient becomes markedly dyspneic, the excessive rise in blood-pressure
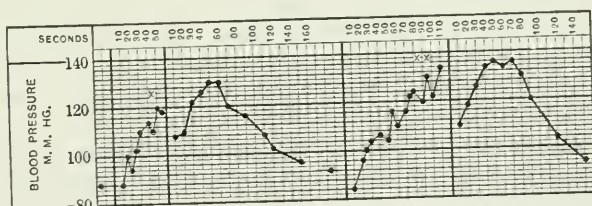
CHART IV.—Curve of systolic blood-pressure during and after work in patient D., suffering from mitral stenosis and regurgitation and small cardiac reserve power. She was able to do light housework and exercise as shown in Table I.   Space between two heavy perpendicular lines represents working periods of sixty and one hundred and twenty seconds respectively.   At x patient dyspneic.   At x^2 respirations were 48 per minute and it was apparent that patient could work but a few seconds longer.

we have described ensues and a temporary insufficiency is produced. The heart's reserve power has been exceeded.   Naturally, when a heart has no reserve power, as in Case II, no exercise, however

4 Personal communication from Dr. F. A. Bainbridge.

small the amount, will produce a normal physiologic reaction. We direct particular attention to the abnormal curves of blood-pressure following excessive amounts of work in these experiments (delayed rise and prolonged fall). When the exercise given to a damaged heart is properly estimated the rise in blood-pressure, whatever its height, is not accompanied by excessive dyspnea, nor is it followed by this type of curve.

The necessity, then, of deciding very definitely the question of overtaxing a damaged heart when prescribing exercise as a thera-peutic measure must be apparent from these considerations.

The Symptoms of Overtaxing of the Heart's Reserve Power. Oertel, the pioneer in the treatment of cardiac insufficiency by physical exercise, depended chiefly upon a patient's sensations to determine whether a given exercise had overtaxed the heart. His rule was that if a patient after walking a short distance experienced palpitation and dyspnea he should stand still and breathe deeply until the disturbance disappeared.[5] Dyspnea, palpitation, pre-cordial distress or pain, faintness and fatigue, are the subjective sensations arising from the overtaxing of a damaged heart. Like all subjective sensations, they must be carefully appraised, and since it is their intensity which is of significance the lack of any standard makes their proper valuation a difficult matter except when they are present in marked degree. On the other hand, there are symptoms which can be observed when the heart is overtaxed —dyspnea, the expression of the face indicating distress or fatigue, the color of the face and lips and the pulse-rate. In marked over-taxing the intensity of both the subjective and objective symptoms does not leave us in doubt. When the overtaxing is inconsiderable, however, and all or a few of the symptoms enumerated above are present in but slight degree we are perplexed. The return of the pulse-rate to the preëxercise count inside of a few minutes has of late been much used to decide the question of overtaxing. In marked instances it is of help, but in the borderline cases I have found it of no value.

There is another means of deciding this question which, in my experience, has been of great value—that is, the plotting of the curve of the systolic pressure after work. A "delayed rise" and prolonged fall,[6] referred to above, indicate, we believe, that the preceding work has overtaxed the heart's reserve force. This definite objective symptom often enables one to decide the question of overtaxing when other symptoms have left us in doubt, and is, perhaps, more reliable than any other symptom of this condition.

It is surprising how few instances we see of cardiac failure directly following physical overstrain. It certainly is an unusual event to see this caused by a single overexertion.

[5] Oertel, M. J.: Ueber Terrain kurorte, Leipzig, 1886, p. 12.
[6] Barringer, T. B., Jr.: Am. Jour. Med. Sc., 1918, clv, 864.

In the great majority of instances cardiac failure or decompensation is caused by a reinfection of the heart and not by physical overstrain.

Forms of Exercise and Test Exercises for Heart Patients. As a therapeutic measure exercise may be divided into two forms, energetic and mild, and a definite guide to prescribing these forms for patients with damaged hearts can be formulated from the facts set down in the two preceding sections. The amount of increase in the systolic blood-pressure after exercise determines the category to which any exercise belongs.

The energetic type is the more important for heart patients. The question of overtaxing the heart must be carefully decided in this form of exercise by the methods previously described. One or two overtaxings have never in my experience done any harm. This energetic type produces an increase of between 20 and 40 mm. of mercury after work, should not produce excessive dyspnea and should show a *normal curve* of *systolic pressure* subsequent to work. From this we know that a somewhat smaller rise has existed during work, that the heart in acting more energetically, is increasing its output and that the heart muscle is being better supplied with blood. The working periods should be of short duration and alternated with periods of rest. Also the exercise should be of such a kind that it can be prescribed in definite amounts and increased or decreased in definite proportions.

Exercise with dumb-bells, stair-climbing, skipping rope, running in place, hopping and all calisthenic exercises in which the body trunk is moved widely are the ordinary forms of energetic exercise useful for heart patients.

I have found the most convenient form of energetic exercise to be different movements with dumb-bells varying between one and fifteen pounds in weight. Swinging a bell from between the feet in an arc up above the head and repeating without a pause; flexing the forearms alternately, with a bell in each hand, the patient sitting or standing; and pushing two bells alternately above the head are the three most useful movements. Each close[7] includes between five and twenty units of exercise. After each close the patient rests until blood-pressure and pulse return to normal.   The closes are repeated from five to ten times at each exercise period, which is generally once in twenty-four hours.

The mild form of exercise is one which stimulates the heart's activity but moderately over longer periods of time, as shown by the small increase in blood-pressure subsequent to the exercise. This form should be used for patients with small cardiac reserve power and also to supplement the first more energetic type.

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[7] The word "close" is used to indicate the period during which the patient is continuously exercising. Its duration is not measured in time but by the number of units of exercise it includes.

Walking is perhaps the best example of the second, milder type of exercise. This should be at first on a level. The patient should not talk and should not walk against a strong wind. A certain distance should be covered at a fairly rapid gait which can be determined only by experiment and then the patient should rest for two or three minutes; then repeat the walk and rest.

Other forms of mild exercise suitable for heart patients are croquet-playing, setting up exercises in which the arms and legs and not the trunk are moved and dancing (limited to one step). As the patient's reserve power increases one of the more energetic types of exercise should be added to the daily regimen. Whatever the exercise it should be determined on two successive days by the methods outlined above if it overtaxes the patient's cardiac reserve power.

A comparison of walking, stair-climbing and swinging dumbbells by the same patient will give a quite correct idea of the relative intensities of these different forms of physical activity.

TABLE I.—D. B., AGED TWENTY–TWO YEARS; MITRAL REGURGITATION AND STENOSIS; SMALL CARDIAC RESERVE POWER. IS WALKING ABOUT AND DOING VERY LIGHT HOUSE WORK.

Date.	Stair climbing.	Walking on level.	Swinging 1-pound bell.
1920. May 16	10 *feet rise in* 15 *seconds.* Pulse before . . . 72 Pulse after . . . . 120 Blood-pressure before . 96 Blood-pressure after . 126 (highest) Delayed rise and prolonged fall present. Respiration before . 28 Respiration after . . 42	400 *feet in* 2 *minutes.* Pulse before . . . 78 Pulse after . . . . 120 Blood-pressure before . 96 Blood-pressure after . 124 Normal curve of blood-pressure. Respiration before . 24 Respiration after . . 36	10 *times in* 20 *seconds.* Pulse before . . . 84 Pulse after . . . . 112 Blood-pressure before . 100 Blood-pressure after . 126 Delayed rise and prolonged fall present. Respiration before . . 24 Respiration after . . 36
	22 *feet rise in* 30 *seconds.* Pulse before . . . 72 Pulse after . . . . 132 Blood-pressure before . 92 Blood-pressure after . 142 Delayed rise and prolonged fall marked Respiration before . 28 Respiration after . . 56	960 *feet in* 4 *minutes.* Pulse before . . . 78 Pulse after . . . . 132 Blood-pressure before . 98 Blood-pressure after . 128 Delayed rise and prolonged fall present Respiration before . 24 Respiration after . . 42	15 *times in* 30 *seconds.* Pulse before . . . 84 Pulse after . . . . 132 Blood-pressure before . 100 Blood-pressure after . 132 Delayed rise and prolonged fall present Respiration before . . 28 Respiration after . . 42
June 7	10 *feet in* 20 *seconds.* Pulse before . . . 66 Pulse after . . . . 88 Blood-pressure before . 90 Blood-pressure after . 108 Normal curve of blood-pressure Respiration before . 24 Respiration after . . 32	1360 *feet in* 6 *minutes.* Pulse before . . . 60 Pulse after . . . . 108 Blood-pressure before . 86 Blood-pressure after . 106 Normal blood-pressure curve Respiration before . 28 Respiration after . . 36	*Swinging* 5-*pound bell* 10 *times in* 20 *seconds.* Pulse before . . . 66 Pulse after . . . . 100 Blood-pressure before . 84 Blood-pressure after . 108 Normal curve of blood-pressure Respiration before . . 24 Respiration after . . 32
	22 *feet in* 30 *seconds.* Pulse before . . . 66 Pulse after . . . . 120 Blood-pressure before . 88 Blood-pressure after . 120 Delayed rise and prolonged fall present Respiration before . 24 Respiration after . . 42		15 *times in* 30 *seconds.* Pulse before . . . 64 Pulse after . . . . 120 Blood-pressure before . 88 Blood-pressure after . 116 Delayed rise and prolonged fall present Respiration before . . 28 Respiration after . . 48

Table I shows that on May 16 this patient could not swing a one-pound bell ten times nor climb a short flight of stairs without overtaxing her heart. She could, however, walk 400 feet on the level with normal reactions. On June 7 she showed decided improvement, for she was able to do some stair-climbing, swing a 5-pound bell ten times and walk much farther without overtaxing her heart. At this date she was put on both energetic and mild forms of exercise.

It is a difficult matter to translate any given amount of a particular form of exercise into other forms of physical activity. It can be stated, however, from a number of experiments on different patients similar to the ones just quoted, that a patient who can swing a 5-pound bell ten times in twenty seconds can climb slowly a flight of stairs with a 10-foot rise, can walk easily on the level and can perform light, physical work without overtaxing the heart. A patient who can swing a 10-pound bell ten times without overtaxing his heart can walk as long as one-half hour up a slight grade and can play nine holes of golf over not too hilly a course.

Stair-climbing and swinging dumb-bells afford, perhaps, the best test exercises for heart patients. The test of hopping on one foot 100 times, which was much used in the army, is thoroughly unsuitable because the actual amount of work performed and the time of performance vary greatly with each individual. The work done depends upon the height which the body rises with each hop. This varies with each person and varies even in the same individual, for the later hops are lower than the earlier ones; again, the time taken to perform this test varies greatly. Obviously, then, with these two variables the amount and the rate of work the circulatory reactions will differ greatly and afford no basis for comparison.

It must be emphasized that exercises should not be given to patients who are suffering from even a mild reinfection of a diseased heart, nor should they be given until such an infection is well over, as shown by a normal temperature for from five to seven days. The administration of digitalis to a patient is not a contra-indication to exercise, for we have exercised such patients many times with benefit. Digitalis favorably influences the action of the heart during exercise, as we shall show in a later paper.

There is another adjunct to exercise of much importance, and that is weight-reduction in patients who are overweight. Heart patients are inclined to grow stout because of the enforced limitation of their physical activities and because of lack of specific dietetic instructions. I have been impressed with the fact that exercise in conjunction with weight-reduction produces a more rapid and more marked increase of the heart's reserve power in these patients than does exercise alone. The reasons for this are not clear. Changes in the total metabolism, the slight increase in the size of the stream bed due to the formation of new capillaries in the fatty tissue, better pulmonary ventilation—probably all these play a part.

The history will be summarized of one patient who represents a class in which particularly excellent results were obtained by this procedure.

Mrs. M., aged seventy years. For ten years she had suffered from angina pectoris. This had steadily grown worse until, in 1919, she was unable to walk at all without causing an attack of pain and dyspnea. On January 8, 1920, I first saw this patient in an attack of pulmonary edema. She was a very obese woman, 5 feet, 2 inches tall, weighing 200 pounds, and seemed to be on the point of death. Her pulse was 120 per minute, regular rhythm, and her blood-pressure 140-80. The heart sounds could not be heard because of the moist rales heard all over the lungs. Her electrocardiogram taken later showed slight myocarditis and a left ventricular predominance. She recovered from the attack and was put on tincture digitalis, diuretin and a strict diet of four glasses of milk, two glasses of water and six soda biscuits daily, with rest in bed. The following table summarizes her course of treatment:

TABLE II.—COURSE OF TREATMENT IN PATIENT MRS. M.

Date.	Weight.	Diet.	Exercise.	Remarks.
1920. Jan. 8	200	800 calories: 6 soda biscuits 4 glasses milk 1 glass water	Rest in bed until Jan. 29	Tincture digital- is and diuretin.
Feb. 12	180	1100 calories: 1 egg 1 portion vegetable 1 slice bread and butter 6 soda biscuits 4 glasses milk $\frac{1}{2}$ grape-fruit Stop fluid restriction	Up and about room	Stop digitalis and diuretin.
Feb. 21	$178\frac{3}{4}$	The same as on Feb. 12	Walk one block—5 closes;	
Mar. 11	$175\frac{3}{4}$	1500 calories: 1 lamb chop 2 slices bread and butter 6 soda biscuits 1 portion vegetable 4 glasses milk 1 lettuce salad $\frac{1}{2}$ grape-fruit	Walk two blocks—8 closes; light calesthenics (flex thighs on abdomen alternately ten times while standing—3 closes)	
Mar. 17	173	The same as on Mar. 11	The same as on Mar. 11	
Mar. 24	$171\frac{1}{4}$	The same as on Mar. 11	Increase walking and calesthenics	
April 14	166	2000 calories	Walk four blocks—10 closes; calesthenics (flex thighs 12 times— 6 closes)	No precordial pain during ex- ercise.
May 26	165	No dietetic restriction except meat but once daily; weight not to be increased	Walk sixteen blocks—3 closes; climb 1 flight of stairs 15 feet	No precordial pain during exercise.

The calisthenics noted above belong to the mild type of exercise, for each close produced no greater rise in blood-pressure than from 10 to 20 mm. of mercury.

Summary. At the end of six months this patient had lost 35 pounds in weight and was able to walk three-fourths of a mile without stopping and climb one flight of stairs without producing any anginoid symptoms. This compares very favorably with her condition during 1919, when she was unable to walk at all because of attacks of angina caused thereby.

I have found fluid restriction of minor importance compared with weight-reduction except in patients who have considerable edema. It has been a difficult matter to convince patients that weight-reduction means less work for the heart to do, and many physicians feel that the reduction of weight in heart patients is a dangerous procedure unless done very gradually and very moderately. In the past five years in approximately thirty patients I have never seen "weakening" of the heart result from even a radical weight-reduction if at the same time the patient was exercised properly.

In the light of our knowledge of the circulatory physiology of exercise it seems quite certain that physical exercise must not only increase the resistance to general infections of patients with heart disease, exactly as it does in normal people, but that in all probability it makes the heart itself more resistant to the serious menace of reinfections.

There can be no excuse in the majority of instances for advising heart patients against exercise nor any reason for not being specific and definite when prescribing this valuable therapeutic measure.

OCCULTISM WITH PARTICULAR REFERENCE TO SOME PHASES OF SPIRITISM.[1]

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THE term, "occultism" is derived from the Latin, meaning hidden or concealed. As sometimes used the word has a special significance, referring to Oriental sects or cults which concern themselves with religious mysteries like the Vedanta or theosophy. Theosophy is a particular phase of occultism, its disciples believing, as the name implies, that they have a direct knowledge of God through spiritual intercommunication. In comparatively recent years the theosophy of the East has found disciples in the Western

[1] Presented to the Philadelphia County Medical Society, January 12, 1921.

World and now is represented by a considerable following in various localities of England, the European continent and America.

Forms of theosophy have flourished under other names as Neoplatonism and Swedenborgianism.

The most exploited apostle of theosophy, at least in the early days of my interest in matters of this description, was Madame Helena Petrovna Blavatsky, a Russian who travelled in India and elsewhere in the East and later became one of the founders of a theosophical society about 1875. She stayed for a time in London, where she attracted much interest in society and in pseudoscientific bodies. Her tricks and false assumptions were exposed by Richard Hodgson. It is interesting to note that in spite of this exposure the theosophists, or many of them, still give their adherence to her teachings and still uphold her as an inspired exponent of spiritistic doctrine. Evidently, from what I have read of Blavatsky, she was a trickster and so-called medium, which often means the same thing.

Even in recent days it has been held, as it was of Blavatsky, that it does not impair the value of a medium's power to communicate with spirits not of this world to prove that she is a fakir.

The term " mysticism," as commonly used, is more or less synonymous with occultism. It has been briefly defined as the " *belief in a third kind of knowledge*," that is, knowledge which is neither perceptual nor inferential. But I must leave a discussion of these points to our friends the psychologists.

The question of paramount interest since the recent revival of spiritualism is whether or not communication can be held between the spirits of another world and the inhabitants of this. The anecdotal literature of such communications has been enormously increased since the beginning of the World War. Millions have " gone west" or to " the other side," and it is claimed that not a few of this immense host have communicated with their bereaved relatives.

Why has the world recently become fascinated by the study of occult phenomena? The horrible sacrifice of life since 1914 has doubtless acted as an exciting cause, but back of this is a more profound reason. The phenomenon is due to a resurgence of that which is primitive. Edward Clodd, in the *Fortnightly Review*, says: " Man felt before he reasoned. As a creature of emotion he has an immeasurable past; as a creature of reason he is only of yesterday."

War, and especially a great and terrible war, arouses the instinctive and emotional in the human race. It removes man for the time being from the control of sound reasoning. On the principle of the first organized the most organized—the first to come the last to go—untutored men, and in particular instances intellectual men, through the domination of feeling and emotion, revert more or less to the same domain of mysticism that held in thrall their savage or half-civilized ancestors. Instinct and emotion for a time largely

hold the field.   Even crime so prevalent today is best psychologically explained as a return under peculiar stress to instinctive tendencies.

It is not altogether true that the only great wave of spiritualism has been since the World War.   In 1855, for instance, Professor Robert Hare spoke to an audience of three thousand people in the New York Tabernacle on the subject of spirit manifestations, a larger audience when the population of that time and this are compared than those to whom Sir Oliver Lodge delivered his lectures.

Some of my critics may say that it is all well enough to talk of the ignorant and mediocre human beings who, at least from the standard of knowledge of such subjects as philosophy and metaphysics, are 90 to 95 per cent. of the people of the world, that they are creatures of instinct and emotion, that their beliefs are founded on their superstitions and general mystic tendencies; but how is it to be explained that not a few of the great men of the earth—in the sense of their literary, scientific or technical accomplishment—should give their adherence to spiritualism?

What is to be said of Robert Hare, chemist and physicist; of Sir William Crookes, another great chemist; of Sir Oliver Lodge, physicist, astronomer and educator; of William James, the eminent psychologist; of Alfred Russell Wallace, Sir Arthur Conan Doyle, Sir W. F. Barrett, Camille Flammarion and Maurice Maeterlinck?

Of course I might in contrast to these men produce a goodly host of scientists and scholars who have not given their adherence to spiritualism.   The list would include great names like Darwin, Huxley, Spencer, Tyndall, Leidy and many others who will be easily suggested.

It has been said with regard to some of the scientists that their conversion to spiritualism was in their advancing years, when their mental powers were probably failing.   This, however, cannot be said of most of them.   It is true that Robert Hare became an open advocate of spiritualism only a few years before his death, which occurred at the age of seventy-eight.

Sir William Crookes, however, who was born in 1832, expressed his belief in spiritualism as early as 1871, when he was scarcely forty years old.

Sir Oliver Lodge went into the " spiritualistic camp" before he was sixty.   Others of the group to whom I have referred entered the same camp at varying ages.

I might advance a partial explanation.   These men apparently at some time in their career have come to lead what might be termed a double mental life—not a double life of the Jekyll and Hyde sort of changing periods of virtue and vice, of criminal propensity and conventional acquiescence—but a life in which reason and investigation pursue their way side by side with instinctive and emotional tendencies.   Some of these men probably

are the victims of inherited temperament; their hereditary strain impels them strongly toward the instinctive and emotional.

In my own experience I have had a few interesting exemplifications of such tendencies. I remember, for instance, a well-known Philadelphia surgeon, one time a teacher in the medical department of the University of Pennsylvania, the author of a text-book on a branch of surgery which long held its place as an authoritative treatise, an admirable practical surgeon in his chosen line of work. This man, nevertheless, side by side with his scientific and practical work, had curious tendencies toward philosophical and metaphysical inquiries in which he showed considerably less stability and power. Under a pseudonym he was the author of various philosophical or pseudophilosophical books, one of which referred especially to Plato and Platonism.

This gentleman was a personal friend of mine and loved to drop in at times and talk of Rosicrucianism, of Heraclitas, Plato, Aristotle or Bruno or some other of the brood of ancient and medieval philosophers. With all his acquirements he was a most childlike being. He would go, as one of our mutual friends told me, to some spiritualistic seance or meeting and allow himself to be fooled by the most crude and obtrusive frauds. Once he came to my house in a state of excitement and told me that he believed he had discovered the explanation of telepathy. He said he was confident that it was through the pineal gland and its peduncles that the phenomena of telepathy received their final accomplishment in the human brain; nor was he able to listen with any patience to my own exposition of the common views regarding the physiology of the pineal gland.

The adherence of some scientists to the more primitive or emotional forms of religion has been thought to have the same explanation as has just been expressed. I might give a number of illustrations of men of this type, but shall refer only to one.

Philip Henry Gosse (1810–1888), whose interesting story is told by his son, Edmund Gosse, in that remarkable book *Father and Son*, was a biologist of high repute. He was a member of the Royal Society and wrote a series of authoritative biological works, among these being *The History of the British Sea Anemones and Corals*, *The Ocean* and *Birds of Jamaica*. One or two of his books were speculative and religious in tone. In one he worked out a theory to justify himself as a strictly scientific observer, who was also a humble slave of revelation.

Philip Henry Gosse had been reared as a Wesleyan, but he became an active and militant member of the Calvinistic sect known in England as the " Plymouth Brethren." He was zealous in prayer and preaching, was narrow in his application of biblical teaching, had the spirit of a proselytizer, and withal he was an honest and upright man in his dealings with others. He and his son Edmund finally separated, after it became clearly impossible

for them to live in accord on religious matters.   As in the case of the scientific spiritualists, the primitive, emotional or instinctive, in spite of his intellectual accomplishment, held the elder Gosse with an iron grip.

Let us now take up briefly a few points of special interest connected with the general discussion of the subject of spiritism. Ghosts or apparitions are intimately associated in the minds of the community with this subject.   Ghost stories are as old, and probably older, than historic time; from Nippur and Babylonia, through all the Egyptian dynasties, in the period of Pericles and Plato, of Cagliostro, Robespierre and Anacharsis Clootz, in the days of the Fox Sisters and Robert Hare, and now in our own time of Sir William Crookes and Sir Oliver Lodge, the belief in spirits, visible or invisible, has held sway.

Close consideration of the voluminous literature of apparitions, as well as attention to one's personal experience, soon reveals certain facts which are applicable to all stories of ghostly visitants. In the first place some of these stories are clearly of the fake or fraudulent sort, of which it is hardly worth while to give examples.

The newspaper story of six mischievous boys arrayed in white, along a cemetery wall near one of our suburban towns, who affrighted several youngsters and female pedestrians, but were ignominiously routed by a detail of police from a nearby station, is one of the crude sort.

In others a hysterical young woman is usually prominent who startles friends and neighbors by ringing doorbells, breaking furniture and otherwise disturbing the night.

I presume that there are few who could not recite unpublished tales of apparitions.   I have myself a growing collection of ghost stories.

My colored chauffeur in reply to my query as to whether he had ever seen a ghost, replied that he was not quite sure, but he thought possibly he had seen the spirit of his grandmother.   His story was that shortly after the death of the said grandmother he had been sleeping with two brothers in the room formerly occupied by the old lady.   Just as he was passing into the sleeping state he heard a rattling at the window of the room, which opened on a porch. He saw the window raised and a form stepped into the room and over to the foot of his bed.   He said she grew bigger and bigger and uglier.   As the features of his grandmother grew he gave a shriek which wakened his sleeping brothers and gave the untimely visitor a chance to escape—for on awakening none of them could see their relative from the other world.

On questioning the man as to the garb in which his grandmother appeared, he said he was not quite sure but thought it was something like the white stuff which they show in the ghost pictures at the "movie" exhibitions.   Whether he saw a ghost or not, he told me

very emphatically that he never slept in the room after that night
and never proposed to do so again.

One of my distinguished friends, who is a cautious believer in
spiritualism, told me a story, which I do not think has been pub-
lished, about a ghost which appeared one night to a well-known
financier and philanthropist of Philadelphia. The gentleman came
from Europe on a liner, accompanied by a military officer, and both
had been invited to be the guests of a New York friend of the latter.

Shortly after the financier had retired he saw near his bedside
a beautiful woman, but on his rousing from sleep the visitant had
disappeared. The next morning on entering the drawing-room the
first thing that met his gaze was the full-length portrait of a beautiful
lady, who he said at once was the visitor of the night before.

During the next day he told this story to his military friend, who,
somewhat startled, remarked that it was extraordinary, as he had
had the same visitation on the same night.

The relater of this story was apparently impressed with the
evidential character of this ghostly yarn. It would not, however,
bear full examination. In the first place the military man had been
a close friend and admirer of the former wife of their host. What
could be more likely than that in the disturbed sleep of this gentle-
man the visitation should have occurred, and in the second place,
what more likely than that the other party to the drama should
have interpreted the picture into his dream rather than the dream
into the picture?

Omitting the plain cases of fraud or fabrication and the instances
of purely literary handiwork, the ghosts which remain are best
explained on the theory of hallucination. In saying this I do not
mean to refer to those cases of visions and voices occurring among
the recognizably insane, of which every alienist could produce
many instances. It is significant, however, in discussing our
subject to remember the intensity and certainty which these appear-
ances and auditive phenomena have in the delusional mind.

A careful consideration of ghost stories which have come to my
direct knowledge, or which have been read in the now enormous
literature of the subject, shows that a large percentage of the
experiences recorded have occurred in the period preceding deep
sleep or in the aftermath of such sleep—in other words, in the pre-
dormitium or post-dormitium. Not only have we a well-marked
predormitium and postdormitium but also what might be called
an intradormitial period in which sleep becomes shallow without
the occurrence of waking.

Under the head of disorders of sleep many interesting physical
as well as psychical phenomena have been described by Weir
Mitchell[2] and others as occurring in the time preceding or following

[2] Some Disorders of Sleep, Am. Jour. Med. Sc., August, 1890, N. S., vol. c, pp.
109–127.

profound slumber, and these, of course, may also occur in an intradormitial period. The probability is that when one is really plunged into deep, natural sleep no dreams occur, although apparitions may be present in the profoundly somnolent state of those who are suffering from toxemia or injuries of the head.

The evidence is fair that visual, auditory and other sensory hallucinatory dreams are as much a mark of disordered cerebral action as are such well-known phenomena as waking numbness, sleep paralyses and sleep clonisms. Time will not allow me to go into a discussion of these phenomena, in connection with which I could readily draw from my own neurological experience as well as from the writings of my colleagues.

In all probability the story told by a prominent clergyman of the visit from the spirit world of his former wife, who sat on the edge of his bed and revealed to him the place of concealment of a certain pen and papers for which he had long sought in vain, belongs in the category of predormitial dreams or hallucinations.

I was interested in reading one of the popular volumes of ghost stories by a woman evidently of considerable literary ability, to note how many of the ghosts which she had seen had come to her in haunted rooms and houses just before she passed into the full sleeping state. If we acknowledge that the insane can have vivid and impressive hallucinations which are fully believed in, and that the normal can have these in the state preceding and following deep sleep, it is not at all difficult to understand that persons of certain temperaments or constitutional tendencies, the so-called psychics of our ghostly literature, may have such appearances at any time. They are at all times cerebrally attuned for the reception of such impressions.

Consideration of occultism with particular reference to spiritualism would scarcely be complete without some discussion of mediums and mediumistic communications, including trance phenomena, table-tipping and automatic writing. The last phase, however, I will leave entirely to my psychological colleagues. It would be hardly worth while to encumber this presentation with any review of the voluminous literature of the subject, past and recent. I will simply refer to a few personal experiences, and very briefly, to Sir Oliver Lodge's *Raymond*.[3]

In the earlier years of my professional life, halcyon days of investigation not to be forgotten, I was deeply interested in hypnotism, and to a much less extent in questions like spiritualistic communication and telepathy. Regarding hypnosis I became convinced of the possibility of its production in one's self or in another. I entered upon the study of the phenomena of hypnotism stimulated by the then recent writings of Charcot and his school,

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[3] Lodge, Sir Oliver: "Raymond," New York, George H. Doran Company, 1916.

with a view especially of clarifying my ideas on hysteria. My studies in so-called spiritualistic communications were far less extensive and rather along side lines of interest.

I became an infrequent attendant upon spiritualistic assemblies and occasionally took part in a so-called seance. I well remember certain gatherings in an old church on North Eleventh Street, where after we had listened to feeble renderings of " Nearer, My God, to Thee," or " Greenland's Icy Mountains," or some similar well-known religious refrain, one or more mediums, fat or fragile, sleek or frowsy, appeared on the platform. Usually after going through a series of extraordinary gurglings and gaggings, poses and contortions, these mediums passed into a real or bogus trance, during which, in somewhat incoherent and usually ungrammatical English, they delivered voluble messages from the " other side," with the assistance of the "Moonstones," " Red Feathers," "Fedas," "imperators, rectors, doctors or mentors— " or whatever names then held the mediumistic control field.

I was soon convinced that these exhibitions were vulgar frauds. These open meetings acted as feeders or advertisements of seances privately held and for a definite and often a considerable charge.

> "And not for nothing these gifts are shown
>   By such as delight our dead,
> They must twitch and stiffen and slaver and groan
>   Ere the eyes are set in the head,
> And the voice from the belly begins.   Therefore,
> We pay them a wage where they ply at En–dor."

I can take time to recall only one or two seances which took the form of " table-tippings," or at least attempts at these phenomena. They serve to indicate my own views and the views of others as to their nature. On one occasion, the medium being a well-known author of novels or stories of Indian life, which appealed to the imaginative views of that time, several of us gathered around the table, the medium sitting opposite the center of the group. Attempts were first made, without any great success, to call up the spirits of some of our departed friends or relatives. I remember that my grandfather was sadly misrepresented as to the time, place and manner of his death.

As we sat around the table, our fingers lightly but firmly touching it, no effect upon the obdurate table became visible, but after a few minutes I noticed that the face of one of my friends had assumed a somewhat dreamy or foolish appearance and that his right hand began to make peculiar rotary movements, at first · slow but gradually increasing in rapidity and amplitude. At once it struck me that he was passing into a unilateral hypnotic state, such as I had studied in one of my patients at the Philadelphia Hospital. I grasped his right arm and placed his hand on his head, remarking that he could not remove it, which he could not or did not. I then

put his head and upper extremities into various positions, where they remained in a cataleptoid state, until with a few strokes and a command I restored him to his usual condition.

In these early days two of my professional friends, both of whom became men of distinction in their chosen lines of biology or medicine, began to hold seances of their own after the manner of the table-tippers. I attended one or two of their exhibitions, one of these being before a medical society. No so-called medium was present, but the exhibitors placed their hands and fingers as in the table-tipping experiments. Their faces soon assumed an abstracted look. The obdurate table, as in my former experience, again refused to respond by tipping or other movement, but not so the experimenters. In a short time a tremulous movement took possession of the hands of one of them. This soon became a twitching. The movements extended up the limbs to the trunk, and after a brief interval the whole body of the participator was thrown into convulsive movements, these, in one instance, being so severe as to cause the exhibitor to be involuntarily thrown from his chair.

To my mind there is a distinct point in this recital which has to do with the explanation of the manner in which table-tippings and movements of a similar kind are brought about. Michael Faraday and others, but none of higher rank, have asserted their belief that such table-moving phenomena are due in some way to the exercise, sometimes unconscious, of muscular activity on the part of those seated around the table. The same concentration or abstraction of attention which could induce the hypnotic phenomena which I have just described might and sometimes does bring about such muscular action. I know it is said that the tables at seances at times continue to move after the removal of the hands which have started them. Most of these reports lack sufficient foundation, and even if correct may perhaps be explained by some sort of fraud.

As I have only space in this connection to refer to one or two other matters, let me turn for a moment to Sir Oliver Lodge's *Raymond*. I read this book, as I have other writings of Lodge, with the hope of obtaining some idea of the ground on which this physicist and philosopher stands. The first part of *Raymond*, which dwells upon the early life and soldier experiences of his gallant son, is full of interest and naturally appeals to the sympathies of those whose hearts go out toward the thousands of families who have been bereaved during the recent war.

In the third part of his book he deals with theoretical considerations and the explanation of spirit communications. While written in a scholarly manner it is simply another exposition by a man of literary ability of the old dualistic theory of spirit and matter. It is about as convincing or unconvincing, according to one's previous point of view, as Sir Oliver's lectures in this country, one of which I attended.

In the second or middle portion of his book *Raymond*, Sir Oliver deals with the mediumistic communications which he and Lady Lodge and other members of his family were supposed to have had with Raymond, talking to them from the "other side" through a medium and control. The gullibility with which he swallows the communications of such proved fakirs as these London mediums reminds me more than anything else of my old friend the distinguished Philadelphia surgeon, to whom I referred in the preceding portion of this paper. Some of the data obtained by Lodge or members of his family are marked as "non-evidential" and others as "evidential," although close scrutiny of all would without much difficulty place them in the former group. I will give but one example, although others might easily be brought forward.

Sir Oliver records that on one occasion, at a table-sitting, he asked Raymond what the boys had called him and he replied PAT, which was quite right. Sir Oliver then asked Raymond if he would like to give the name of a brother, and he replied NORMAN, which Sir Oliver thought was quite wrong. Then Raymond amended the name to NOEL, which was accepted as correct, as applying to his brother Lionel.

About two weeks later another medium, being alone, had some automatic writing in which Raymond said: "Please listen carefully now I want to speak to you about Norman. There is a special meaning to that because we always called my brother Alec Norman." Two days later Sir Oliver and Lady Lodge had another table-sitting, at which the writing medium was also present, and Sir Oliver said to Raymond: "Do you want to say something more about that name 'Norman'? You gave a message about it to Mrs. K., but I don't know whether she got it clearly." The reply spelt out was I TOLD HER THAT I CALLED LIONEL, on which Mrs. K. said she was afraid she often got names wrong and supposed she had got the name of the wrong brother.

Sir Oliver, commenting on these communications, says that it appeared "Norman" was a kind of general nickname applicable to almost any one of Raymond's brothers, especially used when they played hockey together, although Sir Oliver and Lady Lodge were not aware of the nickname at the time of the sittings which he reports. There is more about "Norman" and hockey, but the gist of the matter is that Raymond in his communications speaks of this name "Norman" as applicable to two different brothers.

Sir Oliver with great solemnity states that he could testify that he was not aware that a name like Norman was used, nor was Lady Lodge. Assuredly it is extraordinary how these communications could be swallowed whole as "evidential." During certain phases of the Great War few families in England were better known to the readers of newspapers, illustrated and otherwise, than that of Sir Oliver Lodge. The shrewd London fakirs who ran the "medium

mills" no doubt acquainted themselves with all available facts regarding the Lodge family, as many of their kind always do, and one can easily understand how they might, through conversation or otherwise, have learned of this nickname "Norman."

I well remember with regard to one of my boys how I was suddenly made acquainted with the fact that he was known to a number of his college and athletic friends by a nickname of which I had never before heard, although he had undoubtedly carried it for a year or two. If at a spiritualistic seance I had happened to get a communication from the "other side" about him under this nickname I would certainly have been for a time somewhat confused as to the identity of the individual referred to, although in my temper of mind it would have taken a good deal more than this mediumistic communication to convince me that it was evidence of spirits.

REVIEWS

A TEXT-BOOK OF PATHOLOGY. By WILLIAM G. MacCALLUM, M.D., Professor of Pathology and Bacteriology, Johns Hopkins University. Second edition, thoroughly revised. Pp. 1155; 575 original illustrations. Philadelphia and London: W. B. Saunders Company.

THIS unique text-book of pathology has been carefully revised by the author, with the inclusion of much new matter developed by the exigencies of war, and particularly on the infectious diseases, including those caused by animal parasites, wounds, the effects of poisonous gases and the results of malnutrition. The author has summarized this new work by inserting paragraphs or by rewriting whole chapters.

The sections on shock, acid base equilibrium, hydrocephalus, immunity in tuberculosis, meningococcal infections, pneumonia after measles, influenza, cholera, leprosy, etc., have been rewritten in large part on the basis of the author's own experience. Parasitic diseases are treated in greater length because of their wider recognition and importance.

The illustrations of this valuable work are superb and a great improvement over those commonly found in text-books; in this edition several new ones have been included.

The book is now well and favorably known and constitutes a refreshing and in many respects a remarkable departure from the style of systematic text-books on pathology. It is particularly valuable for the practitioner; from the student standpoint it is lacking in certain fundamentals, which, however, may be easily supplied by lectures and works of reference.   J. A. K.

ZIEGLER'S GENERAL PATHOLOGY. Revised by DOUGLAS SYMMERS, M.D., Director of Laboratories, Bellevue and Allied Hospitals of New York. From the eleventh revised German edition. Pp. 594; 604 illustrations. New York: William Wood & Co., 1921.

THIS standard text-book has been revised to meet primarily the needs of the medical student while preserving its usefulness as a

convenient reference for the practitioner. The revision by Dr. Symmers appears eminently satisfactory, and he has taken advantage of the opportunity of making many changes in the text and illustrations with the introduction of considerable new matter. The general arrangement of the book, which has proved so satisfactory from the standpoint of both teacher and student, has not been disturbed. There is, however, considerable room for improvement in references to literature, and the value of the book could be considerably enhanced by including a table of contents.

<div align="right">J. A. K.</div>

THE AMERICAN YEAR-BOOK OF ANESTHESIA AND ANALGESIA, 1917–1918. F. H. McMECHAN, A.M., M.D., EDITOR. Pp. 483; many illustrations. New York: Surgery Publishing Company, 1921.

THE year-book on anesthesia and analgesia for 1917–1918 presents in a volume of 483 pages a well-edited review of the papers of nearly one hundred authors on the various phases of this branch of medicine and its related problems. These papers are arranged in sections dealing with the subdivisions of anesthesia and the topics pertinent to them.

A collection of twenty papers on the methods of anesthetization used during the war, both in the battle zone and in base hospitals, furnishes a most interesting and instructive review, and describes all the worth-while advances of anesthesia and analgesia in the surgery of the war.

The many meritorious papers on the pharmacological, physiological and pathological aspects of anesthesia illustrate well the large amount of attention and investigation which this branch of medicine is receiving. As the principles elaborated in these studies are closely concerned with the clinical application of anesthetic agents they become as significant and valuable to the surgeon as to the anesthetist.

The special methods of anesthesia and analgesia are fully covered. The specialist in almost any branch of surgery will find here a recapitulation of the advances in anesthesia of definite advantage and import in his work. The section on anesthesia, both local and general, and analgesia in obstetrics is deserving of particular mention. Besides an index to the text, a very complex index of all literature on anesthesia and analgesia for the years 1917–1918 is included.

Barton likens anesthesia to "a game of skill in which chance also figures to some degree." A study of this year-book will tend to eliminate chance in favor of safety in anesthesia.

<div align="right">P. F. W.</div>

DIE THERAPIE AN DEN BONNER UNIVERSITÄTSKLINIKEN. By
PROF. DR. RUDOLF FINKELNBURG, in Bonn; Dritte, vermehrte,
Auflage, Bonn. A. Marcus & E. Weber's Verlag.

THIS paper-bound volume is one of the many German works
now rapidly coming to this country after the war. It presents
the therapeutic methods used in the clinics at the University of
Bonn. Every phase of medicine is covered in a brief, somewhat
outlined style. The preface promises in this third edition the
inclusion of methods consequent upon war experience as they
have been found useful at Bonn.

A rather careful search gives one the impression that the Allied
advance in therapeusis has been a much more extensive one than
that of the Germans. The therapeutic sheet anchor for the German
internist, as it seems to be for all European physicians, remains
in the natural springs and their waters. Much is promised for
the various cures. Many of the newer synthetic preparations are
used and advocated in various conditions. Treatment is for the
most part along conservative lines. Many of the newer proved
practices in this country are not included. Perhaps they have
not filtered in with those Bonn clinics.

This volume still continues to show the pre-war spirit of German
medicine, a spirit that never decided anything to be worth while
unless it was of Teutonic origin. American medicine when it
appeared on the Allied fronts, even though it began with almost
a three-year handicap, suffered nothing by way of comparison
with medicine of Europe. T. G. S.

THE PRINCIPLES OF THERAPEUTICS. By OLIVER T. OSBORNE,
M.A., M.D., Professor of Therapeutics, Department of Medicine,
Yale University. Pp. 881. Philadelphia and London: W. B.
Saunders Company, 1921.

WHEN the reviewer prepared to review this volume, he antici-
pated a profitable but rather uninteresting evening. To sit down
and go over carefully a book on therapeutics, does not seem alto-
gether the most agreeable method of passing one's leisure hours.
To read over the action of drugs, some of which are never used and
rarely heard of, and to look over pharmaceutical data, does not
seem particularly interesting. But, on the contrary, only the first
few pages of this book were scanned when the reviewer became
intensely interested, and before he knew it the hour was late and the
book had been reviewed partially in the rapidly fleeting hours.
The reviewer does not know when he has studied such an interesting,
well-written book.

While upon a rather trying subject the material is presented in an extremely individualistic style, which stamps the author not only as one well able to impart what he knows, but also marks him as a man of good common sense, and incidentally one very much of a philosopher.

Osborne has divided his book into fifteen parts. These fifteen parts contain not only a thorough discussion of valuable and useful drugs, vaccines and serums, practical therapeutic measures, treatment of emergencies and various other related studies, but he also has a section on practical advice to young physicians, medical ethics, and related subjects.

The reviewer has sung the praises of the book sufficiently to indicate how much he has appreciated it. A word of criticism may possibly be not amiss. In a book which is for the greater part filled with such clean, clear-cut, definite instruction and advice it does not seem rational for the author to have spent so much time and to have given so much space to the hazy endocrines, nor to have suggested quite so frequently the use of a drug, calcium, about the pharmaceutical action of which we know relatively little.

<div align="right">J. H. M., Jr.</div>

A PRIMER FOR DIABETIC PATIENTS. By RUSSELL M. WILDER, PH.D., M.D., MARY A. FOLEY, Dietitian, DAISY ELLITHORPE, Dietitian. Pp. 76; W. B. Saunders Company, Philadelphia and London, 1921.

THIS little book is a brief outline of the principles underlying the dietary treatment of diabetes. It emulates in spirit the somewhat larger and therefore more detailed *Diabetic Manual* of Joslin. The word "primer" is a very apt and relatively descriptive term as applied to this volume. It should be another book "to help make the home safe for the diabetic."   T. G. S.

HORDER'S MEDICAL NOTES. By SIR THOMAS HORDER, M.D. (LOND.), F.R.C.P. (LOND.), Physician with Charge of Outpatients to St. Bartholomew's Hospital. London: Henry Frowde Oxford University Press: Hodder & Stoughton, 20 Warwick Square, E. C. 4.

THIS small book of one hundred and eleven pages is a very unusual little volume. It is a collection of remarks let fall by the author in the out-patient room and in the wards of old St. Bartholomew's Hospital. These remarks are for the most part brief notes; some of them trite; some of them dogmatic; yet all of them are golden and intensely stimulating.   T. G. S.

THE MEDICAL CLINICS OF NORTH AMERICA. New York Number. Vol. IV. Pp. 1637; Philadelphia and London: W. B. Saunders Company, March, 1921.

THE March number of The Medical Clinics contains some very interesting case reports by prominent clinicians of New York City. In all, there are nineteen authors who have contributed to this number. The articles are well presented, and deal with conditions and diseases which are of unusual interest for the most part. The clinic of Dr. Longcope and that of Dr. Mosenthal seem particularly timely to the reviewer. Dr. Geyelin and Dr. Rosenthal also add two very valuable contributions. Dr. Draper, as always, writes very interestingly, but seems to delight in wandering off from the beaten track into the vague mazes of diseases of the endocrines.

J. H. M., JR.

HISTORY AND BIBLIOGRAPHY OF ANATOMIC ILLUSTRATIONS. By LUDWIG CHOULANT; translated and edited by MORTIMER FRANK, B.S., M.D., late attending Ophthalmologist, Michael Reese Hospital, Chicago. Pp. 435; 100 illustrations. Chicago: University of Chicago Press, 1920.

THIS is a book which everyone interested in anatomy must wish to possess. It is a fascinating study of anatomic illustration, a history of anatomy in pictures, and will be of unfailing interest. From the crude drawings of the thirteenth century to Rembrandt's well-known anatomy lesson is an instructive survey of human development and advancement. It seems hardly credible that the misshapen and grotesque efforts of the early illustrators were made by beings of the same race as the beautiful and correct drawings of da Vinci, of Jan van Calcar, the illustrator of Vesalius, and of H. V. Carter, the illustrator of Gray.

This grouping of the illustrator's art serves again to point out the great advance which was marked by the appearance of the Vesalian treatise. Short biographies being given, one may easily pass from century to century, and Dr. F. H. Garrison's note in the appendices brings us down to our own day and Professor G. A. Piersol's *Anatomy* with its excellent illustrations by the Fabers.

Since Choulant's day, the whole field of microscopic anatomy has opened, and it is strange to think that he was one of those who bitterly opposed the introduction of pathologic anatomy.

Dr. Frank's translation, so carefully edited and annotated, is a noteworthy achievement. We only regret that he did not live to enjoy the success and appreciation which his work has gained. The University of Chicago issues this edition as "The Mortimer Frank Memorial." In it a difficult and little known book has been made easily accessible.

W. H. F. A.

THE DISEASES OF THE NEWBORN. By DR. AUGUST RITTER VON REUSS, Assistant at the University Children's Clinic and Director of the Department of the Newborn at the First University Women's Clinic in Vienna. Pp. 626; 90 illustrations. New York: William Wood and Company, 1921.

DR. VON REUSS has written a book that considers separately the first period of infancy. This division into a separate specialty is a new idea for America, and is probably only carried out in the clinic of which the author is director. The period of the newborn is usually considered as terminated when the umbilical stump is sloughed. Here it is extended beyond this time, or until the initial weight loss has been recovered and the weight of the infant corresponds to the weight at birth. It is claimed that it is not until this time that the mechanism of the infant has adjusted itself to the different mode of existence. After this time begins the period of infancy. The book is well written and sensibly published in English. It should be of value to obstetricians and pediatrists, as well as to others having the care of new babies. While books on obstetrics and pediatrics usually devote some space to the consideration of this epoch of child life, space does not permit of the detail and elaboration that has been possible in this work. Medical literature has been thoroughly searched for additional information. Authorities are quoted in the text, and the references are given in the bibliography at the end of the volume. The original publication in German was in 1914. It is to be regretted that the present publishers did not have the references brought up to date and edited into the text. A. E. S.

TRANSACTIONS OF THE AMERICAN PEDIATRIC SOCIETY. Volume XXXII. Pp. 353; 23 illustrations. Edited by DR. OSCAR M. SCHLOSS, 1920.

THIS volume comprises the report of the thirty-first annual meeting of the American Pediatric Society, which was held at Highland Park, Illinois, May 31 to June 2, 1920. Sixty papers were presented before the society of which thirty-nine are published in this book. The discussion aroused is printed with each paper; many and varied phases of pediatric thought were covered by these reports, all of which represented either the results of clinical observation or laboratory investigation. Many of these article have appeared in the current medical periodicals and the others will doubtless be made available to the profession in the same manner. In addition to the report of the scientific program the minutes give the names of the members in attendance, the report of the executive session, as well as lists of officers, members, meeting places and other information of the activities of the society. A. E. S.

EDEMA AND NEPHRITIS.   By MARTIN H. FISCHER, M.D., Eichberg
   Professor of Physiology in the University of Cincinnati.   Third
   edition.   Pp. 922; 217 illustrations.   New York: John Wiley
   and Sons, 1921.

IN 1915 the author published in a composite second edition his
1909 Nathan Lewis Hatfield prize essay of the College of Physicians
of Philadelphia, entitled "Edema, a Study of the Physiology and
Pathology of Water Absorption by the Living Organism," with his
1911 Cartwright prize essay of the Association of the Alumni of the
College of Physicians and Surgeons, Medical Department of Col-
umbia University, New York, entitled, "Nephritis, an Experimental
and Critical Study of its Nature, Cause and the Principles of its
Relief."   This second edition contained additional evidence to
substantiate the author's iconoclastic theories promulgated in the
original monographs and calculated to calm the storm of adverse
criticism.

The present, third edition includes the original monographs
unaltered together with a more detailed colloid chemical study of
edema and nephritis. The author still more vehemently insists upon
the lack of relationship between the so-called symptoms, signs and
complications of nephritis and actual disease of the kidney and
unequivocally gives infection as the cause of vascular disease and its
consequences, including chronic interstitial nephritis.

Whatever view is taken of the validity of the theories presented,
much information of practical value to the physiologist, pathologist
and practitioner can be obtained and, on account of the logical
arrangement of the text, with a minimum of effort.   The author has
followed his customary method of abstracting the entire volume
under the caption "The Argument," so that the general principles
may be gleaned in a short time.   The more detailed discussion and
the experimental evidence of the text and body are referred to by
page number in the argument.

The appendix contains an excellent practical summarization of
the knowledge concerning the relation of mouth infection to sys-
temic disease.   The book closes with a classification of the nephri-
tides apparently as unorthodox as the author's theory of edema
appeared in 1909.

That the author's polemic tone and his sarcastic contempt for his
critics, so evident in the second edition, have not been softened, is
shown in the preface which states, "It is an ironic fact that I can
cite today as best proof for the correctness of the general notions
for which I have pleaded for more than a decade the observations
of the very workers who have been most violent in their criticism
of what I have written.   The colloid-chemical notions of water
absorption by protoplasm with their many physiological and patho-
logical corollaries, so long a jest, are now embodied by those workers
in their scientific discussions as self-evident truths in which the

original sponsor needs never to be mentioned. High commissions
find alkali, glucose and colloid injection mixtures the chief things
of service in shock; surgeons suddenly discover that their bad
operative risks are 'acidosed' and that food and alkali may save
them; while those who thought the acid content of the living mass
an unchangeable value are running about their wards with respira-
tion bags and hydrogen ion determinators."

That circle of scientists known as colloid chemists, of which the
author is a recognized leader, is so small that very few persons are
competent to give authoritative criticisms of his theories. Though
the clinician, the physiologist, the pathologist, the chemist, is not
convinced of the validity of the theories, he cannot deny that Pro-
fessor Fischer's work is an emulable model of logical arrangement
of the data and deductions from a masterful scientific research
covering a period of more than a decade.   W. H. S.

THE HEALTH OF THE INDUSTRIAL WORKER. By EDGAR L. COLLIS
    and MAJOR GREENWOOD, containing a chapter on Reclamation of
    the Disabled by ARTHUR J. COLLIS, with an introduction by SIR
    GEORGE NEWMAN. Pp. 450. Philadelphia: P. Blakiston's Son
    & Co.

THIS book, although written by Englishmen, has as wide an appeal
to Americans as it has for the author's own countrymen. The sub-
jects under discussion are international in scope and the character
and conditions of employment in England and America are so nearly
identical that what applies to one country applies also to the other.

The section on industrial fatigue, dealing as it does with the length
of working day, seems very apropos in view of the widespread dis-
cussion on this subject that is going on all over this country at the
present time. The question is dealt with from a scientific rather
than an economic standpoint, but an effort is made to show that in
this instance science and economics go hand in hand.

The incidence of morbid states with industrial conditions is shown;
a large part of the book being devoted to this purpose. The close
association of unhealthy working conditions with tuberculosis,
cancer, diseases of the female genitalia, and the general health of the
workers is brought out in a series of chapters that go into the matter
very exhaustively. Statistics are used in an effort to prove their
contentions in a very extensive and intricate way, so much so at
times that it seems as though one would have to be an expert statis-
tician fully to understand them.

The questions of home diet and food at the factory; the effect of
alcohol on health and efficiency; ventilation, lighting and sanitary
arrangements; labor turnover; methods of maintaining and improv-

ing the health and efficiency of the individual employees; and the reclamation of disabled workers are the subject that are fully and satisfactorily covered in this work.

The bibliography is complete and conveniently placed at the end of each chapter.   S. J. R.

SCURVY PAST AND PRESENT. ALFRED F. HESS, M.D., Clinical
    Professor of Pediatrics, University and Bellevue Hospital Medical
    College, New York City. Pp. 279; 25 illustrations. Philadel-
    phia: J. B. Lippincott, 1920.

HESS has compiled an instructive and interesting volume com-
prising a complete review of the literature and scientific studies
made on scurvy. The historic sketch is of value as showing how very
recently knowledge of this disease has become generalized. One
might state that a definite recognition of this disease only dates
back over the last twenty to thirty years; before this time but few
observers were able to differentiate this affection from the other
hemorrhagic diatheses. One cannot but be impressed with the lack
of recognition of the means of prevention and to even a greater
degree to the lack of adaptation of proved preventive measures.
Prevention has become still more complicated by that compara-
tively newly recognized group of food essentials, termed "vitamines."
According to the author, "It has become increasingly evident that
the attention of physiologists and clinicians has been focussed too
sharply and too narrowly on the caloric value of foodstuffs." Study
has proved that our former dependence was correct, that a small
amount of orange or lemon juice is essential for the eradication or
prevention of scurvy. These dietetic articles are not alone curative
or preventive, but there are others almost equally effective, such as
a moderate quantity of fresh cabbage, raspberries and canned
tomatoes. Other foods in large quantity, such as milk and fresh
uncooked meats, have definite preventive qualities.

The subject is discussed under the following headings: History
of scurvy; pathogenesis and etiology; the antiscorbutic vitamine;
pathology; experimental scurvy; antiscorbutic foods; symptomatol-
ogy and diagnosis; prognosis; treatment; metabolism; relation of
scurvy to other diseases.

The volume can be recommended to amplify a not too well known
disease.   F. C. K.

PROGRESS

MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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Visceral Syphilis.—WILE (*Arch. Dermatol. and Syphilol.*, 1921, iii, 117 and 122). *Syphilis of the Spleen:* In the early stages of acquired syphilis splenic involvement is indicated by an acute splenomegaly, frequently symptomless, occurring coincident with the general lymphadenitis. WILE and ELLIOTT determined its presence by palpation in over 35 per cent. of their cases of early syphilis and feel that it probably represents the earliest syphilitic visceropathy. In only one case was the presenting symptom severe abdominal pain referable to the spleen. Of 36 cases 19 presented themselves with soft spleens, the remainder showing firm tumors. Usually under treatment the tumor rapidly decreases, and pain, if present, disappears. In a few cases, however, the splenomegaly persisted, the condition changing from an early syphilitic hypertrophy to a chronic interstitial splenitis. In the later stages of syphilis splenic involvement is rare and occurs as (1) chronic interstitial splenitis, (2) gummatous splenitis and (3) amyloid disease. Chronic splenitis is most frequently found associated with syphilitic disease of other viscera (liver, kidney, etc.), and except for the increase in size of the organ the condition possesses no clinical characteristics. It seems most likely to the author that syphilitic anemia, sometimes found in association with syphilitic splenomegaly, is due to bone-marrow changes rather than the splenic involvement, since the anemia also occurs in cases of syphilis without demonstrable splenic changes. Gummatous splenitis is common in congenital syphilis but exceedingly rare in the acquired disease. Two pathological types have been noted: (1) A diffusely enlarged spleen with palpable gummatous nodules, and (2) miliary gummas. The first form may be recognized clinically by palpation. Amyloid disease of the spleen can be clinically recognized

in the presence of evidences of the condition elsewhere, and a positive Wassermann reaction. However, amyloid disease due to syphilis is a pathological rather than a clinical entity. *Syphilis of the Pancreas:* While common in syphilis of the newborn, clinical syphilis of the pancreas in the acquired form is one of the rarest of syphilitic visceral manifestations. From a pathological standpoint Warthin believes that chronic interstitial pancreatitis is one of the most frequent visceral lesions found in latent syphilis. The condition may occur either as a gummatous pancreatitis or an interstitial pancreatitis or as a combination of the two. The symptoms are not pathognomonic. The author feels these points are suggestive of syphilis when the pancreas is the site of the disease: jaundice without other cause, glycosuria and pancreatic tumor without cachexia. The therapeutic test is the most efficient diagnostic aid.

Studies on Measles.—Blake and Trask (*Jour. Exp. Med.*, 1921, xxxiii, 385 and 413). Of seven monkeys receiving intratracheal injections of unfiltered nasopharyngeal washings from cases of measles in the preëruptive and early eruptive stages of the disease, five developed symptoms closely simulating those of the disease in man. Similar symptoms were induced in one monkey by inoculating the nasal and buccal mucous membranes with unfiltered washings and in two other monkeys by the intratracheal inoculation of washings which had previously been passed through Berkefeld N filters. The characteristic group of symptoms which follow the inoculations was successfully carried through six passages by intratracheal injection of saline emulsions of the skin and buccal mucous membranes of monkeys killed from two to six days after the onset of the reaction. From the fourth passage monkey the reaction was successfully induced in three monkeys by the transfusion of citrated whole blood. Blood cultures were negative. The symptoms induced were constant and definite, the only conspicuous difference between the experimental disease and human measles being the absence of respiratory symptoms in the former. Moreover, histological examination of the lesions of the skin and buccal mucosa revealed no essential differences in the two conditions. The conclusion is drawn that monkeys (*Macacus rhesus*) are susceptible to inoculation with the virus of measles.

Experimental Studies on the Nasopharyngeal Secretions of Influenza Patients.—Olitsky and Gates (*Jour. Exp. Med.*, 1921, xxxiii, pp. 125, 361 and 373). These investigators communicate, in a series of three papers, the results of their studies at the Rockefeller Institute on influenza. Their work to date may be summarized as follows: (1) An active transmissible agent present in the nasopharynx in early cases of influenza produces characteristic clinical and pathological effects in rabbits and guinea-pigs (fever, leukopenia, lung hemorrhage, edema and emphysema). This active substance disappears or diminishes in the nasopharyngeal secretions of cases of epidemic influenza early in the disease and seems to be absent in healthy persons and in other pathological conditions. (2) This agent passes through a Berkefeld filter and the filtered material produces the same effect in experimental animals as the unfiltered material. The agent withstands the action of glycerol 50 per cent. for periods up to nine months (thus resembling

the virus of poliomyelitis, smallpox, etc.). (3) Concurrent infections occurred in the experiments described and are regarded as accidental. Experiments were performed which indicated that the presence of the "influenzal agent" in the pulmonary tissue encouraged the invasion of the lung by ordinary bacteria such as the pneumococcus, streptococcus and Bacillus pfeifferi. In no instance did death occur in rabbits as the result of the uncomplicated effects of the "influenzal agent." When death occurred there was always present infection of the lungs by ordinary bacteria (pneumococcus Type IV and atypical Type II, streptococci and hemoglobinophilic bacilli, etc.).

Focal Infection and Selective Localization on Streptococci in Pyelonephritis.—Bumpos and Meisser (*Arch. Int. Med.*, 1921, xxvii, 326). In a study of six patients with pyelonephritis and dental sepsis the authors have attempted to ascertain by the intravenous injection of the Streptococcus viridans obtained from the teeth whether or not there exists a relationship between the two conditions. The technic of Rosenow was employed and 27 rabbits were injected with the primary cultures. At autopsy 24 of these had lesions in the kidneys, 8 in the bladder, 4 in the muscles, 3 in the stomach, 3 in the endocardium, 2 in the myocardium and 4 in the joints. The extra-urinary lesions were relatively slight in each instance. On subsequent animal passage of these strains this affinity for the urinary tract was shown to decrease. The conclusion is arrived at that ."pyelonephritis may often be due to focal infections harboring streptococci which have a selective affinity for the urinary tract and that the colon bacillus which is commonly found and generally believed to be the cause, is of secondary importance.

The Cause of So-called Idiopathic Hydrocephalus.—Dandy (*Johns Hopkins Hosp. Bull.*, 1921, xxxii, 67). It is recalled that until recent years all cases of hydrocephalus were considered to be idiopathic. It seems certain now that one group of these cases has, as its underlying pathology, lesions occluding the ventricular system (obstructive hydrocephalus). The present communication deals with human experimental cases of so-called communicating hydrocephalus in which free communication was proved to exist between the ventricles and subarachnoid space, and an attempt is made to "correlate all the anatomical variations of communicating hydrocephalus into a single disease with a fundamentally similar pathology." Extracts from the author's summary and conclusions follow: The cerebrospinal fluid circulates in a closed vascular system. This is just as well defined as the vascular system for blood, lymph, bile or urine. In the ventricular system the fluid is produced but not absorbed; nearly all the cerebrospinal fluid is absorbed in the cerebral sulci (to which it passes from the ventricles via the cisternæ). Collateral circulation is almost precluded either in the ventricles or in the cisternæ. An obstruction in these spaces, therefore, results in hydrocephalus—if the obstruction is situated in any part of the ventricles an "obstructive" type of hydrocephalus is produced; if it is situated in the cisternæ or in the main branches of the cisternæ a "communicating" type of hydrocephalus results. That the latter type of hydrocephalus is due to obstruction in the cisternæ or their main branches is demonstrated by its experimental production in animals and by the demonstration of such an obstruction in living patients by

cerebral pneumography. Adhesions, which follow meningitis and occlude the cisternæ, cause the vast majority of cases of communicating hydrocephalus, although in two cases cited the condition seemed to depend upon a congenital failure of the cisternæ or of its branches to develop. Brain tumors may also be a cause.

Experimental Inoculation of Human Throats with Avirulent Diphtheria Bacilli.—Moss, Guthrie and Marshall (*Johns Hopkins Hosp. Bull.*, 1921, xxxii, 37). The authors summarize the results of their extensive investigations as follows: " (1) The carrier state was easily produced in human beings by inoculation of the throat with avirulent diphtheria bacilli. (2) When thus produced the carrier state lasted for a long time, two of the carriers still harboring avirulent diphtheria bacilli after fifteen months. (3) The previous administration of diphtheria antitoxin subcutaneously did not prevent the lodgment and growth of the organisms. (4) Inoculation of avirulent diphtheria bacilli into the throats of human beings did not produce: (*a*) clinical diphtheria; (*b*) any subjective symptoms; (*c*) any objective change in the appearance of the throat. (5) The results of the guinea-pig test for virulence were confirmed when thus tested with human beings. (6) No cases of clinical diphtheria developed among the associates of these artificially produced "healthy carriers" of avirulent diphtheria bacilli. (7) When isolated in pure culture after prolonged sojourn in the human throat the bacilli were not altered in morphology or in their staining or cultural characteristics. (8) The bacilli showed no tendency to become virulent as a result of this type of animal passage, either in the carriers who had received diphtheria antitoxin or in those who had not. (9) Spraying the nose with gentian violet in a strength which could be tolerated seemed to be without effect in eradicating avirulent diphtheria bacilli." The following are the conclusions of the investigators: "(1) Avirulent diphtheria bacilli retain their characteristics despite long residence in the human throat or transfer from one human being to another. (2) Avirulent diphtheria bacilli are devoid of pathogenic importance for man. (3) The carrier of avirulent diphtheria does not constitute a menace to the health of the community."

SURGERY

UNDER THE CHARGE OF

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Subphrenic Abscess.—Ullman and Levy (*Surg., Gynec. and Obst.*, 1920, xxxi, 594) review the literature on this subject and report a case cured by operation. Of 890 cases collected by Piquand in 1908, 28 per cent. followed gastric and duodenal ulcers and 21 per cent.

appendicitis; 15 per cent. were associated with the liver and biliary passages; 6 per cent. with intestinal diseases; and the remaining 3 per cent. with various conditions. Of Barnard's series of 76 cases collected from the London Hospital, gastric and duodenal ulcers were responsible for one-third of the cases (34 per cent.), appendicitis for one-sixth (15 per cent.), tropical and hydatid diseases of the liver for one-sixth (17 per cent.); the remaining were distributed among rare conditions, such as cancer of the pancreas, pyosalpinx, splenic infarct, gall-stones, etc. Since 1908, appendicitis as the cause of subphrenic abscess appears to assume the principal etiological role. This view was vigorously suggested by Heffinger in 1912. Subphrenic abscesses are apparently not so common today as formerly. The improvement in diagnostic skill, and the almost universal employment of the roentgen ray for thoracic and abdominal diagnosis, together with the realization of what clinical diseases may be complicated by a subphrenic abscess, have apparently rendered this condition an uncommon occurrence today. In the present paper they reported a case of a patient who developed a subphrenic abscess while under care, showing that such a condition may occur even under hospital supervision; secondly, the case is worthy of record in view of the interesting roentgenological findings of an abscess with gas formation. Moore has pointed out that roentgenological illustrations of subphrenic abscesses containing gas are very rare.

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Two Hundred and Fifty Operations on the Gall-bladder and Ducts.—McGuire (*Surg., Gynec. and Obst.*, 1920, xxxi, 617), says all gall-stones have their origin in a primary cholecystitis. Typhoid bacilli are present in only 7 to 10 per cent. of gall-stones. The mode of transmission of the primary infection is not positively determined. He is of the opinion that it is almost always carried by the blood-stream, and rarely, if ever, by direct extension. It is probably more frequently associated with a primary lesion elsewhere in the abdomen. A diseased appendix is very frequently present when stones are found in the gall-bladder. It is probably the cause of the primary cholecystitis in more instances than is commonly believed. Gall-stones are rare in young people. In less than 15 per cent. was the patient under thirty years, while over 60 per cent. occur between the ages of thirty and fifty years. Jaundice has received too much emphasis as a diagnostic symptom. Probably when the primary cholecystitis is present, a goodly proportion have a mild jaundice, but it is slight and usually forgotten. Stones in the gall-bladder or the cystic duct produce jaundice only by pressure on the common duct or by associated cholecystitis. Attacks of pain in right upper quadrant are most frequent symptoms of stones. Cholecystectomy is the operation of choice where there are stones in the gall-bladder or cystic duct. It is probably the operation of choice where stones are in the common duct, if one is positive all stones have been removed, because stones in the common duct are so often associated with an old contracted gall-bladder. The mortality from cholecystectomy is now sufficiently low so that decision for or against the operation should be judged largely by the percentage of ultimate cures. In cancer of pancreas, the mortality is so high that operative procedure is prohibitive. If operation be done, anastomosis between gall-bladder and stomach is the one of choice.

PEDIATRICS

UNDER THE CHARGE OF

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The Necessity of Clear Thinking in Milk Modification.—HILL (*Jour. Am. Med. Assn.*, March 5, 1921) states that there are several methods of milk modification in good use. It is not of great importance which one is used provided the physician gives enough food in total quantity and the proper combination of the individual food elements to suit the digestion of the baby he is dealing with. It is necessary that he should know approximately the amount of each food element in the mixture in order that he may vary these quantities at will, that he may be able to proceed in a rational manner and that he may be able to express clearly to others in the exact language of figures what he has done. The modification of milk is the mechanical part of infant-feeding. He thinks that the best thing for the average physician to do is to learn the whole milk method and the gravity cream and skimmed milk method. He should discard the methods of top milk dilutions. With these two methods he will have at his hand a large range of formulas, and if he desires to give more fat than can be obtained by the whole milk method he can turn to gravity cream and skimmed milk method.

Clinical Investigations of Xerophthalmia and Dystrophy in Infants. —BLOCH (*Jour. Hygiene*, January, 1921) states that there are fats which are indispensable for children because they contain specific bodies essential for normal growth. If these lipoid bodies termed "fat soluble A" bodies by McCollum are absent from the food for a long time an inhibition of growth will occur and the conditions which the writer has termed Dystrophia alipogenetica will finally appear. This condition involves a great susceptibility and lowered resistance to all infections and often leads to xerosis of the conjunctivæ and cornea associated with night blindness. The xerosis has a great tendency to result in keratomalacia. In its first stage xerophthalmia resembles a slight conjunctivitis. The children develop photophobia, their eyes are red and there is a slight secretion. Xerophthalmia generally occurs in spring, the time when its growth is at its maximum. The disease is most frequent among the children of the poorest country people, and it is always due to an unsuitable artificial diet, generally the replacing of whole milk partly or completely by centrifuged milk, buttermilk or flour preparations. It may appear in children who have received whole milk and cream, but in these cases the milk and cream have been boiled for too long a time or have been subjected to other kinds of drastic treatment, which have destroyed the specific lipoid bodies. Xerophthalmia is easily cured when it is recognized in time. The best treatment is cod-liver oil, but whole milk, cream and butter and also eggs contain the necessary lipoids. It is important to remember that these foods should be only subjected to the ordinary short boiling. The disease is fairly common in Denmark and apparently more so than

in other countries. This is explained by the fact that milk and dairy products are a great part of the exports and the natives deprive themselves to furnish these products for market. Many of the cases of blindness and leukoma attributed to the eye diseases are perhaps due to xerophthalmia. This is perhaps emphasized by the fact that this blindness is increasing, whereas the incidence of gonorrheal and other forms of conjunctivitis is becoming less in Denmark.

Lactic Acid Milk.—SHERMAN and LOHNES (*Jour. Am. Med. Assn.,* October 2, 1920) undertook this study for the purpose of investigating the variations of this preparation of milk and to devise a means to prevent their occurrence. Lactic acid milk differs from ordinary sour or spoiled milk in that it is a sour uncontaminated sterile milk. The authors have used it for more than eight months with very good results. With their method of mixing, four of the points of advantage which are emphasized in protein milk are obtained. There is a relatively high protein, a full fat, the fine curd during digestion and the concentrated food. They believe that it is the lactic acid in the protein milk that stimulates digestion, both gastric and intestinal, and sterilizes the intestinal content. Lactic acid milk contains only 1.5 per cent. more of lactose than protein milk. Lactic acid milk contains nearly twice the amount of the soluble salts as does protein milk and less of the insoluble salts. They use two sorts of lactic acid milk, one made from skimmed milk and the other from whole milk. This makes the formulas very flexible as regards the use of fats. Their policy is to begin with the product made with skimmed milk and gradually lessen the dilution, and when undiluted lactic acid milk is reached the form made from whole milk is begun well diluted and the dilution gradually eliminated. In order to make the formula smooth barley water is used in the formulas. This is of a strength of from 0.5 to 0.75 per cent. The first method is to warm the milk, which has been boiled and then cultured, and put it away in a fireless cooker or in a nursery refrigerator. If put away in the evening at 85° F., in the morning it will be found to have undergone a proper fermentation with an acidity of from 70 to 90. To prevent further fermentation it is put on ice or preferably boiled rapidly. While being boiled it must be beaten with an egg beater. The other method is more simple. They take the milks, either skimmed or whole, and in the morning add the ferment in the proportion of 1 ounce of ferment to 31 ounces of milk. This is placed in a warm place until the next morning. The whole or skimmed lactic acid milk is then diluted with an equal part of whole or skimmed sweet milk that has been boiled, and as the acidity of the lactic acid milk will be from 170 to 190, we thus get the desired acidity of from 75 to 95. This mixture is boiled or not as desired and is placed away on the ice, where it will keep well for twenty-four hours. Modifications can be made according to the need of the case. To supply the carbohydrate needs corn syrup is used. Infants show improvement of appetite and they like the formula better and are more liable to retain it by this method. They soon lose their ashy-gray color. Their temperature becomes more stable. They are less fretful. Their sugar tolerance seems less easily broken and gas formation is less likely to occur. The loss of weight is overcome by a substantial weekly gain.

Acrodynia.—WESTON (*Arch. Ped.*, September, 1920) reports 8 cases. They began with loss of appetite and listlessness. Some had infections of the upper respiratory tract and some did not. Intestinal symptoms were seen in some and not in others. All had loss of appetite, loss in weight and diminished reflexes. Knee-jerks were sometimes absent for weeks. Profuse perspiration all over the body with scratching and more or less maceration of the skin was a common feature. In every case the hands and feet became cold, bluish red and swollen and tender and painful to touch. One case had photophobia and inflamed conjunctivæ, and this patient also had a small area of necrosis about two erupting teeth. Two patients had necrosis of the gums and alveolar processes in both upper and lower jaws. One lost six and the other eight teeth. None had a temperature of more than 102°. The predominance of opinion seems to be that this condition is a food deficiency disease like pellagra. The disease is self-limited and therefore treatment should be directed toward making the patient comfortable and sustaining the strength by giving a well-balanced diet.

The Effect of Tonsillectomy on the Recurrence of Acute Rheumatic Fever and Chorea.—ST. LAWRENCE (*Jour. Am. Med. Assn.*, October 16, 1920) studied 85 children, all of whom had presented one or several rheumatic manifestations before the tonsils were removed. The time elapsed was an average period of three and a half years. The tonsils were markedly hypertrophied in 13 per cent. of the cases, moderately so in 69 per cent. and not enlarged in 18 per cent. of the cases. They were the site of recurrent inflammation before the tonsils were removed in 73 per cent. of the cases. Sore-throat recurred after removal in 7 per cent. of these cases. At least two operations were necessary before the tonsils were completely removed in 22 per cent. of the cases. The tonsillar lymph nodes were enlarged in 100 per cent. of the cases before the operations were performed, while in 59 per cent. they were not palpable afterward. One or more attacks of acute rheumatic fever had occurred in 42 cases before the tonsils were removed. After tonsillectomy there were no recurrences in 35 cases, or 84 per cent. One or more attacks of chorea had occurred before the removal of the tonsils in 40 cases, and there were no recurrences after operation in 20 cases, or 50 per cent. Sixty-one cases showed myositis and bone or joint pains before the operation, and there were no recurrences in 47 cases, or 77 per cent. Fifty-eight cases of organic disease of the heart were present in the series. Twelve of these patients had suffered at least one attack of cardiac failure before operation. One patient suffered one attack after operation. The exercise of tolerance in the cases of cardiac disease seemed to be favorably influenced by tonsillectomy in the instances in which indication existed for the removal of the tonsils. Nutrition and general health were improved and intercurrent diseases were less common after the tonsils were removed.

Experiences with Luminal in Epilepsy.—GRINKER (*Jour. Am. Med. Assn.*, August 28, 1920) has treated 100 cases of epilepsy with this drug. In this paper he enumerates a number of cases in which the drug was used. In some of his cases the patients have been free from attacks for a period of three to four years, others from one to two years,

and many more for periods of a number of months. During the war, he often used sodium luminal. The dose of this is much larger and the effects are not nearly so good. Luminal in small doses of from $1\frac{1}{2}$ to 2 grains once or twice a day was found capable of causing the arrest of the convulsions of epilepsy. Larger doses are seldom required, but may be safely given. Large doses may be given when beginning treatment, especially after withdrawing the bromide. In these cases the dose may be reduced to the average dose. No harmful effects have been observed from the long-continued use of luminal, and it does not seem to have a habit-forming tendency. The effect on the mentality of patients taking luminal has been surprising. The patients taking average doses do not manifest the mental torpor of those taking bromides.

OBSTETRICS

UNDER THE CHARGE OF

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Disturbance of the Circulation in Pregnancy.—HERRICK (*Med. Clin. North America*, 1920, iv, 179) describes the case of a woman admitted to the hospital while pregnant, with dilatation of the heart and insufficiency of its valves, high blood-pressure, congestion of the lungs and liver, dropsy and dyspnea. In the treatment of the case a diet was given free from salt and the quantity of fluid had been limited to 1200 c.c. each day. Digitalis was given three times daily. The diet was varied and drugs were given to stimulate the action of the kidneys. Under the influence of digitalis the pulse was kept between 60 and 80. The patient improved under this treatment and during the first month there were no attacks of dyspnea and the patient became much more comfortable. The area of cardiac dulness became less, while systolic blood-pressure was somewhat less but the diastolic pressure continued to be 100. After ten weeks of treatment the patient left the hospital in the sixth month of pregnancy and had had no material loss. There was no evidence in any way of syphilis. Since going to her home the patient has been asked to limit strictly the quantity of animal food and also of salt taken. It has been observed that where this is done the blood-pressure is not so high. Regarding prognosis, many of these cases greatly improve. There is usually, however, some essential change in the myocardium and in the small vessels and serious and permanent disease usually follows. If advice is given as to the safety of pregnancy in these cases, patients and their friends must be warned that during pregnancy the woman must be kept constantly under the care of a competent physician.

Suppression of Urine in Pregnancy and Puerperal Period.— In the *Lancet*, 1920, No. 199, p. 116, JARDINE and KENNEDY publish

details concerning 12 patients who had suppression of urine during pregnancy and the puerperal state. In 11 of these cases the report was detailed. It was possible to study the state of the kidneys in 8 and in 6 of these in the cortex there was developing a symmetrical necrosis, 3 showed signs of chronic inflammatory condition and 3 had what was termed "necrosis of the cortex" of the kidney. In the remaining 2 of the 8 cases, the woman had practically a chronic nephritis. It is obvious that the fact that the urine was not secreted might be due to some of these causes. It may, however, not be possible from the clinical study of the patient to say definitely which pathological condition is present. In 6 patients there was necrosis in other organs than the kidneys. The changes in the urinary organs seem to be due to focal necrosis and the location of these lesions was largely dependent upon the arrangement of the blood supply. Wherever there was necrosis the vessels in the adjacent tissues were thrombosed. There are well defined arteriosclerosis in three and there was evidence to indicate that some wound or bruising of bloodvessels produced the thrombi seen in these patients. Curiously enough the lesions were suggestive of those seen in the toxemia of pregnancy. As regards preventive treatment, decapsulation and drainage of the kidney do not give good results because, as a rule, operation is done after the disease has fully developed. These cases furnish another indication for preventing and remedying toxemia in pregnant women.

Pregnant Women Subjected to Vaccination Against Typhoid Infection.—VALMALE–VAYSSIERE (*Gynec. et Obst.*, 1920, i, 217) give the result of their observations and experiments. A vaccine was prepared which was monovalent with 500,000,000 bacilli to each cubic centimeter. Injections a week apart were made into the extensor surface of the arm, doses varying from 1, $1\frac{1}{2}$ to 2 c.c. When animals were studied there was a positive agglutination in the young but not to so great an extent in the others. When rabbits were injected the young die before birth or soon after, but the vaccine was given in doses very large in comparison with the size of the rabbit. During the last six weeks of pregnancy women received vaccination averaging four injections each. It could not be seen that this treatment had any bad effect on the child. The reaction in pregnant women was essentially the same as in the non-pregnant, nor was the blood altered. When the breast milk was studied up to the third injection the agglutinating power of the milk increased. If the serum of the blood and the serum of the milk were tested, the milk serum was always lower than that of the blood. This seems to depend on the action of the epithelia of the breasts. In the majority of cases the serum of the fetus had less agglutinating power than the mother's. This would indicate that in most cases the fetus was passively immunized through the mother although this is not true of all.

An Interesting Illustration of the Extension of the Sphere of Cesarean Section in Its Classical Form.—This is given in a paper by BLANKO ("A Classical Cesarean Section in Pregnant Women Suffering from Bronchopneumonia," *Siglo med.*, 1920, lxvii, 204). After the sixth month of pregnancy, bronchopneumonia is very fatal for the

mother, some have a general septicemia with high fever, weakness and changes in the heart muscle. Pregnancy usually terminates prematurely with the loss of the embryo or child and treatment in the mother is usually without effect. In other patients the disease is localized and the mother's general condition is fairly good, when pregnancy is interrupted in these patients they become much worse. Among others threatening symptoms develop caused by the mechanical effect of pregnancy upon the circulation. These patients are threatened with heart failure, becoming partially asphyxiated with a rapid weak pulse. Some of these cases the writer has treated by the classical Cesarean section under spinal anesthesia, the mother making a good recovery. It is obviously necessary to use great care and judgment in selecting such cases for operation, for if section be done in unsuitable cases the result will be disastrous.

Amniotic Hernia.—FRIEND (*Surg., Gynec. and Obst.,* September, 1920) described a case of this comparatively rare condition. This is found about once in 6000 cases and goes back to the period when the embryo is forming and the umbilical cord developing. Among the different kinds of umbilical hernia, we find described congenital hernia of the cord, amniotic hernia, infantile umbilical hernia and adult umbilical hernia. The writer believes that the term "congenital hernia of the cord" is incorrect and should be supplanted by the term "amniotic hernia." The coverings of this type consist of the amnion, then a layer of Wharton's jelly, and then a thin sac continuous with the peritoneum, and usually so transparent that its contents can be seen. In size the hernia may vary, from the tiny protrusion to an almost complete evisceration. Under the title of "amniotic umbilicus" some writers describe what is practically this condition. The writer narrates and illustrates the case of a newborn child having a large ventral hernia, the size of the child's head, together with undescended testes. The hernial mass was covered with peritoneum and amnion. This seemed to be reflected on to the mass and contained a considerable amount of Wharton's jelly. Through the thin walls of these coverings, one could plainly see the stomach, liver and intestines. The child lived for two days and at autopsy the case apparently belonged to the common type of congenital abdominal hernia, in which amniotic adhesion was an important factor in causation. So far as treatment is concerned, operation immediately after birth is imperative. This must be done before the thin membrane covering the abdominal wall has a chance to become hard through drying and also before the size of the hernial protrusion has been increased by the accumulation of fluid in the stomach. Operation can be done only on those cases where the contents of the tumor can be reduced into the abdomen and the opening in the abdomen closed. If the attempt is made to resect the liver or other abdominal organ, the child usually dies. In Olshausen's method, the skin around the sac is separated, Wharton's jelly is removed and the hernia is reduced entirely, without opening the sac, followed by suture of the skin. Where the protrusion is small, operation is not desired; much can be done by keeping the parts carefully clean, using aseptic precautions and making pressure on the tumor with adhesive plaster which goes around the entire abdomen. The writer lays considerable stress

upon the fact that the term "amniotic hernia" should be substituted for "congenital umbilical hernia" which is often employed.   A photograph and a roentgen-ray picture accompany the article.

The Death of Newborn Child from Broken Neck. — HERSMAN (*Surg., Gynec. and Obst.*, September , 1920) reports 8 cases of newborn children in which the child's life was lost because the axis and atlas were separated, causing death by pressure on the spinal cord.   One case had been delivered by a midwife, 4 were forceps deliveries and 3 were breech presentations.   In each case labor was difficult, sometimes prolonged, and considerable force was employed in extracting child.   To make a diagnosis of the condition, the child's head should be allowed to drop severely forward with the chin on the chest.   If the thumb of the physician is passed along the spinal column, a depression between the spinous processes of the axis and atlas large enough to admit the ball of the thumb will be found; in the normal condition no such depression exists.   The writer believes that many cases formerely ascribed to apoplexy are due to such separation.   Unfortunately the writer had no opportunity to hold autopsies, nor could he have the advantage of examination by the roentgen-ray.

The Influence of Cesarean Section upon the Fertility of Patients Who Have Had the Operation.—WEBER (*Inaug. Diss.*, Giessen, 1919), believes that Cesarean section has a remarkable influence upon the fertility of those patients in whom the mortality of children during normal birth becomes very high, or in whom the birth of a living child in a natural manner is impossible.   Among these he would class cases of placenta previa and contracted pelvis of the third and fourth degrees. In placenta previa Cesarean section reduces the mortality of viable children to less than 10 per cent.   He quotes statistics of normal mortality for Cesarean section in all classes of cases at 14 per cent. These statistics evidently do not include the results of late years in contracted pelvis.   It must be remembered that most of these patients, without operation, could not produce a living child.   In placenta previa many cases occur in multipara who are near the end of their child-bearing activity.   In contracted pelvis of the second or other grades, the conditions are different.   Many of these patients give birth to children through the pelvis.   It is estimated that in these cases the highest possible maternal mortality is 5 per cent.   It is true that the operation offers the possibility of sterilization.   Where the operation is performed for contracted pelvis of considerable degree, it is estimated that at least 60 per cent. of these patients subsequently produce children.   In the lesser grades of contracted pelvis it must be remembered that 80 per cent. give birth to living children with little or no especial difficulty in a natural way.   It is only in the more pronounced grades of contracted pelvis that radical interference becomes necessary.

The Induction of Labor by Modified Champetier de Ribes Bags.— MAXWELL (*Am. Jour. Obst.*, November, 1919) observed the different opinions of obstetricians regarding the ability to measure the fetus while still in the uterus.   In his series of cases there were 161 infants weighing $8\frac{1}{2}$ pounds or more; 108 of these were born at or before term

and 53 after. The average duration of labor was 12.1 hours; 15.1 hours for those over one week overdue; 19.6 for the 16 cases overdue; 10.2 for 9 cases in which pregnancy was prolonged 3 weeks over time and 12.2 hours in 8 that were a month later. Moreover, labor lasted in 15 per cent. of the cases for 16 hours or more. This was a very favorable showing compared to other statistics. In this group of cases there were only four forceps applications; 2 for transverse position of the head and 2 when the head was low down. One child was delivered by Cesarean section after pelvic indications in version were done and operative delivery was employed in $5\frac{1}{3}$ per cent. In a series of 821 cases reported by Enge in this series 8.4 per cent. of the pelves were contracted, of which 80 per cent. were flat, a very common pelvis where the size of the child is large. In this series there were 7 Cesareans, 2 symphysiotomies. There were 10 generally contracted pelves; 76 simple flat; 17 rachitic flat; 1 generally contracted flat; 2 transversely contracted and 1 oblique coxalgic patient. Furthermore, it was not found that fetal death from overretention in the uterus was of common occurrence. Sendykowski studied the literature of the subject over a period of thirty years and was able to find but 50 cases of true delayed or missed labor. In 2750 cases at the University of California Hospital bags have been employed to induce labor in 60. The average duration of these labors was twenty-three and a half hours. The shortest was four hours. The very longest 94; in 49 of 60 cases the bag was weighted sufficiently to keep up tight against the cervix. The lack of uterine irritability becomes evident when we know that 79 per cent. of these patients demanded treatment because labor had ceased or uterine contractions were very weak. The membranes were ruptured in 17 (98 per cent.) shortly after the bag was expelled. Pituitrin was given in 30.3 per cent. to stimulate contraction. On an average the bags remained within the cervix for thirteen hours, although the greater number were expelled within ten hours. Twice the bag was withdrawn because convulsions developed and twice labor failed to appear after the bag had remained in the cervix thirty hours. The average time of pains following the insertion of the bag was five hours and ten minutes. From these and other statistics it becomes evident that differences in the irritability of the uterus must be very pronounced. Castor oil and quinin have been tried, but in the majority of cases they were useless. Operative interference was necessary, although 21 per cent. of the cases were due at term in 40 per cent. or excluding breech extraction 33 per cent. It is also difficult to accurately check the mortality of the fetus in induced labor, but it is known that obstetric operations for the termination of induced labor where the fetus is premature is followed by high fetal mortality. There is no evidence that in good hands the use of bags predisposes to septic infection. In comparison with other reports of similar nature these reports show that the induction of labor at term is considerably different from the induction of premature labor. The difference lies in the varying behavior of the uterus and in the fact that the uterine muscle is ready for labor at term, but unprepared when labor is brought on promptly. The reviewer believes there are many valid objections to the use of bags in the induction of labor. It is admitted that bags frequently displace the presenting part and cause an abnormal presentation. The use of bags is, if one can believe patients, frequently very painful. Bags

do not stimulate retraction of the uterine muscle, and this is the most important because without the dilatation and retraction of the cervix the head cannot advance and labor cannot go on. It is not uncommon experience in the induction of labor with bags to find that when a bag is expelled or removed the cervix is surprisingly little opened. The fetal head cannot descend far when a bag is used as the bag occupies a great portion of the cervix. The reviewer much prefers to induce labor by the use of bougies. If these are inserted under gas anesthesia an opportunity is given to dilate the cervix considerably with the fingers, to separate the membranes from the cervix and lower segment and thus to prepare for the dilatation of the cervix and its retraction. Two bougies rarely fail to bring on labor efficiently, while in cases in which time cannot be lost the reviewer has inserted three bougies, with very good results. The bougie tends distinctly to a softening of the cervix because its presence acting as an irritant to the uterine muscle produces not only dilatation and retraction, but also stimulates the secretion of the muciferous glands in the cervix.

GYNECOLOGY

UNDER THE CHARGE OF

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Varicose Veins of the Female Pelvis.—Perhaps no other subject in the large field of gynecology has been treated so negligently as the one on varicose veins of the female pelvis. This subject has, however, received considerable attention at the hands of EMGE (*Surg., Gynec. and Obst.*, 1921, xxxii, 133), who states that the symptomatology centers around one point, and that is the pain complained of and which must be carefully analyzed. One usually hears that beginning with a definite time there have appeared either bilateral or unilateral, usually left-sided pains of a dull, deep, aching character felt low down in the abdomen which grow worse on long standing and are relieved quickly when the patient assumes the recumbent position. This one complaint is just as typical for women as it is for men who suffer from varicocele and to which the condition in the female has been likened. If sufficient attention is paid to this point the history becomes suggestive enough to make the examiner look for these veins. All of the other symptoms are obscure and may hold good for almost any pelvic disturbance. There is commonly a sense of heaviness in the pelvis and the patient often

suffers from constipation. As the patient is usually examined in the recumbent position her veins are well drained and, therefore, they are not palpable. One would never fail to examine a man standing up if he would complain of anything pointing to trouble anywhere around the genital organs but custom has made the recumbent examination in women a standard. If one will take the trouble to examine the patient by rectovaginal touch in the recumbent position and then have the patient drop her legs and raise her upper body, the author believes that it is often as easy to feel these veins in the female as in the male, for the veins will fill quickly and bring out the dilatation and tortuosity in the shape of an easily compressible and doughy tumor that is much less tender than either an inflamed or an ectopic tube. The tumor will disappear again when the patient resumes the recumbent position. Furthermore, the author believes that ovarian varicosities are frequently overlooked during exploratory operations for pelvic disturbances, because the habit of having the patient put into the Trendelenburg position before the incision is made is quite common, thus putting the veins in the most favorable position for good drainage. Considering the treatment of this condition, if the distention of the ovarian or uterine venous units is directly traceable to constipation, the first principle naturally must be to regulate the bowel and if visceral ptosis is present a proper abdominal support must be added. During the period of any conservative treatment it is essential that the patient keep off her feet as much as possible so that the veins of the broad ligament may be in the most favorable position for free flow and all sexual excitement should be prohibited. Hot douches should not be given as they increase congestion, but slow lukewarm douches with 2 or 3 per cent. of menthol and 5 per cent. of alum will produce a pleasant cooling effect. When the veins have distended to such a degree that one must suppose that they cannot return to normal, operative procedures must be considered. The author does not advise resection of the distended veins nor resection of cystic ovaries, as the number of symptomatic reliefs that he has obtained is sufficiently large to indicate that suspending operations, if carried out properly and in conjunction with uterosacral shortening, will give the desired result in the cure of varicose veins of the broad ligaments and of the ovarian veins in particular.

Tuberculous Salpingitis.—An analytical review of 200 cases of tuberculous salpingitis that were observed in the gynecological department of the Johns Hopkins Hospital has been presented by GREENBERG (*Bull. Johns Hopkins Hosp.*, 1921, xxxii, 52), as a result of which he has been able to draw some rather interesting and instructive deductions. It was noted that tuberculosis of the tube occurred in nearly 1 per cent. of all women admitted and was found one and one-half times as frequently among the colored women as among the whites. Out of every 13 abnormal tubes removed at operation, one was tuberculous and nearly three-fourths of the patients who had tuberculous salpingitis were between twenty and forty years of age, while 60 per cent. of the married patients were sterile. A family history of tuberculosis was reported in 22.5 per cent. while in an additional 2.5 per cent. the con-

sort had active pulmonary tuberculosis. The chief complaint of the patients was pain (74.5 per cent.), usually situated in the lower abdomen. Not much information was obtained from the menstrual history, although it was noted that 62 per cent. of the patients had dysmenorrhea and 41.5 per cent. menorrhagia. Amenorrhea occurred in only 6.5 per cent. of the patients. Nearly half of the patients had dysuria, nocturia and pollakiuria and more than half of the patients were constipated. Approximately one-fourth of the patients attributed the onset of their trouble to some uterine activity (menstruation, pregnancy, etc.). Half of the patients had lost weight during their illness but the physical examination presented no characteristic findings, except that one-fourth of the patients had pulmonary tuberculosis. Pre-operative elevation of temperature was recorded in 62.5 per cent. The blood usually showed either an absolute or a relative leukopenia and a reduced hemoglobin. The correct diagnosis before operation was made in only 13 per cent. of the cases, and in more than half of these the diagnosis was aided by the presence of ascites. In 53 per cent. of the cases it was necessary to perform a radical operation and complications during the operation occurred in 14.5 per cent. of the patients. One hundred and four cases were drained and of these 17.3 per cent. developed fecal fistulæ. In one-third of all the patients there was suppuration of the abdominal incision. In 99 per cent. of the cases both tubes were involved, in 68 per cent. the peritoneum was involved and in 3 per cent. the appendix was tuberculous. The operative mortality in this series was 7.6 per cent., but the prognosis is grave in the presence of tuberculosis elsewhere in the body, where fever exists and where the peritoneum is involved. By means of follow-up letters 90 patients were traced and of this number 78 were found to be living from two months to thirty years after the operations and nearly all of those who are alive are in good condition.

Gynecologic Significance of Appendicitis in Early Life.—It seems to be well established that the appendix may undergo considerable grades of inflammation and yet eventually be restored to a condition of approximate normality. It is entirely probable that during the inflammatory periods of a chronic appendicitis, a serous or serofibrinous exudate is produced which finds its way by gravity into the true pelvis since one often encounters such an exudate in apparently uncomplicated pelves and wonders whence it came. Therefore, GRAVES (*Arch. Surg.*, 1921, ii, 315) believes that it is quite reasonable to suppose that, although this exudate is usually absorbed by the peritoneum, under certain conditions it may be sufficient either through bacterial or chemical influence to destroy the superficial epithelium of the pelvic peritoneum and to stimulate the subserous connective tissue into the formation of organized plastic adhesions; or it may itself become organized and form the basis of adhesions. In this way may be explained theoretically the cases not infrequently encountered in which, without sign or history of gonorrhea or puerperal sepsis, adhesions are found in the posterior cul-de-sac or implicating the surfaces of the adnexa while the appendix shows only mild evidence of disease, or perhaps none at all, to gross appearance. If besides the pelvic adhesions there is added a well-defined chronic appendicitis, or the scar of an

appendix operation performed in youth, the author believes his explanation is still more plausible; certainly more so than the attempt to ascribe the condition to an entirely improbable gonorrheal infection. For this reason appendicitis in childhood or young girlhood is an affection which must be regarded not simply with reference to the diseased organ itself but to the serious harm which it may exert on the pelvic organs, if left to work out its own destiny in a state of chronic inflammation. Early operation is therefore indicated in children when there is any suspicious evidence of appendicular infection. In the acute stage the appendix should be removed immediately to forestall if possible a secondary involvement of the adnexa. If pus is present, every effort should be made to drain the pelvis, it being feasible in certain cases to drain the pouch of Douglas through the vagina. Excepting in cases of localized abscess it is advisable to make a median line incision in order that the pelvic organs may be inspected, and that any abnormalities of position or plastic adherence may be remedied by a proper surgical procedure.

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

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Studies in the Treatment of Malaria.—MAYNE and MOSS (*Public Health Reports*, 1920, xxxv, 3082) review certain experimental observations on the use of quinin and other remedies in the treatment of malaria. The frequency of relapse under quinin is emphasized, even though large doses are given; for example, 45 grains daily for from three to eight weeks and smaller doses lead to high percentages of relapse. The maximum tolerated dose is 120 grains of quinin sulphate on each of two consecutive days. Neoarsphenamine in doses of 0.45 to 0.9 gram control the febrile paroxysms but do not cure, but this drug, in combination with quinin, is more effective in simple tertian infections than is either drug alone.

Syphilis as a Cause of Insanity.—DONALDSON (*Public Health Reports*, 1921, xxxvi, 67) by means of a questionnaire, ascertained the following facts with respect to state institutions for the insane: Percentage of male inmates whose insanity is due to syphilis, 6.2. Percentage of female inmates whose insanity is due to syphilis, 2.2. Percentage of inmates (male and female) whose insanity is due to syphilis, 3.9. Percentage of male admissions whose insanity is due to syphilis,

15.5. Percentage of female admissions whose insanity is due to syphilis, 6.1. Percentage of admissions (male and females) whose insanity is due to syphilis, 10.4. The much larger figures for admissions over inmates are due to the short period of survival of cases admitted for syphilitic mental disorders.

Venereal Disease Incidence at Different Ages.—KING and SYDEN-STRICKER (*Public Health Reports*, 1920, xxxv, 3091) summarize their studies as follows: (1) For the purpose of throwing some light upon the question of the age incidence of venereal infections, and in the absence of complete data for any definitely and accurately observed population group, certain tabulations were made of approximately 8400 case reports of venereal diseases among white persons in Indiana. (2) Considering these cases as fair samples of the total cases of that type which actually exist in the population under consideration, indices of venereal disease incidence according to age of onset were computed for persons of both sexes and of different marital condition by adjusting the age distribution of cases to that for the population of Indiana in 1910. (3) While the data cannot be considered conclusive, they suggest the following points: (*a*) The greatest incidence of venereal infections occurs in early adult ages, between seventeen and twenty-five. This is true of both males and females. (*b*) The incidence of venereal infections is earlier among females than males. The modal or peak age for females is nineteen years, while that for males is approximately twenty-one years. (*c*) While the data are not definite on this point, the evidence suggests that among persons married at the time of report, venereal infections were largely premarital in the case of males and postmarital in the case of females. (*d*) There is a wide divergence in the incidence curves for males who were married previous to the time of report and for males who had remained single. In the one case, infections were confined chiefly to the younger adult ages (under twenty); in the other, the incidence in the adult ages (twenty to twenty-four) was considerably higher than in the younger ages. The effect of marriage apparently was to greatly lessen the incidence of venereal infection among males. (*e*) Gonorrhea apparently occurs at slightly younger ages than syphilis or chancroid among both males and females. (4) In view of the limitations of the data with respect to the number of cases reported, the stage at which disease was reported, the possible errors in determining accurately the age at which infection occurred, and the use of the 1910 age distribution of population, these observations cannot, of course, be regarded as definitely conclusive.

Studies on the Lethal Action of Some Meningococci on Mice, with Special Reference to the Protective Properties of Antimeningococcic Serum.—NEILL and TAFT (*Hygienic Laboratory Bulletin*, November, 1920, p. 93) endeavored to determine the value of protection tests as a method of estimating the therapeutic value of antimeningococcic serum. It was found that dead meningococci were about as fatal for mice as were living ones, though large doses were required in either case. The method does not show relative value except when practically the difference is very great. The irregular results do not lend encouragement to the use of the method for practical purposes.

Report on Investigation of Typhoid Fever Epidemic at Greenville, Tenn.—HARRUB (*Public Health Reports*, 1921, xxxvi, 72), a Sanitary Engineer, reports an outbreak of 61 cases with seven deaths due to contaminated spring water used as a municipal supply. The supply was treated with hypochlorite but the disinfectant was not properly employed, and analysis of the water showed it to be of a poor sanitary quality.

The Tropin Reactions of Antimeningococcus Serum.—EVANS, (*Hygienic Laboratory Bulletin*, November, 1920, p. 43) gives the following summary of the work reported: The phagocytic test for bacteriotropins is a workable test which distinguishes clearly between a normal serum and a serum containing the specific antibodies. The important phagocytic antibodies in meningococcus serum are bacteriotropins. That is, they are not dependent upon complement for their activity. A high concentration of tropins does not inhibit phagocytic action, but there is in serum a poisonous substance active against leukocytes of a foreign species, which suppresses phagocytic activity in low dilutions of the serum. No stains of meningococci were found which resisted phagocytosis after treatment with serum containing the specific tropins. All strains of meningococci tested produced tropins in inoculated rabbits. But not every inoculated rabbit produced tropins, presumably because of individual differences in the animals. Some strains regularly produced tropins in higher titer than other strains. After long artificial cultivation meningococci may lose their tropinogenic power, and their power to respond to active tropins. The tropin reactions of meningococci are specific, dividing them into well-defined groups, with no cross-reaction between the typical strains of the main groups. Sixty-three strains of meningococci were available for classification according to their tropin reactions. They were divided into four distinct groups, designated R, S, T, and U. Group R included 61.9 per cent. of the strains; group S included 25.4 per cent. of the strains; group T included 4.7 per cent. of the strains and group U included 1.6 per cent. of the strains. Groups R, S, T, and U are distinct groups. Every strain belonging to those groups was equal to every other strain of the homologous group in its power of absorbing tropins from serums of the homologous group. The typical strains of groups R, S, T, and U did not absorb tropins specific to a heterologous group. But 4 atypical strains were found which did, in a slight degree, absorb tropins of another group. A fifth group (Z) included 6.4 per cent. of the total number of strains of meningococci. Unlike the other four groups, group Z is not distinct but is related to the others. This relationship is shown by a partial absorption of tropins specific for those groups. Moreover, the strains of group Z differ in their relationship to one another, and they differ in their relationship to the four main groups The strains of group Z are further distinguished by a tendency to spontaneous phagocytosis. In the majority of immune serums a good tropin content is accompanied by a good agglutinin content. But agglutinins may be produced without tropins, and tropins may be produced without agglutinins. Under unfavorable conditions the deterioration of agglutinins and tropins did not follow a parallel course. Certain conditions destroyed the action of the agglutinins without injuring the tropins,

and other conditions destroyed the action of the tropins without injuring the agglutinins. One hundred and twenty-eight commercial serums were tested for their content in tropins. The tropin content was compared with the agglutinin content as determined in the official test. The results of the two tests agreed for 71.8 per cent. of the serums. For the remaining 28.2 per cent. the results were discordant.

Differentiation between Various Strains of Meningococci by Means of the Agglutination and the Absorption of Agglutinins Test.—Butterfield and Neill (*Hygienic Laboratory Bulletin*, November, 1920, p. 9) present their Summary and Conclusions as follows: (1) Classification of strains according to their geographic distribution is not possible. (2) When the agglutination test with type serums prepared from Gordon's types was applied to the Hygienic Laboratory strains, 90 per cent. of them were classified without further work. (3) If the meningococcus suspension agglutinates in a titer of 1 to 100 or higher, with only one of the type serums, provided the homologous coccus agglutinates in over 1 to 400, it may, in 100 per cent. of the cases, be classified at once without resorting to the absorption test. (4) If a meningococcus suspension agglutinates with two or more type serums in equal titer, it may in 100 per cent. of the cases be classified by the absorption test. (5) If a suspension agglutinates with two or more type serums in unequal titer the highest titer probably indicates the type. This was true in 77 per cent. of the cases tried. (6) In the monovalent serums tried the complement-fixation bodies have the same specificity as the agglutinins, the complement-fixation titer being, as a rule, somewhat higher than the agglutination titer. (7) During the course of a year's time the apparent changing of certain strains of meningococci from one type to another has been observed.

The Fate of the First Molar.—Butler (*U. S. Public Health Reports*, 1921, xxxvi, 434) states that it is a generally conceded fact that the human tooth is undergoing a process of involution due to lack of hard usage. Recent investigations by the U. S. Public Health Service not only bear out the above statement but furnish also much food for serious thought. The first molar, the first permanent tooth to make its appearance in normal dentition, is easily the most important tooth in the mouth. Not only does it present the largest masticating surface but it also largely determines the position of the other permanent teeth to follow it in eruption. In the examination of 6388 children the age varied from six years, or the year of the appearance of the first molar, to seventeen, or ten years after the eruption of this tooth. The first molar was found to be the most neglected of all the permanent teeth and the one most frequently lost. One reason ascribed to these facts is given as a failure on the part of parents to recognize this tooth as other than one of the deciduous set. Among the children of six years, the year of the eruption of this tooth, 4.8 per cent. of all these molars was found to be undergoing carious processes. This means 14.3 per cent. of all the six-year-old children were found to have one or more of these molars defective. Five years later 9 per cent. of all six-year molars were found to have been extracted or to be appearing as necrosed roots; 54.5 per cent. of all

children of this age examined were found to have one or more defective or missing first molars, regardless of such as had received professional attention. In order to determine the possibilities of successful prophylactic measures 1000 carious areas in first molars were plotted as to the location in which they occurred. For this purpose only the mouths of children of from nine to twelve years were considered, this for the reason that during this period the tooth would have been in position from three to five years, during which period no tooth would be contiguous to it upon the distal surface but upon the mesial there would have been a deciduous tooth. Thus the distal surface would have had the advantage of being polished in mastication, an advantage which could not be enjoyed by the mesial surface because of the presence of the deciduous tooth. The following findings were thus obtained: Occlusal cavities, 877; mesial cavities, 110; distal cavities, 8; buccal cavities, 3; lingual cavities, 2; total, 1000. It would appear that the difference between 110 and 8 would indicate the advantage of the distal surface over the mesial as a result, the abrasion of this surface by mastication, but as seen, the preponderance of cavities occurs upon the masticating surface, in the fissures or sulci. To faulty development is ascribed the large proportion of occlusal cavities. This seems to be of three types: (1) an arrest in the deposit of enamel at this point; (2) a lack of calcification in the enamel and (3) a failure of union when the enamel rods approximate each other in a more or less horizontal position. The writer urges a specialization in care of children's teeth and a systematic encouragement of early visits to the dentist, pointing out that only by early detection and most careful operative procedures may this important tooth be preserved for the necessary years of usefulness.

Epidemic Encephalitis (**Encephalitis Lethargica, Nona**). — SMITH (*U. S. Public Health Reports*, 1921, xxxvi, 207) made an investigation of epidemic encephalitis which he summarizes as follows: (1) Clinically the disease presents a series of symptoms which are found in no other affection. (2) The lack of positive epidemiological data renders the determination of the length of an incubation period impossible. (3) The clinical course of the disease may be divided into three stages: A prodromal period with fatigue, lethargy, headache, giddiness, and disturbances of vision; the stage of acute manifestations, with vomiting, fever, paralysis of certain cranial nerves, changes in tendon reflexes, alterations in speech, marked general weakness, and, in the majority of cases, coma of varying intensity; and the period of convalescence, which varies. In some cases recovery is complete within ten days or two weeks after the subsidence of the acute symptoms. In other cases, however, convalescence is prolonged and is accompanied by changes in the mental state, definite loss of function of certain muscles, and obstinate palsies of the cranial nerves. (4) There was a distinct outbreak of the disease in the United States during the latter part of 1918 and the early part of 1919. Beginning with the first case in the city of New York in September, 1918, there was a gradual increase in the monthly incidence up to and including March, 1919, during which month 61 cases occurred. This was followed by a sharp break with only 12 cases in April and 5 in May. (5) The age distribution of the cases

in epidemic encephalitis is entirely different from that in poliomyelitis, and is, it is believed, in itself alone to be sufficient grounds for the belief that the two diseases are separate and distinct affections. (6) The appearance of encephalitis in epidemic form has, with the exception of the cases reported by v. Economo, apparently always been preceded by an epidemic outbreak of influenza. This apparent relation between the two diseases remains as yet unsolved, and consequently, therefore, leaves a field for considerable discussion. Of the 122 cases of epidemic encephalitis on which definite data were obtainable, only 56 cases, or 46 per cent., gave a history of having had a preceding attack of influenza; whereas in 66 cases, or 54 per cent., the history of a recognized attack of influenza was negative. As shown in a previous section of these studies, this influenza attack rate is higher in the group of persons having had epidemic encephalitis than in the general population. The question naturally arises, "Why?" In seeking a solution to this problem two lines of thought present themselves: (a) Believing that epidemic encephalitis is a disease unto itself, may not this difference be due to the fact that those persons who have had influenza suffer a certain lowering of vitality, immunity, or resistance, which would render them more susceptible to the invasion of the causative agent of epidemic encephalitis when exposed to such a factor? If this be so it would account for the difference in the attack rate above mentioned. (b) If, however, the belief that epidemic encephalitis is a distinct disease is erroneous, may it not be possible that those cases classified as having had a previous attack of influenza are really recurrent invasions of the same person with the causative agent of influenza, whatever this agent may be, the second invasion involving or invading the central nervous system? An invasion of the central nervous system direct as a primary attack by this same agent, if such a thing be possible, would account for those cases which give no history of a previous attack of influenza. In the absence of definite positive laboratory findings in connection with the etiology of epidemic encephalitis, this thought is merely offered as a possibility. (7) Sex distribution shows 60 per cent. of the cases males and 40 per cent. females; whereas in influenza the attack rate for males and females is about equal. In the cases of epidemic encephalitis without a previous attack of influenza, the ratio of males to females is 1 to 1. In those cases having had a previous attack of influenza, however, the ratio of males to females is 2.5 to 1. (8) Onset was gradual in 71 per cent. of cases and sudden in 29 per cent. The case fatality rate, however, was 60 per cent. in the cases with sudden onset and 22 per cent. in the cases where the onset was gradual. (9) Lumbar puncture and subsequent examination of the spinal fluid, while revealing very little of a positive nature, should be done in all cases where it is possible, as it is by this means that other conditions which might be confused with epidemic encephalitis may be eliminated to almost a certainty. (10) Blood examinations reveal very little data which may be used for diagnostic purposes. (11) As for communicability, approximately 900 persons were exposed in the immediate families of the cases reported in the United States, and among this number no secondary case occurred so far as reports and inquiries show. (12) The case fatality rate was 29 per cent. (13) The results of animal inoculation with brain material from two fatal cases in connection

with these studies were negative. The fact must be borne in mind, however, that the brain material used had been retained in 50 per cent. sterile glycerine for a period of six months prior to the inoculation.

The Incidence of Tuberculosis Among Polishers and Grinders in an Axe Factory.—Drury (*U. S. Public Health Reports*, 1921, xxxvi, 159) made a study of tuberculosis in a Connecticut industrial community covering a period of twenty years, with the following results: In the group of "polishers and grinders" the maximum number of deaths occur at the age of forty-five years instead of at twenty-five years, as among other mill workers. The dust produced in "wet grinding" is held responsible as the chief cause of the excessive mortality. Death-rate from pulmonary tuberculosis per 1000 population: Polishers and grinders from 1900 to 1919, 19.0; others in mill from 1900 to 1919, 1.6; entire mill population from 1900 to 1919, 6.5; general population of town A from 1900 to 1919, 1.5; general population of town B from 1900 to 1919, 2.4; general population of town C from 1900 to 1919, 2.1; general population, mill district as a whole, from 1900 to 1919, 2.0; general population, town of H from 1900 to 1919, 1.1; general population, state of Connecticut, from 1900 to 1919, 1.5; male population, state of Connecticut, from 1900 to 1919, 1.7.

Four Years of Framingham Demonstration.—Armstrong (*Am. Rev. Tuberc.*, 1921, iv, 908) states that tuberculosis as a cause of illness in Framingham is apparently being brought under control. This is particularly true as reflected in the decreasing number of advanced cases. As to mortality the tuberculosis death-rate per 100,000 corrected for certification was 121.5. For the entire demonstration period thus far, with similar corrections, including the rate for 1920, the figure is 84.2 per hundred thousand—a reduction of about one-third. For 1920 the rate was 64.5 per hundred thousand—a reduction of about one-half under the predemonstration rate after four years of intensive work. This rate would mean that the same measures if successfully applied to 100,000 people, with 100 deaths a year at the start, would save fifty lives a year. For the United States as a whole this would mean the saving of 75,000 lives annually. In Framingham at the beginning of the demonstration the community was spending approximately 40 cents per capita per year on all kinds of health work. The community is now spending about $2 per capita per year from public and private funds combined. In a city of 100,000 people this would mean an annual health expenditure of about $200,000.

A Statistical Study of Recent Experience with Measles and Whooping-cough in Massachusetts.—Henry (*Am. Jour. Public Health*, 1921, xi, 302) states that approximately 33 per cent. of the whooping-cough and 18 per cent. of the measles in Massachusetts are in children under three years. For a period of years (1913 to 1918) 90 per cent. of the deaths from whooping-cough and $79\frac{1}{2}$ per cent. of those from measles have been under three years old. The apparent fatality rates for the group under three in 1918 were $23\frac{1}{2}$ per cent. for whooping-cough and 8 per cent. for measles. For each thousand reported cases of measles in 1918 in Massachusetts there were 18 deaths,

and 14 of these were under three. In the same year each thousand cases of whooping-cough represented 92 deaths, and 77 of these were under three. Even though there has been on an average four or five times as much measles the whooping-cough fatality leads for the six years (1913 to 1918) with 2065 deaths compared with 1908 for measles. This is a total of 3973 deaths from the two diseases and 3378 were under three. Measles is more prevalent but less fatal; whooping-cough less prevalent but more fatal. In the end they cause almost equal numbers of deaths and should cause us equal concern. Measuring our success by a reduction in deaths from these diseases it is at once apparent that our results depend very largely on how successfully we prevent measles and whooping-cough in children under three, among whom about 85 per cent. of the deaths occur (90 per cent. whooping-cough; $79\frac{1}{2}$ per cent. measles). Propaganda and methods of control should be more specifically directed at the age group under three. It cannot be emphasized too strongly that in these dangerous years, when so many children die of measles and whooping-cough or their complications, the most careful medical attention and nursing are needed to prevent dangerous complications.

The Destructive Effect of Oxidation on Antiscorbutic Vitamine.— Hess (*Proc. Soc. for Exp. Biology and Medicine*, 1921, xviii, 143) states that the antiscorbutic vitamine was destroyed when 4 c.c. of a normal solution of hydrogen peroxide were added to a liter of raw milk, which was then placed in the incubator over night. Bacteria did not develop in the incubator under these conditions. When 80 c.c. per capita of this milk was fed to guinea-pigs in addition to oats they all developed scurvy in about three to four weeks, a result similar to feeding experiments with milk which had been autoclaved for one hour at 120° C. The addition of orange-juice to the dietary served either to protect or to cure animals on this dietary. Orange-juice subjected to oxygen for a short period was likewise found to have lost some of its potency. It was previously found that milk or tomato-juice which had been shaken had lost some of this vitamine. Probably this deleterious action is partly due to the effect of oxidation. The harmful effect of "aging" may also be interpreted in this way. As foodstuffs undergo oxidative processes frequently in the course of various manipulations no doubt this factor plays an important role. This action probably explains the differences in the antiscorbutic potency of foodstuffs which have been treated in apparently similar ways, for example, of milk which has been heated in open pans or in hermetically sealed bottles.

ORIGINAL ARTICLES.

ACUTE ARTERITIS COMPLICATING PNEUMONIA.

By George Douglas Head, M.D.,

MINNEAPOLIS, MINN.

Microörganisms may enter the arterial wall either directly into the intima from the blood stream, or into the media and adventitia by way of the vasa vasorum, or through lymphatic channels, or by leukocyte carriers from diseased tissue in close proximity to the artery itself. We know the organisms are there because they have been isolated from the vessel walls in typhoid fever, diphtheria, septicemia, pneumonia, tuberculosis, syphilis and gonorrhea. When such an accident occurs in the course of an acute infection, acute inflammation of the artery may result. If the vessel is completely occluded by the thrombus, gangrene of an extremity may occur. Such cases have been observed and reported in smallpox, rheumatic fever, influenza, gonorrhea and cerebrospinal meningitis. In so widespread and common a disease as lobar pneumonia the occurrence of acute arteritis with thrombosis and gangrene should be encountered with some degree of frequency. An examination of the reported cases proves, however, the rarity of this complication.

Douillet's case is a true instance of such a complication, as is probably the case reported by Fussell, and that by Brouardel and Giroux. Abstracts of these three cases are as follows:

Douillet's case.[1]

[1] Arch. de Méd. et de Pharm. Militaire, September, 1901; Abstracted, Am. Jour. Med. Sc., 1902, cxxiii, 538.

Male, aged twenty-one years, who on the second day of defervescence from a mild pneumonia of the right lung began to complain of much pain in the left leg, which was soon followed by gangrene, and the leg was amputated at the point of election. The patient recovered. After amputation the dissection of the leg showed complete obliteration of the posterior tibial artery, the anterior tibial and the peroneal being unaltered. The obliteration was not due to an embolus but was the result of an arterial thrombosis. No bacteriologic or microscopic examination of the arterial walls was made. The patient's circulation was extremely poor during the pneumonia and during convalescence.

Fussell's case.[2]

Male, aged forty-one years, an alcoholic. Seen November 5, 1906, with a temperature of 103°, pulse 120, respirations 48 and complete consolidation of the right lung. Resolution occurred and the temperature was normal on November 8. On November 11 the man developed edema of both hands and cyanosis of the fingers of both hands. There was no cyanosis of the lips. There was also cyanosis of the lower half of both forearms, with petechiæ along the lines of the superficial veins. The afternoon of the same day the fingers became black and almost gangrenous. On November 12 the fingers of both hands were black, cold and shrivelled at the first joint. The gangrene advanced, death occurring on November 13. The postmortem revealed a bluish-black discoloration from the forearm downward. The tips of the fingers were black, shrivelled and dry. A thrombus filled the interossei arteries to a distance one inch proximal to the digital division and completely filling the digital branches. Apparently the thrombosis began in the terminal branches and spread upward.

M. G. Brouardel and M. R. Geroux,[3] relate a case of acute arteritis of the humeral artery, following pneumonia without gangrene, as follows: In 1911 Madame H., aged fifty-eight years, was seized with a violent chill and pain in the right chest, and a diagnosis of frank acute pneumonia of the lower lobe of the right lung was made. On the seventh day she complained of pain in the right shoulder and arm, with increased temperature and chills. Palpation of the humeral artery caused increased pain. Pulsation in the radial artery became lost and the limb became white and pale. No cardiac findings of an abnormal nature. No complete arrest of circulation but simple ischemia of the arm. The author concludes there was complete obliteration of the humeral artery by thrombosis, but circulation was maintained by collateral circulation because there was no thrombosis in the branches.

The large number of cases of pneumonia occurring in the army camps during the winter of 1918 and 1919 offered a splendid oppor-

[2] AM. JOUR. MED. SC., 1909, cxxxvii, 70.
[3] Société Méd. de Hôpitaux, 1913, xxxv, 1268,

tunity for observing some of the rare complications of pneumonia. In our large experience at the Base Hospital, Camp Wheeler, Macon, Ga., one proved instance of acute arteritis with gangrene was observed (Case I). A second case (Case II) with localized gangrene of the skin of the toes was probably of like origin, and the reports of the cases are as follows:

CASE I.— *A case of lobar pneumonia complicated by arteritis and thrombosis of the right femoral and popliteal arteries. Gangrene of the leg; amputation and recovery.*

Sam. B., colored, aged twenty-three years; soldier; of good habits. Admitted to Base Hospital, Camp Wheeler, Macon, Ga., November 1, 1918. Complained of headache, nausea, vomiting and cough with fever.
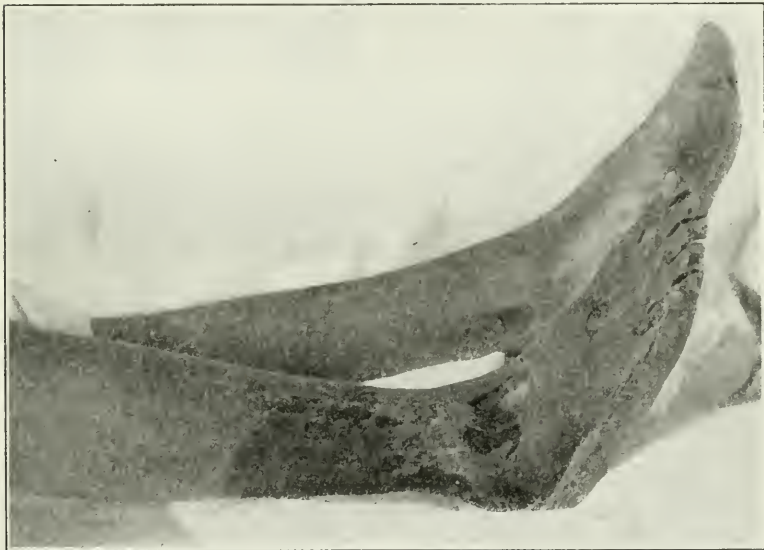
CASE I.—Lobar pneumonia complicated by acute arteritis and thrombosis of the right femoral and popliteal arteries; gangrene of foot and lower third of leg; amputation; recovery. Sam. B., aged twenty-three years; soldier. Base Hospital, Camp Wheeler.[4]

Family History. Negative. The man had syphilis in 1916 and influenza in 1917. On the day of admission, the patient was taken with a chill, headache, pain in the chest on cough or deep breathing and fever (100.8°). The physical examination was negative for organic disease except the presence of a few fine crackling rales with slightly impaired percussion note in the lower right lung posteriorly.

[4] Photograph published through the courtesy of Dr. Warren Sisson, of Boston, Mass.

The diagnosis of influenza with possible lobar pneumonia (right lower lobe) was made. The second day after admission the patient's temperature was 104°, pulse 110, respirations 30. The physical examination was negative for organic disease except for an impaired percussion note at the bases of both lungs posteriorly, more marked on the right, where increased bronchophony and bronchovesicular breathing were present. The clinical diagnosis of lobar pneumonia in the right lower lobe was made by the ward surgeon and confirmed by the chief of the service. The patient had his crisis upon November 5, and on November 8 the clinical note stated that the right lobe was clearing but moist rales were still present at the base. On this date, eight days after his admission, the patient began complaining of a severe pain in the right lower leg and knee. This came on rather suddenly without apparent cause. Slight swelling was present and the tenderness was extreme from the knee downward, especially in the calf of the leg. There was no discoloration of the skin, but the leg was cold. On November 14 the patient still complained of extreme pain in the right leg. The skin of the leg looked white, wrinkled and pinched. There was slight swelling in the right foot and a mottled appearance of the leg from just above the ankle downward. A total absence of pulsation in the right dorsalis pedis was noted and the right popliteal artery showed only slight and feeble pulsation. A diagnosis of acute arteritis or embolism with thrombosis of the popliteal and anterior tibial arteries was made.

On November 29 the note of the condition of the right leg read as follows: "A line of demarcation is clearly defined on the inner aspect of the limb 10 cm. above the internal malleolus. The foot and ankle are almost completely mummified and black up to this point. There are small areas suggesting moist gangrene over the foot. There is also some swelling of soft parts in the calf of the leg. There is slight increase of temperature. The tissues of the leg are hard and indurated. No marked tenderness is present although the patient complains of extreme pain in the right leg. This, however, is not constant. There is no pulsation in the popliteal or anterior tibial arteries. The arteries of the left foot, leg and groin show normal pulsation. The pulsation in the iliac arteries can be palpated on both sides; physical signs in the lungs are clear. The heart is normal."

Urine Examination. Negative.

Blood Examination. Leukocytes, 14,800. Hemoglobin, 80 per cent. Differential count: Polynuclears, 88 per cent.; small mononuclears, 8 per cent.; large mononuclears, 3 per cent.; transitionals, 1 per cent.

Nose and throat cultures were positive for Streptococcus hemolyticus. The sputum showed a Type IV pneumococcus. Wassermann reaction positive. Inasmuch as a line of demarcation and

gangrene was established the patient was referred to the surgical side for amputation of the leg. The leg was amputated above the knee December 2. After amputation a large clot was noted plugging the cut lumen of the femoral artery. After this was removed the vessel bled freely and had to be ligated. The patient made a slow and complete recovery. A pathological study of the bloodvessel submitted for examination was reported as follows (Earl Gilroy): "There are multiple round cells in the adventitia of the femoral artery. There is slight endarteritis in the media. The interna of vessel is thick and there is a laminated collection of blood elements extending three-fourths across the lumen of the vessel."

Pathological Diagnosis: Arteritis of femoral artery with thrombosis of this artery and the popliteal artery of the right leg.

CASE II.— *A case of localized gangrene of the skin of the toes complicating bronchopneumonia.*

Hazelton, Arthur C., aged twenty-six years; white; single; soldier. Admitted to the Base Hospital, Camp Wheeler, October 28, 1918, complaining of headache, pains in the chest, cough and fever. His family history was negative. He had had measles, mumps, scarlet fever and chicken-pox. Denied venereal disease. No history of dead fingers or chilblains. One day prior to admission, while doing his work in the development battalion, the patient was taken with cold in the head and cough and pains in the back and legs. He had no distinct chill. The patient was admitted to the hospital with a temperature of 102°, pulse 88, respirations 28 and the physical signs of bronchopneumonia in the bases of both lungs. The clinical diagnosis of bronchopneumonia, bilateral, was made. The patient was very sick in the hospital from October 28 to November 4, 1918, when his temperature began dropping and the pneumonic process began gradually to resolve. On November 1, 100 c.c. of antipneumococcic serum was given. The patient showed no anaphylactic reaction following the giving of the serum or during the convalescence. On November 25, one month subsequent to entering the hospital, the patient began complaining of considerable pain on the dorsal surfaces of the third, fourth and fifth toes of the left foot. A few raised, blister-like patches appeared over the corresponding toes on the right foot, but not as marked as on the left. The appearance of the toes suggested Raynaud's disease. During November 29 and 30 the patient complained of considerable pain and a good deal of oozing from blistered-like areas on the toes. The color began to change and the toes took on a bluish, dark color and localized areas of necrosis, while ulceration appeared in the skin of the toes over the area where the blisters had first appeared. By December 4 the skin began peeling off and the ulceration areas began filling in. The patient still complained, however, of some pain in the toes. The color of the toes was now a light, greenish

color.   By December 8 the skin on the toes had entirely cleared up and, aside from slight discoloration, the skin appeared healed, but the nail on the fourth toe of the left foot began to show evidence of necrosis, and on the twelfth this nail came off.   Repeated careful physical examinations of this man during this interval of time showed no evidence of disease of the heart.   He complained from time to time of numbness in the left thigh, some headache and general nervousness, but had no fever.   The urine examination showed specific gravity, 1022; no albumin; no sugar; few granular casts.

Blood Examination.   Leukocyte count, 8400; polynuclears, 54 per cent.; small mononuclears, 35 per cent.; large mononuclears, 8 per cent.; transitionals, 2 per cent.   Sputum examination showed a Type IV pneumococcus.   The Wassermann reaction was negative. The blood culture November 25 was negative.   The patient was treated symptomatically during his sickness.   At various times he was given digitalis, nux vomica and atropin (small doses).   No ergot or adrenalin was given at any time.   It did not seem reasonable to attribute the skin necrosis to the medication given.   The diagnosis settled upon was bronchopneumonia, bilateral, complicated by gangrene of the skin of the toes of the left foot.

PERIARTERITIS NODOSA.

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AND

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The rare diseases have, as a rule, a clean-cut, clinical picture which enables one to recognize them readily.   Periarteritis nodosa, however, is most bizarre in its manifestations, and the fact that the disease at its onset or during its course in not a few instances resembles that of an acute surgical abdominal condition makes it of interest to both internists and surgeons.

It is not our intention to present a full historical, clinical and pathological study of periarteritis nodosa, since this has already been so well done in a number of monographs.   Dickson[1] brings the

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[1] Jour. Pathol. and Bacteriol., 1908, xii, 31.

subject down to 1907; Longcope[2] to 1908, Lamb[3] has given the most complete discussion of this subject and has brought the literature down to 1914. Since then the most valuable contribution has been that of Klotz.[4] The most recent is that of Spiro,[5] which has appeared since this report was begun. Including our own case, the number of definitely proved cases is only 42. About a dozen or more additional cases have been properly eliminated because they do not definitely belong to this group.

As to the rarity of this disease, Schroetter[6] has given testimony when he regretfully admits that he never encountered a case of it in spite of being constantly on the watch for it in the enormous material which came under his observation in Vienna and elsewhere. While it is true that the fully developed disease is so rare, yet, as will be referred to later on, it is probable that rudimentary lesions of this type may be by no means so infrequent an occurrence, as stated by Klotz and Spiro.

The case which we shall report here is unique even for this rare disease, since it is one of the few in which the diagnosis was made during life. This has been done in four other cases, in only one of which has the diagnosis been verified by autopsy. As, fortunately, the diagnosis of our case was made early in the course of the disease, we had the unusual opportunity of studying the vascular lesions both in the early inflammatory stages as well as in the stage of healing toward which it had progressed when death occurred from the secondary nephritis. By being thus able to follow the different stages of the process and to compare them with the findings of the autopsy we have been able to correlate the varying pathological and clinical pictures described in the previously reported cases.

W. S., aged thirty-nine years, was admitted to Mount Sinai Hospital on June 6, 1919. His previous history was that he had had measles and typhus fever in childhood. As an adult his only complaint was recurrent attacks of peritonsillar abscess. His venereal history was negative.

Present History. Seven weeks before admission he had severe, cramp-like pains in the left calf which radiated into the foot. Within a few days he had similar pains in the right leg. One week later, while these were subsiding, he had severe pains in the right lumbar region which radiated into the testis. In a few days he had similar pains in the left lumbar region. Six days before admission he had bad pains in the epigastrium which did not radiate and were accompanied with marked distention and a fever of 102°. The pains and the fever have persisted. During one of the attacks of lumbar pain he passed bloody urine.

[2] Bulletin Ayer Laboratory, Pennsylvania Hospital, 1908, v, 1.
[3] Arch. Int. Med., 1914, xiv, 481.
[4] Jour. Med. Research, 1917, new series, xxxii, 1.
[5] Virchow's Arch., 1919, ccxxvii, 1.
[6] Nothnagel's specielle Pathol. und Therap., 1901, xv, ii Theil, 31.

When he was admitted to the hospital he was apparently suffering from an acute abdominal condition and he was sent to the surgical service of Dr. Edwin Beer. Shortly after his admission he was seen by Dr. L. Buerger, who, thinking that he had to deal with some lesion in the upper urinary tract, cystoscoped him and catherized the ureters. No ureteral obstruction was found. The urine was negative except for a few epithelial and red blood cells. The urea of the right kidney urine was 0.9 per cent.; that of the left kidney was 1.3 per cent.

On the next morning, when he was first seen by Dr. Beer, the patient was cheerful and felt perfectly well; in fact, when he was taken to the roentgen-ray department he asked whether he could not go home that day. It is worth noting that this curious condition of being well in the morning and being very miserable in the afternoon continued until the time of the operation. The examination showed nothing more than a vague epigastric tenderness and diseased tonsils, with a marked pharyngitis. He complained of no pain, and yet there was a very high leukocyte count of 36,000, with 75 per cent. polynuclear cells and a fever of 102°! For the following week the same condition continued. For four days he had an intermittent fever of 102° to 103°, when it suddenly dropped to normal and remained so for several weeks. The pulse and respiration ran parallel to the fever. The leukocyte count continued very high, ranging between 36,000 to 54,000, with the polynuclear cells from 76 to 90 per cent. At the end of the first week Dr. Beer could elicit some tenderness in the right hypochondrium on jarring the patient. Later on, in the same way, he found some tenderness higher up in the same area and also in the splenic region. Save for these few signs repeated examinations were negative.

The other clinical data were the following. The blood-pressure was 160/90. The blood Wassermann was negative. The chemical examination of the blood showed 35 mg. urea nitrogen; 95 mg. incoagulable nitrogen; 2 mg. creatinin; 0.136 cholesterin per 100 c.c. blood. The urine was negative save for a few red blood cells. The phenolsulphonephthalein test gave an excretion of 64 per cent. in two hours. The white cell counts and the results of the catheterization of the ureters have already been given. The blood culture was negative. From the smears of the throat a pure culture of hemolytic streptococci was obtained.

Roentgen-ray examinations of the chest, gastro-intestinal tract and kidneys were all negative. Examinations of the gastric and duodenal contents were also normal.

Gradually Dr. Beer came to the conclusion that there might be some suppurative process in the retroperitoneal glands behind the lesser omental bursa or perhaps a localized peritonitis in the lesser sac. An exploratory laparotomy, which was performed by Dr. Buerger on June 19, revealed periarteritic nodules in the mesentery,

a finding which at once cleared up many of the points in the history which had been so obscure.

All the arteries in the mesentery and in the pancreatic region were involved. Each vessel had one or more small nodular swellings, about the size of a pea, which involved the vessel uniformly like small aneurysmal enlargements. Similar nodules were found in the mesentery and in the intestinal walls. The head of the pancreas was enlarged. There was also a large solid area of fat necrosis in the omentum. The nodules were at once recognized as those of periarteritis nodosa, a diagnosis which was confirmed by the pathological examination which was made by Dr. F. S. Mandlebaum of one of the nodules excised for this purpose. The cultures from the nodule were sterile.

Five days after the operation he passed bloody urine, but this time there were no colicky pains. Two weeks later, shortly after his transfer to the Second Medical Division, he had very severe pains in both arms, the right being especially sore. This led to the finding of the first external nodules, which were felt as definite small nodes along the course of the right brachial artery. They were the size of a small pea, each of which had a small area of inflammatory reaction about it. Eleven days later (July 15) similar nodules appeared along the course of the left brachial artery and two were also found on the face, one in each anterofrontal region. The latter were the first in which there was distinct pulsation and had no inflammatory reaction. Within the following week a few not tender and uninflamed nodules appeared on each shin and also along the course of the third right intercostal artery. One of the latter was excised for pathological examination, the report of which will be found later on. Four days later two fresh nodules were found on the right side of the neck and one on the left side. Pulsation could only be detected in the nodules which had appeared on the face. At this time he also had a diffuse maculopapular rash on the hands and forearms.

He remained in the hospital for two months after the operation and he left it at his own request considerably improved; his general condition was better, although he still ran a low, irregular fever. His leukocyte count was also lower, ranging around 20,000. The pains also became much less and there were no further crops of nodules. The only new symptom was failing vision, which was due to a fibrinous exudation on the temporal side of the optic nerve heads; this was associated with a low grade of nephritis, which had been present for some weeks.

On September 3, 1919, he was readmitted to the hospital, He stated that he had been quite well for a fortnight, when he again felt sick. He had lost much weight and his chief complaints were weakness and marked dyspnea. The physical examination showed an advanced nephritis, with generalized edema. There were also

irregular patches of consolidation scattered through both lungs. Both ventricles of the heart were considerably enlarged. The liver reached to the umbilicus; the spleen could not be felt. There was a marked neuroretinitis. The urine showed an advanced nephritis. There was no fever on admission or subsequently. No glands could be felt anywhere.

The only nodules which could be found were several small hard nodules along the right temporal and brachial arteries. All the other nodules had disappeared. It is to be noted that no other nodules developed during the rest of his life.

The leukocyte count was 12,000, with 80 per cent. polynuclears, 19 per cent. small lymphocytes and 1 per cent. eosinophils. The blood-Wassermann test was again negative. The blood-chemical examination showed urea nitrogen, 49 mg. incoagulable nitrogen, 100 mg. per 100 c.c. blood. The blood-pressure was 140/100. The sputum was pneumonic in character and amounted to 30 to 60 c.c. daily. It contained streptococci and pneumococci, but no tubercle bacilli.

The most interesting findings were those in the lungs, which were naturally interpreted as being associated with vascular changes of the periarteritis nodosa in branches of the pulmonary artery. It was thought that they might be due to hemorrhages and consolidation about the aneurysmal dilatations or hemorrhagic infarcts. No information on this point could be gained from the roentgen-ray examination, which only showed dense shadows from the bases up to about the second rib. These shadows suggested pneumonia or tumor.

The electrocardiograms showed inverted T waves in all the leads, but were otherwise normal.

The terminal stages were those of a chronic bronchopneumonia and advanced nephritis. Death occurred on October 8, 1919.

Autopsy Report. *General.* The body is that of a rather emaciated man of large frame. No icterus or petechiæ. Moderate postmortem discoloration of the back. On the forehead, about one inch above the outer end of the left eyebrow, is a small nodule about the size of a split pea, which is apparently along the course of the temporal arteries. It is elastic in consistency. Irregular thickenings can be felt along the course of both brachial arteries.

Heart. Of normal size. The coronary vessels show a thickening of the walls, though no calcification and no distinct atherosclerotic patches. In addition, many of the descending branches of both arteries show irregular thickenings along their course. At the very apex, lying just beneath the visceral pericardium, are two nodes, pea size and apparently springing from terminal branches of the descending ramus of the left coronary. These are solid, semielastic in consistency. One consists of a sac which is filled with old blood clot, the second appears to be filled with a thrombus which

has been almost completely organized and converted into dense fibrous tissue.

Lungs. Both upper and the left lower lobes appear to be diffusely involved by a subacute lobular pneumonia; their cut section is pinkish gray in color and in places is very friable. The pleura at both apices is densely adherent. The lower lobes of both lungs and the intervening patches, between the areas of lobular pneumonia appear to be in a state of chronic edema. The tracheobronchial lymph nodes are moderately enlarged and markedly anthracotic.

Liver. Of normal size. Surface smooth; on section there appears to be a uniform thickening of the walls of the hepatic arteries. The cut ends of these vessels in Glisson's capsule stand up prominently above the cut section.

Gall-bladder and Bile Passages. Appear to be normal.

Spleen. Weight, 120 gm. About one-half normal size. Outer aspect is densely adherent to the diaphragm and anterior abdominal wall. The walls of the splenic arteries are uniformly thickened and inelastic. Two of the branches of the splenic, just as they enter the hilus of the organ, present at one side a large aneurysmal sac filled with old blood clot. At the hilus just beneath the capsule are felt three such sacs about the size of a small marble. On section these are found to be filled with old blood clot, the periphery of which is undergoing transformation into connective tissue. The spleen on section presents a rather dry appearance, with complete absence of lymphoid elements. In the center of the outer aspect is a small infarct about 1 x $\frac{1}{2}$ cm., yellowish brown in color and completely cut off from the rest of the organ by a zone of dense connective tissue.

Pancreas. Of normal size and presents no gross lesions.

Kidneys. The right kidney is slightly larger than normally and weighs 240 gm. There is a marked chronic perinephritis, so that the fatty and true capsules are densely adherent. On the outer aspect of the organ is a mass the size of an egg. On section what is left of the kidney appears to be compressed by this large hematoma, consisting of clotted blood which occupies a fibrous sac on the outer aspect of the organ. On its periphery the hematoma is limited by the fibrous capsule of the kidney. It is apparently a false aneurysmal sac belonging to some vessel in the cortex of the organ. It is roughly the size of an egg. The rest of the deformed organ presents on section a yellowish-pink appearance and is dense in consistency. The cut surface is glassy; the cortical markings are completely obscured. The arteries, including the interlobular and arcuate, show a thickening of their walls and in a few places an aneurysmal dilatation. The latter, as well as nearly all the branches of the renal arteries in both cortex and medulla, are occluded by a recent thrombus. The left kidney is about one-half the normal size and weighs 125 gm. The capsule strips easily, disclosing a reddish surface which is everywhere studded with smaller and larger yellowish-white scars. The ureter

and pelvis are implanted in the center of the anterior aspect. The organ is of a dense elastic consistency and on section presents an irregular narrowing of the cortex, due to the above described scars, apparently the result of old infarctions. The cortical striations are rather obscured. Here and there throughout the cortex the arcuate, interlobular and larger branches of renal artery are thickened and along their course present occasional spherical aneurysmal sacs. On cross-section of the kidney these are seen to vary in size from a pin-head to a few which are about the size of a pea. All are filled with red thrombus, apparently deposited some time ante mortem.

Adrenals. Of normal size. Cortex narrow and contains relatively little lipoid material. The organ otherwise shows no abnormalities.

Gastro-intestinal Tract. Stomach: The entire mucosa is intensely congested and on the posterior aspect near the lesser curvature shows four shallow ulcers. The largest is the size of a thumb nail. The base of these ulcers is apparently formed by the muscularis and in the base are seen both recent and old hemorrhages. The edges of the ulcers are neither thickened nor undermined. Along the lesser curvature both the coronary arteries and the gastric branch of the gastroduodenalis artery are thickened and present along their course eight or nine aneurysmal sacs. About five of them, which are the largest, are along the course of the coronary artery. The very largest is about the size of a small grape. They are filled with red thrombus, which is undergoing organization. The entire mesentery, especially of the small intestines, is studded with numerous nodes varying in size from a pinhead up to a few the size of a small grape. They are lying along the branches of the mesenteric arteries, most of them being about one to one and a half inches from the intestinal insertion of the mesentery. Others are found in various places in the mesentery, a few also on the surface of the intestine at the mesenteric attachment. The intestinal tract, however, aside from irregular patchy congestion of the mucosa, shows no circulatory disturbances.

Brain. Shows no gross changes.

Systemic Arteries. Including the aorta they show moderate thickening of the wall and loss of elasticity. In the aorta are a few small patches of atherosclerosis beneath its intima. As to the frequency of occurrences of periarterial nodes along the course of the systemic vessels, nothing can be said because of the limited permission for the autopsy. Only a few small pieces of brachial and temporal and intracranial vessels could be excised for microscopic study.

Microscopic Examination. Numerous sections were made from each organ and from arteries and veins in various parts of the systemic, splanchnic, coronary, intracranial and pulmonary circulation. The material was studied with hematoxylin-eosin, Van Giesen and Weigert's elastica stains.

I. *Branch of the Superior Mesenteric Artery Which Was Removed at the Operation* (June 19, 1919). The section shows a fusiform dilatation of the artery, the lumen of which still contains fluid blood. In the wall of this vessel the lesions consist of two types: (1) An acute and subacute inflammatory process in the adventitia on one side of the vessel. Both the adventitia and the periarterial connective tissue at this side are extensively and densely infiltrated with small round cells, plasma cells and polynuclear leukocytes. The relationship of this inflammatory lesion to the vasa vasorum cannot be definitely ascertained. (2) The second conspicuous lesion consists in a remarkable homogeneous appearance of the media throughout the greater part of the circumference of the vessel, which gives the appearance of an actual necrosis of the muscle fibers in this coat. Here and there in this degenerated media there are collections of round and polynuclear leukocytes. Scattered through the degenerated media are fibroblasts which are apparently undergoing some proliferation. The damage has apparently occurred so acutely that the intima as yet shows no changes.

II. *Aneurysmal Node from Intercostal Artery* (Removed July 17, 1919). The vessel shows an extensive sacculated aneurysmal dilatation, the lumen of which is occluded by a mixture of blood-platelet thrombus and red clot. The wall of this aneurysmal sac for two-thirds of its circumference consists of dense connective tissue, whereas in the other one-third of the circumference the various layers of the arterial wall can still be made out. Here, however, the musculature of the media is markedly atrophic, and between these scattered muscle fibers is a peculiar bluish staining material, apparently a hyaline form of degeneration of connective tissue. In the expanded two-thirds of the circumference the wall consists solely of dense connective tissue which contains a large hemorrhage, probably a dissecting aneurysm. The elastic-tissue stains show no elastic tissue fibers in this part of the wall. Only in the small segment previously described as presenting some remnants of the structure of the arterial wall are still to be seen some strands of elastic tissue undergoing marked fibrillar degeneration.

III. *Autopsy Material* (October 8, 1919). Heart Muscle, Left Ventricle: Muscle fibers are rather thin and atrophic. The striations are poorly marked and there is considerable bipolar pigmentation. The small arteries in places show a slight uniform thickening of their walls.

Heart Muscle, Left Ventricle: This section has been taken perpendicular to the serous surface and in addition to the thickness of the ventricular wall contains the visceral layer of the pericardium and several large arteries. These vessels present a remarkable appearance. In places the arterial wall is enormously thickened, due to a productive inflammation in the media and intima. The thickened area consists of young interlacing fibroblasts lying in a

peculiar pale blue staining intercellular substance. The media at this site shows a replacement of large areas of muscle fibers by the same peculiar pale bluish substance containing occasional young fibroblasts. At times this degenerative process involves the inner part of the media, in other places the peripheral part, whereas in still other sites it forms a patchy streaking throughout the musculature of the media. The process appears to be the end-stage of some degenerative phenomenon in the media, which has resulted subsequently in a compensatory proliferative and nodular thickening in the intima. The adventitia shows relatively little change. Where the thickening of the intima and scarring of the media are most marked the adventitia is often involved by a dense connective tissue in which small collections of round cells are to be found. The vasa vasorum occasionally show a uniform thickening of their walls and occasionally show a small tendency toward round-cell infiltration in their immediate vicinity.

Deeper in the heart muscle, branches of the coronary arteries just described show in places a similar involvement. In one such branch almost the entire vessel has been replaced by a loose connective tissue, leaving only a minute lumen in the center. In this small vessel the structure of the media has been almost completely obliterated by dense hyaline connective tissue. In addition to the changes described in the last section the heart muscle presents occasional small areas of interstitial scarring.

Coronary Artery: This section passes through the site of one of the small aneurysms on the descending branch of the left coronary artery. The greater part of the circumference of this structure is occupied by old, dense, connective tissue, muscle fibers of the media being present only in one small segment of the circumference. The entire lumen of the vessel has been closed by a recent blood clot which on its periphery is undergoing active fibroblastic invasion. The vessel looks as if it had undergone a marked uniform expansion previous to the occurrence of the thrombosis. Weigert's elastic stain shows an almost complete disappearance of all the elastic tissue in the vessel wall, no trace of the internal elastic membrane being visible. Only in the periphery, in the adventitia, are small elastic fibers to be discerned.

A second section, also through the thrombus of the coronary artery, presents almost an identical picture except that in one-half of the circumference of the vessel the muscle fibers of the media are still fairly well preserved. The rest of the media in this portion of the vessel wall, especially the peripheral layer, has been replaced by an enormous mass of loose connective tissue consisting of thin spindle-shaped fibroblasts running circumferentially in a peculiar granular blue-staining intercellular substance. This bluish staining material is probably the remains of a degenerative process. One of the small vasa vasorum in the region has been completely closed by young vascular connective tissue and then recanalized.

Small Descending Branch of Right Coronary Artery Near the Apex of the Heart: This vessel, which grossly appeared to be a sacculated aneurysm, appears microscopically to consist chiefly of a completely organized thrombus which has been recanalized. The wall of the vessel consists chiefly of old, dense, connective tissue, only a narrow band of muscle fibers being still present three-quarters of the way around the periphery. The internal elastic membrane is ruptured and shrunken so that it can be traced less than half the distance about the circumference of the vessels. The portion that remains is thin and atrophic and in places has undergone a fibrillar degeneration. In the other half of the circumference of the vessels only occasional small degenerated fragments of elastic tissue are to be seen.

Medium-sized Branches of the Coronary Artery: Show an irregular patchy scarring of the media, in places almost completely replacing the muscle fibers except for the circumferential ones on the periphery. The media shows an enormous nodular thickening, irregular in distribution. The internal elastic membrane shows a remarkable fibrillar degeneration which in places amounts almost to complete absorption. There is a small amount of newformed elastic fibrils in some of the scars in the media. In one place on the periphery of the vessel a rupture of the external elastic system has occurred.

Lung: Moderately anthracotic. Many of the alveoli as well as the interstitial tissue of the interalveolar septa contain heart failure cells. Pleura is moderately thickened by old, dense, connective tissue containing considerable anthracotic pigment. Here and there throughout the lung there is a considerable increase in the interalveolar connective tissue, but this is very irregular in distribution. The branches of the pulmonary artery appear to be normal. Some branches of the bronchial artery, however, show a fibrous thickening of the intima and media. The essential lesion in this lung, however, is a brown induration. In the elastic stains the bronchial vessels show an irregular fibrillar degeneration of the internal elastic membrane.

Liver: Marked parenchymatous degeneration, probably postmortem. There has apparently been an intense passive congestion. The centers of the lobules show marked dilatation of the sinuses, with atrophy and a brown pigmentation of the liver cells. In the periphery of the lobules the cells are large and are apparently undergoing some compensatory hypertrophy. The small branches of the hepatic artery in this section show no change. Liver capsule is slightly thickened.

Hepatic Artery, Medium-sized Branch: Shows an advanced degree of the characteristic pathological changes described in the coronary artery. The media is diffusely studded with bluish staining scar tissue. There is a similar irregular fibrous thickening of the

intima. In another medium-sized branch the patchy scarring of the media is found to be chiefly in the circular coat. In this branch the lumen is completely closed by dense connective tissue, apparently an organized thrombus. Between this dense connective tissue and the circular coat of the media there is a zone of pale blue staining material, homogeneous in character and containing a few fibroblastic nuclei. This is probably merely a degenerated connective tissue. The elastic stain shows that there has been a marked fibrillar degeneration of the interstitial elastic membrane which has ruptured so that it can only be traced about two-thirds of the way about the circumference of the artery. On the side where rupture of the elastica has taken place the vessel wall has undergone a bulging so as to form a shallow, sacculated aneurysm.

Spleen: Marked dilatation of the sinusoids and lymphoid hypoplasia. The trabeculæ show a marked thickening. On one large septum there has been a tremendous increase in dense connective tissue and in the center are the remains of old extensive hemorrhage. In places the reticular tissue is distinctly increased. Many of the smaller vessels show an irregular hyaline thickening of the intima, but no typical changes.

Splenic Artery: This is one of the main branches of the splenic. It is completely occluded by a mixture of blood-platelet thrombus and red clot. The thrombus is beginning to undergo organization at the periphery. Almost the entire media is replaced by old connective tissue, some of which stains bluish in the hematoyxlin-eosin preparation. As a result of this diffuse fibrosis of the media no line of demarkation can be made out between the intima and the media. In the Van Giesen stain some muscle fibers are still found to be present in one-half of the circumference of the vessel, but these can only be positively discovered in the peripheral portion of the circular layer and in the longitudinal layer. On one side of the vessel a tremendous expansion has apparently so thinned the wall that it merely consists of a narrow layer of dense fibrous tissue which is apparently upon the point of rupture. Although the entire vessel wall has been stretched by this aneurysmal dilatation the bulging of the wall is more marked at this particular point. The elastic stains show practically a complete disappearance of all elastic tissue in this vessel wall.

Pancreas: Shows a moderate degree of chronic diffuse interstitial pancreatitis. In the interstitium is one vessel which is completely occluded by old, dense, connective tissue taking a pale blue stain and containing relatively few fibroblastic nuclei. This organized thrombus has been partly recanalized. On the periphery it fades off into pink staining scar tissue of the media. Only in the periphery of one-half of the circumference of the media are there any muscle fibers. In the other half of the circumference the fibrous wall had apparently undergone a marked aneurysmal dilatation

before the lumen became thrombosed and the thrombus organized.
The elastica can only be traced in the former half of the vessel and
shows a fibrillar degeneration. The other half of the circumfer-
ence contains no elastic tissue, apparently due to a rupture of the
internal and external elastic membrane before the aneurysmal bulg-
ing took place. Other smaller vessels show similar though less
marked changes.

Stomach: The sections show a shallow ulceration the base of
which consists of acutely inflamed submucosa. The polynuclear
leukocytes infiltrate downward into the musculature. Some of the
small arteries in the submucosa in this region show fibrous scarring
of their media. Near one such vessel there is an old hemorrhage.

Branch of the Superior Mesenteric Artery: The vessel shows a
uniform expansion to about three times its normal diameter and is
occluded by a mixture of blood-platelet thrombus and red clot, the
former of which is already undergoing fibroblastic invasion. The
media of the vessel, except in its most peripheral portion, is com-
pletely replaced by a dense, hyaline, connective tissue. Throughout
the entire circumference no trace of an elastic membrane is to be
seen in the Weigert elastica stains; in fact, all elastic tissue has dis-
appeared from the vessel wall except for the irregular fibers which
normally are present in the adventitia.

Branch of the Inferior Mesenteric Artery: Shows changes simi-
lar to the previous one, namely, aneurysmal dilatation which has
recently been followed by thrombosis and beginning organization
of the clot. The musculature of the media has been almost com-
pletely replaced by hyaline connective tissue in which the elastic
system has completely disappeared. Some smaller branches in the
section show a patchy scarring of the media at some one place and
thickening of the intima opposite this site. The elastica in these
smaller vessels is well preserved except on the diseased side of the
vessel, where fibrillar degeneration has taken place.

Kidney: Presents a remarkable appearance throughout most of
the cortex. The tubules have shrunken to solid cords, consisting
chiefly of nuclei which are buried in a dense connective tissue. The
glomeruli are everywhere well preserved except for a moderate
dilatation of Bowman's capsule. The cause of the remarkable
atrophy of the tubules with subsequent replacement fibrosis is to
be seen in the extensive disease of the arteries throughout the
sections. This is very similar to that which has previously been
described, consisting either of patchy scarring of the media or a
more or less complete replacement of the muscle fibers of the media
by hyaline scar tissue which often takes a pale blue stain in the
hematoxylin-eosin preparation. The medium-sized and larger
branches are most extensively involved, though even the inter-
lobular and arcuate arteries show extensive disease amounting often
to complete occlusion due to narrowing of the lumen or to throm-

bosis. Many of the medium-sized vessels, down to arteries the size of the interlobular, often show aneurysmal dilatation either fusiform in shape or sacculated due to bulging of one side of the vessel wall. Many of these aneurysms are thrombosed and the thrombus more or less completely organized. The elastica stains show varying degrees of fibrillar degeneration in all the arteries. In vessels which are most extensively diseased this amounts to complete disappearance. In vessels in which no dilatation and no thrombosis have taken place the lumen is often markedly narrowed due to the tremendous increase in hyaline connective tissue in the intima. It is this gradual reduction in the blood supply which has apparently been responsible for the atrophy of the tubules, the more or less diffuse fibrosis and the subsequent shrinking of the organ.

Renal Artery: This shows very much less disease than do the smaller branches just described in sections of the kidney. There is some patchy scarring of the media. In the Weigert elastic stain the internal elastic membrane shows a fairly marked fibrillar degeneration which is most pronounced at one side of the vessel where the intima shows a marked fibrous thickening.

Adrenal: Both cortex and medulla are of normal size, the cortex containing a normal amount of lipoid material. No vessel changes are discoverable.

Brachial Artery: Shows small patches of scarring scattered through the media. This, however, is not very marked. The elastic system is also well preserved. In one of the branches of the brachial, however, there is a large scar in the media at one side of the wall and an extensive fibrillar degeneration of the media which has here ruptured, permitting aneurysmal sacculation.

Brachial Vein: Shows no changes.

Common Iliac Artery: Shows peculiar pale blue staining material between the muscle fibers in the inner portions of the media. In the elastic stain this appears to be due to a fibrillar degeneration of the elastic tissue. In one-half the circumference of the vessel this degeneration of the media is most marked and there is extensive hyaline thickening of the intima. In places this thickening of the intima appears to be of an atherosclerotic nature in that it contains masses of cholesterin.

Aneurysmal Node on the Temporal Artery: This appears to be an aneurysmal expansion of the vessel whose walls are extensively degenerated. Very few muscle fibers can be found in what remains of the media, which consists almost entirely of hyaline connective tissue, in places taking a pale blue stain. The lumen of this aneurysmal sac has been occluded by a thrombus of the blood-platelet type, which is about two-thirds organized. In the vessel wall one cannot differentiate between the intima and media, especially as the elastic stains fail to show even a trace of the internal elastic membrane.

Vertebral Artery: Shows only occasional small patches of scar-

ring in the media. The intima is markedly thickened and the internal elastic membrane shows a very extensive fibrillar degeneration, especially on one-half of the circumference.

Middle Meningeal Artery: Here the same degenerative processes are to be seen in the media and on one side of the vessel wall. There is a very marked fibrillar degeneration of the internal elastic membrane which has ruptured. An extensive thickening of the intima at this side has, however, apparently prevented rupture of the vessel wall or sacculated dilatation.

Summary of Pathologic Studies. In the branch of the superior mesenteric artery removed at operation on June 19, 1919, while the patient was still in the acute stage of his illness, the lesion was essentially an acute and subacute inflammatory process involving chiefly the adventitia and the periarterial connective tissue. This periarterial inflammatory process was associated with and probably directly responsible for a true necrosis of the muscle fibers in the media of the vessel. Although we were unable to prove the mechanism of this necrosis, we believe it to have been due to occlusion of the circulation in the vasa vasorum by the periarterial inflammatory infiltration.

In the material removed one month later, on July 17 (an aneurysmal node of an intercostal artery), little evidence of an acute inflammatory process could be discovered. The lesions were similar to those found in the arteries at autopsy.

At the autopsy which was performed three and a half months after the operation (October 8) the disease was found to involve all the systemic vessels, including the coronary, splanchnic, bronchial and cranial arteries. Vessels the size of the brachial and common iliac arteries showed the least damage, the most extensive lesions being found in medium-sized arteries, such as main branches of the renal, splenic, coronary, intercostal and superficial temporal. Much to our surprise no trace of the acute periarterial inflammatory process, which was so conspicuous in the material removed at the operation, could be found in spite of an extensive search. The vascular lesions as they existed after death apparently represented the end-stage of the disease, namely (1) extensive fibrillar degeneration of the internal elastic membrane amounting in some vessels to complete absorption, (2) fibrous-tissue replacement of the degenerated muscle fibers of the media, and (3) compensatory thickening of the intima, apparently a vain attempt to strengthen a much weakened arterial wall.

The intense degeneration of the elastica and the fibrous scarring of the media often resulted in rupture of the former and stretching of the latter, so as to form a sacculated aneurysm on one side of the vessel. When this did not occur the compensatory thickening of the intima on the side of the vessel, which presented the more extensive degeneration of elastica and fibrosis of the media, often gradually narrowed the lumen until the vessel was completely occluded or

finally became obstructed by the formation of a blood-platelet
thrombus.

This case is remarkable because the vascular lesions found at
autopsy represent the end-stage of a periarteritis nodosa, in which
the acute periarterial inflammatory process has long subsided and
the disease was progressing toward healing. Death occurred from
renal insufficiency, due to the gradual atrophy of tubules and replace-
ment fibrosis in the interstitium consequent upon the gradual and
progressive reduction in the circulation through the diseased renal
vessels. The one other case of similar nature in which all the arterial
lesions found at autopsy had advanced to the stage of healing was
reported by Spiro.[5]

From the standpoint of *etiology* our case is also important. It
gives very positive support to the contentions of those writers who
maintain that syphilis is not the cause of the disease. The two
Wassermann tests which were made, one early, the other late, in
the course of the illness were both negative, and, furthermore,
nothing of a syphilitic character was found in any of the pathological
examinations. Syphilis, if it plays any role at all, is purely second-
ary. Klotz, Dickson and Spiro have discussed this point very fully
and we agree with their conclusion that syphilis may have had some
predisposing effect on the bloodvessels in the patients in whom it was
present. It is true that a number of cases have been reported
(Benedikt, Schmorl, Lamb, Klotz, Spiro and others) in which the
Wassermann test was positive, yet nothing of a luetic nature was
found in the gross or histological specimen. The pathological
differences between periarteritis nodosa and syphilitic arteries are
very great and spirochetes have never been demonstrated by any
observer in the former. The fact that great improvement was
noted after specific treatment in the patients of Benedikt and
Schmorl has no significance, since Benedikt's case was never proved
by autopsy, and Schmorl's case, on which so much stress has been
laid, was very poorly observed and the report of it is very unsatis-
factory. The only reference to it which we could find is that which
is contained in a discussion on Benda's paper on specific arteritis
before the Deutsche pathologische Gesellschaft in 1903, when
Schmorl took exception to Benda's statement that periarteritis
nodosa was not specific. His remarks, in full, are as follows:[7] "A
fifty-three-year-old woman, who had had vague symptoms, devel-
oped nodules in the right lower abdominal region and right thigh.
These were excised and proved to have all the characteristic of
periarteritis nodosa. An energetic antiluetic treatment caused the
rapid improvement of all the symptoms and the disappearance of
the nodules on the right thigh. Two years later she died of an acute
portal thrombosis. At the autopsy no changes could be found in the

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[7] Verhandlungen der deutsch. pathologisch. Gesellschaft, 1903, 203.

vascular system which would correspond to those of periarteritis nodosa; what was found were residues of the same in the form of small fibrous foci in the kidneys, liver and heart, which were very closely related to the bloodvessels. He believed that the excellent results of the specific treatment would surely leave no doubt as to the syphilitic origin of the disease."

The fact that the patient improved under specific treatment is no proof at all, since the improvement may have been independent of this treatment, for in our own patient the pathological examinations of the autopsy material gave definite proof of healing without any such treatment. It is also to be noted that Schmorl's case was observed in 1903 before the days of the spirochete and salvarsan. Additional proof, if any is demanded, is afforded by the observations of Lamb, Spiro and others that a similar disease exists in stags and other animals.

It is true that one may easily fall into the error of confounding specific arteritis with periarteritis nodosa. We are indebted to Dickson, who laid the greatest stress on the necessity of the differentiation of the two conditions. He even went so far as to propose a new name, polyarteritis nodosa acuta, for the cases of true periarteritis nodosa and to allow the latter name to be used for the cases which are syphilitic. This suggestion has wisely not been adopted, as it would only cause added confusion, and the name originally proposed by Kussmaul is too firmly established to be discarded.

It is to be regretted that our case has shed no light on the possible bacteriological relations of the disease, for aërobic and anaërobic blood cultures which were taken during life were sterile as well as all the cultures from the various nodules. All the other blood cultures which have been reported have also been sterile. But the same cannot be said concerning the nodules from the cultures of which a variety of organisms have been obtained. These include streptococci, staphylococci, Bacillus coli and Bacillus influenzæ. These varied results tell their own story and it is needless to add to the discussions of this topic which have already been published by Lamb, Klotz and Spiro. Their findings and their animal experiments have led to no definite results. As regards Klotz's suggestion of the possible relations of the Streptococcus viridans, it is to be noted that it was absent in the throat cultures in our patient and it was never found in any of the other bacteriological examinations.

Nevertheless, all the evidence which has been presented would indicate that the disease is of an infectious nature, the cause of which is as yet unrecognized, and which, for some unknown reasons, attacks the walls of the medium-sized arteries, with a predilection for the mesenteric, renal, hepatic, pulmonary, cardiac and cerebral vessels, as well as those in the skin and in the muscles of the extremities. After a time, if the patient survive, these structural changes become less marked and undergo involution; the symptomatic

evidences of the acute infection become less marked and finally disappear. Death in the cases of long duration is caused by the structural changes which have been left behind in the tissues attacked. Thus our patient made a symptomatic recovery from his periarteritis nodosa, but died of the resultant nephritis.

Closely allied to the question of the etiology are those of whether the periarteritis nodosa is a disease entity and whether there are similar changes in the arteries in other conditions. These subjects have been carefully considered by Klotz and Spiro. In his discussion Klotz emphasizes the importance of the perivascular lymphatics in the study of the distribution of bacteria in and about the walls of the vessels: "It is not uncommon to observe the advance of infection and inflammation in tissues surrounding the small arteries of the mesentery of the appendix. It is probable that the thromboses so commonly occurring in the vessels of these outlying tissues have their cause in the damage induced through infections of the arterial coat arising from the perivascular involvement. The same perivascular responses are also observed in the Fallopian tubes, the broad ligament, the umbilical cord and elsewhere. . . . This migration of the inflammatory exudate is not a condition which, *per se*, tends to follow the artery, but which, because of the lymphatics, is the line of least resistance in this process. This is true not only of infections of the suppurative type but also of the non-suppurative lesions. Of the latter it has been frequently demonstrated that the infections associated with acute rheumatic fever and the various rheumatoid processes are for the most part periarterial in their distribution. The focal inflammatory deposits that are so constantly found in the myocardium in rheumatism are excellent examples illustrating the localization in the lymphatic spaces and channels of the nutrient vessels. Thus we are led to believe, and we have further demonstrated in experiment, that periarteritis nodosa differs from the common periarterial inflammations only in the peculiar manner of the damage in the arterial wall. The distribution and the progress of the disease along particular branches of arteries are not unique for this lesion which has received a special name."

Spiro also takes the view that periarteritis nodosa is not a disease, *sui generis*, and he directs attention to the similarity of the nodules to those which occur in the coronary artery as described by Wiessel[8] and Wiesener.[9] Spiro believes that periarteritis is not a distinct entity but that it belongs to the category of mesarteritis which may result from various infective agencies. The cases which run an acute course are those which occur in individuals who have weak vascular systems either congenitally or as the result of overexertion, increased blood-pressure or possibly neuropathic changes.

From the clinical side our patient was also most interesting. The

[8] Wiener klin. Wchnschr., 1906, 726.   [9] Ibid., 723.

striking feature was the occurrence of abdominal symptoms which simulated those of an acute surgical condition. This simulation of an acute surgical condition can readily be understood when we recall that the branches of the celiac axis are the most frequent site of the lesions. These abdominal pains may occur at any time during the course of the disease and may even usher it in. The frequency of this mode of onset is estimated at 25 per cent. by Lamb in the series of cases which he studied. Abdominal symptoms may also be the leading complaint during the course of the disease, and abdominal pain of some kind is present at some time or another in nearly all the cases. The pains come on in severe colicky attacks and are usually referred to the upper abdomen. They may also be felt in the region of the kidney, or they may be diffuse pains all over the abdomen. They may be localized or they may radiate to the back. These attacks may last several days and are usually associated with abdominal tenderness and distention. If to this local picture we add the general symptoms of fever, a very high polynuclear leukocytosis and albuminuria we need not wonder that these patients are suspected to be suffering from an acute surgical condition. That the severe attacks of abdominal pain were the leading feature of our patient's complaints was evidenced by his admission to the surgical division when he applied for relief. Although he was under very careful observation for two weeks no definite conclusion could be reached with such a varied array of symptoms, and he was finally operated on with the expectation of finding some unusual condition in the upper abdomen.

This type of the disease is also well shown in Lamb's Case II: A girl, aged ten years, had a sore-throat and acute abdominal symptoms nine days before admission to the hospital. When admitted she had a fever of 102.6° and a leukocytosis of 33,000 with 93 per cent. polynuclears. A diagnosis of acute appendicitis was made and she was operated on. The appendix and peritoneal cavity were found to be normal and nothing could be found to explain the acute abdominal symptoms. Both of the cases reported by Klotz have interesting abdominal features, and it is a curious coincidence that in both patients death resulted from hemorrhages into the peritoneal cavity from ruptured aneurysmal sacs. His first patient was a woman, aged thirty-three years, whose final illness was four weeks in duration, beginning with a severe cold which followed exposure. Her chief complaints were pains in the muscles and joints; later on she had intense, cramp-like pains in the abdomen. She ran a low, continuous temperature and had albuminuria, a slight icterus and a leukocytosis of 12,000, with 76 per cent. polynuclears. In the presence of a tender and palpable gall-bladder a diagnosis of empyema of the gall-bladder was made. The contemplated operation was deferred, as the patient improved very much. On the following day (six days after the onset of the acute abdominal

symptoms) she suddenly went into collapse and died. The autopsy revealed the typical lesions of periarteritis nodosa, with aneurysms on the hepatic and cystic arteries. One of the aneurysms on the hepatic artery had ruptured and had led to an extensive hemorrhage about the liver and into the peritoneal cavity.

Klotz's second case was equally unusual, and by a curious coincidence occurred within a month of the first one. A fifty-three-year-old man was admitted for vague symptoms and a history of not feeling well for a year and a half. A recent cold had accentuated these symptoms. Two weeks after admission he had a slight fever, a sore-throat and a purpuric rash on the legs, thighs and chest wall which suggested erythema nodosum. One of these nodules became larger and fluctuating. On incision a thick, brownish gelatinous material escaped. The cultures from it were sterile. From the time of the onset of the tonsillitis he ran a low, continuous fever; there was a leukocytosis of 13,000. The blood Wassermann was four plus. Some of the nodules which suggested erythema nodosum disappeared and new ones came. One of these nodules was excised, but a diagnosis of the arterial lesion could not be made, owing to the extensive disintegration and hemorrhage which were present in the excised tissue. Cultures from the excised nodule and the blood were negative. Clinical manifestations of an intra-abdominal condition were not present, his main complaints being those of a decompensated heart. After a five-weeks' stay in the hospital he died rather unexpectedly, although during the last week he became progressively weaker. At the autopsy a very extensive periarteritis of the branches of the celiac axis was found, together with a hemoperitoneum; the latter was the result of hemorrhages from the vessels of the gastrocolic omentum and pancreas. The nodules in the skin were also due to periarteritic nodosa changes. Chronic endocarditis, evidently of long standing, and syphilitic cirrhosis of the liver were also found.

The subcutaneous nodules are most important in making the diagnosis. In the few cases in which the diagnosis was made during life it was only established by means of them. Ours is the only case in which it was reached without them. Unfortunately they are present in only 25 per cent. of the cases. It is interesting to note that the diagnosis may be missed even when they are present and examined for diagnosis in a suspected case, as happened in Klotz's Case II. The subcutaneous nodules are small and firm and feel like shot along the course of the artery; they are quite superficial. They have been found in the face, neck, thorax, abdomen and extremities. They are usually painless; rarely are they inflamed and tender. Pulsation is seldom observed in them, as thrombosis occurs early. Very rarely their size is larger than a pea; a few have been reported which reached the size of a hazelnut. In Benedikt's case, besides other nodules, there was a tumor the size of a fist in the lower right abdomen. As this simulated an appendicular abscess an

operation was performed. The mass proved to be an intramuscular hematoma due to the rupture of an aneurysmal sac on one of the intramuscular arteries. They rarely suppurate; the only exceptions are the two instances which have just been referred to.

A maculopapular rash was also present in our case. Eruptions of the most varied types have been reported by other observers; they are either hemorrhagic or toxic. They may usher in the disease or they may occur later on in successive crops. Desquamation of the entire body without a preceding rash has also been reported. These rashes, when associated with the other confusing general symptoms, are most misleading and the possibility of their occurrence should be remembered in a suspected case. The other skin manifestation which deserves notice is edema, which may involve the ankles, the face or the entire body. In some form or another it has been observed in a large majority of the cases. As nephritis is so frequent in this disease it is a fair inference to assume that it is renal in origin.

The very high leukocytosis deserves special mention. In our patient it ranged between 30,000 and 50,000 in the acute period, and long after the fever had subsided it persisted at 20,000. Even in the terminal stages when, as the autopsy showed, the vascular lesions were far advanced in the process of healing it was still as high as 13,000. Blood counts have only been reported in the cases which have been observed in the last decade; they have uniformly been very high. The polynuclear cells have also been very high in the percentual relation. We wish to direct attention to the possible diagnostic value of these high white cell counts in doubtful cases of irregular pains, especially in the abdomen, when associated with fever and doubtful rashes.

Pains in the voluntary muscles and along the peripheral nerves are also important symptoms which are rarely absent. They may be so pronounced as to lead to the suspicion that the case may be one of poliomyositis or trichinosis. Indeed, in the classical case which gave the disease its name, Kussmaul believed that he was dealing with an unusual type of trichinosis until the development of atrophies and other symptoms convinced him of his error. The pains in the muscles are of varying degrees of intensity and may be tearing or cramp-like in character. There may also be pains in the joints. Lamb noted their occurrence in 39 per cent. of his series. They may be acute enough to simulate acute articular rheumatism, especially if several joints are involved.

Attacks of tonsillitis or a history of sore-throat are reported in so many cases that attention should be directed to the throat in any discussion of this disease. Recurrent attacks of tonsillitis or quinsy are of frequent occurrence in the previous history, and the patients often refer the beginning of their illness to an attack of sore-throat. This is well demonstrated in our own case and in those reported by Lamb and Klotz.

Lamb has directed attention to the fact that symptoms and physical signs referable to the heart are strikingly absent, although the coronary arteries are so frequently involved. We can corroborate this statement, and it is difficult to conceive that a heart whose structure was so extensively diseased as shown by the pathological studies should have functionated so normally.

It is also surprising that the case records which have been published do not show more evidences of renal involvement, since the small arteries of the kidneys are attacked in nearly every case. In Lamb's series of 38 cases no mention of the urine is made in 10 cases. In 5 it is definitely stated that albumin was not present. Often, however, there was only one examination, and the condition of the kidneys at the necropsy indicated that albumin would have been found if repeated examinations had been made. In 23 cases, or 82 per cent. of those in which the condition of the urine is given, albumin was present, generally in moderate amount, but varying from a trace to as high as 6 per cent. In the cases in which repeated examinations were made albumin was not always present but showed exacerbations and remissions. In 14 cases casts, generally hyaline and granular, were present. Blood was reported in 9 instances.

Our case sheds some light on these apparent discrepancies and demonstrates that the condition of the urine does not necessarily correspond with the changes in the kidneys. That the kidneys had been involved early in the course of his disease is evidenced by the severe attacks of renal pain and ureteral colics and hematuria, which made him seek relief at the hospital. The urine was negative, however, save for a few red blood cells. And this in the presence of a marked nitrogen retention in the blood, i. e., urea nitrogen, 35 mil.; incoagulable nitrogen, 95 mil.; creatinin, 2 mil. The urinary evidences of the nephritis did not appear until he had been in the hospital for five weeks, and even then the urinary changes were only those of a mild nephritis. The eye changes, however, appeared very early. But when he returned to the hospital after an absence of only three weeks, so rapidly had the disease in the kidneys advanced that he presented the appearance of an advanced nephritic, from which he died within five weeks.

The alluring temptation to enter into a discussion of the diagnosis and differential diagnosis of periarteritis nodosa must be resisted. Our case has not made this task less difficult. The reader is therefore referred to the publications of Schroetter, Dickson, Longcope, Lamb and Klotz, where the subject is well presented. How difficult the diagnosis of this disease may be is well demonstrated by the experience of Klotz. Although he had encountered a case in which the diagnosis had been established by the postmortem examination only a month previously, yet the examination of an excised nodule failed to verify the correct suspicion in his second case.

URTICARIA, CLASSIFICATION OF TYPES AND ITS CAUSES.
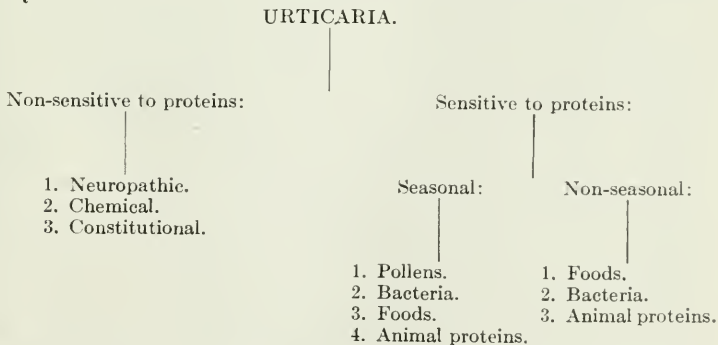
By George L. Lambright, M.D.,

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It has been shown by Walker,[1] Rackemann,[2] Talbot,[3] Fordyce,[4] Blackfan,[5] Fox and Fisher[6] and many others that protein hypersensibility in predisposed persons is a cause of asthma, hay fever, eczema and urticaria. The etiologic information that has been obtained by cutaneous reactions to various proteins exceeds all others and has made it possible to actually cure some of the cases and relieve a number of others.

The causative agents in urticaria seem to be closely related to those of the above diseases. It is a common experience to find one or more associated in the same individual or family. Often when studying asthma, hay fever or eczema, hives may suddenly appear and relief of the foregoing disease may cure the urticaria. From this close relationship one naturally thinks of studying urticaria along the lines of protein sensitization.

From the number of cases seen in my practice and that of others with whom I have been associated I have been able to select cases which show the manner in which protein sensitization may occur. I have tentatively drawn a graphic chart, after the plan of Walker for asthma, which I will show later. In cases studied I have not confined myself to cutaneous tests alone but have had the benefit of careful examinations, special investigation for evidence of focal conditions and roentgen-ray studies. A combination of such evidence is necessary to make intelligent skin tests.

Types of Urticaria.—The following classification of urticaria is based upon etiologic lines. I have found it of assistance as a means of study:

URTICARIA.

Non-sensitive to proteins:

1. Neuropathic.
2. Chemical.
3. Constitutional.

Sensitive to proteins:

Seasonal:

1. Pollens.
2. Bacteria.
3. Foods.
4. Animal proteins.

Non-seasonal:

1. Foods.
2. Bacteria.
3. Animal proteins.

[1] Causation Urticaria, Eczema and Angioneurotic Edema by Proteins Other than Those Derived from Food, Jour. Am. Med. Assn., March 30, 1918, lxx, 897.

[2] Specific Treatment of Hay Fever, Boston Med. and Surg. Jour., March 18, 1920.

[3] Eczema in Childhood, Med. Clinics of North America, January, 1918, p. 983.

[4] Cutaneous Reactions from Proteins in Eczema, Jour. Cutan. Dis., 1911, xxix, 129.

[5] Cutaneous Reaction from Proteins in Eczema, Am. Jour. Dis. Children, May, 1916, p. 441.

[6] Protein Sensitization in Eczema in Adults, Jour. Am. Med. Assn., October 2, 1920, 75, 14, p. 907.

It can thus be shown that urticaria may occur as a result of protein hypersensitization or otherwise. There seems to be a need of classifying the sensitive type further into seasonal and non-seasonal. For instance, in the seasonal type urticaria may be brought on by inhalation or contact with pollens. In certain seasons epidemic infections are numerous and hives may occur from this cause. Recent cases were reported associated with the epidemic of influenza. Stokes[7] reported cases that occurred following the administration of influenza vaccine. Certain food, fruits, vegetables and seafoods are seasonal and therefore included in both groups. Animal sensitiveness is placed in both divisions, as it may be seasonal from close relationship by being indoors, or in certain other seasons when on vacation in summer resorts, mountains, etc. In the non-sensitive column I have made some rather broad classifications.

Under No. 1 of the neuropathies I have placed the cases seen in which psychoneuroses, hysteria and neurasthenic conditions without discoverable organic or protein sensitization were present. The chemical group had to be represented on account of the fact that certain chemicals when applied locally will produce hives.[8] I have seen hives associated with organic conditions as nephritis, goiter, etc., and so far as I could prove, metabolic disturbances were the cause. I realize that in the non-sensitive group there is need for a broader understanding and the classification may be further extended.

Method and Specificity of Skin Tests. The cutaneous method has been used entirely by me. It is sufficiently sensitive and yet not too sensitive, without danger, simple, and is therefore the method of choice. It is briefly as follows:

"The skin surface, preferably the forearm, is cleansed with 40 per cent. alcoholic solution. Abrasions one-eighth inch in length are made with a sharp scalpel. A small amount of protein of food, animal, bacteria or plant in solution is placed thereon. Solution is either made by adding a drop of one-tenth sodium hydrate solution to the powder and mixing on abrasion with a toothpick or solution made on a watch-glass and placed on the cut. Within ten to thirty minutes, if the reaction is positive, a small wheal develops which may or may not be accompanied by an area of erythema and swelling. One of the abrasions is left as a control, and by this method a comparison of the natural reaction to a cut and the application of the soda solution may be obtained. Wheals less than 0.5 cm. in diameter are not considered positive. According to the amount of reaction a classification may be made from 1+ to 4+."

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[7] Etiologic Analysis, Chronic Urticaria following Influenza Vaccination, Med. Clinics of North America, November, 1919, iii, 821.

[8] Sollman, J.: By Animal Aromatics and Urea Derivatives, Jour. Phar. and Exper. Therap., August, 1917, x, 147.

The above is briefly the method in common use, and under ordinary circumstances will be sufficiently clear in its reaction. Occasionally one meets with a dermatographic skin in which wheals will develop larger than 0.5 cm. in all cuts, or there may be some slight variation in the size.

In cases of multiple sensitization a wise plan is to make up various dilutions of the solutions, to which reaction occurred, and determine the amount of sensitiveness.

A positive reaction means that sensitization exists to foods parenterally. It does not prove that such a condition exists otherwise. This perhaps may explain why elimination of proteins has no effect on hives in some cases. In single sensitization it is more liable to be the cause. In children this is more prone to be true to certain classes of food. It has seemed to me that a wise plan would be to test a series of normal individuals to proteins to determine what proportion would give positive reaction without evidence of disease. By this method we have modified our ideas as to value of findings in other tests, particularly as to acidity of stomach contents. It would no doubt be found that a number would react from inherited tendencies. The method of exciting the latent sensitization would be next in order.

Urticaria from Foods.—In childhood it is a simple matter without skin tests to determine foods producing urticaria. The diet is simple and the outbreak often follows promptly from the addition of a new article. Eggs, wheat and oats are the chief ones to which children are most often sensitive. As has been shown by Blackfan in his studies of eczema a family history of specific sensitiveness to a certain food often exists. In adult life it can readily be seen that the determination is not so simple. I have found quite a number of adult cases to be sensitive to foods when applied to the skin, but have been disappointed in the results obtained when they were eliminated from the diet. In such a capricious skin condition it is very difficult to draw conclusions in regard to the effect of the withdrawal of certain susceptible foods. In the last eight cases I found multiple sensitization present. In all of these, in so far as could be determined, there was no change in the urticaria by eliminating the foods. I am quite sure others have met with disappointment in this respect, for I notice that McBride and Schorer[9] in their report of cases met with a number of failures. Also that Engmann in his work at the Children's Clinic, St. Louis, Mo., has had similar experiences. I am unable to explain the cause of the failures other than that there must be other factors and the food reactions are purely secondary. There have been a few cases examined in which favorable results have been obtained, as for instance in the following two cases:

[9] Urticaria and Erythema from Foods, Jour. Cutan. Dis., February, 1916, xxxiv, 70.

CASE I.—Child, aged two years. Was seen in May, 1920. Eggs were added to the child's diet for the first time that morning. One hour afterward the child broke out with giant hives. The child was sensitive to whole egg and egg-white by a skin test. Eggs were not added to the diet until August, when a small amount of egg-white was given and the child again broke out with less severe hives.

CASE II.—Female, adult, aged thirty-eight years, has had hives periodically for the past three years. They first came on while on a camping expedition in Canada. The diet contained at that time an excess of pork and beans. There was a family history of migraine. Skin tests were positive to beans, pork, beef and wheat. All were eliminated from the diet. The hives, which were present over various parts of the body at the time of the tests, cleared up within two weeks. The patient has had a slight return of the hives only when dietary restrictions have been broken.

Pollens as a Factor Pollens as a cause of urticaria have not been considered to be a factor until within recent years. The following case exemplifies an urticaria brought on during ragweed pollinating season in all probability from mass ragweed protein inhalation:

CASE III.—Girl, aged fourteen years. Has had hay fever, commencing about August 15, for four years. Sensitive to ragweed in dilution of 1–10,000. For the past three years, within a week after onset, has had urticaria. Condition usually lasts about a week and subsides without treatment. The past two seasons has had some relief of hay fever by treatment. This year had hives only for one day.

Psychoneuroses. The nervous manifestations present in a number of cases cannot fail to attract attention. Osler stated in his report of cases that a family history of nervous disorders was present in angioneurotic edema. The following is an example of hives from a neurosis:

CASE IV.—Young married woman, aged thirty years, was seen February 5, 1920. Had had hives for five months before seeking relief. They appeared while on a boat trip. Lesions over various parts of the body. Highly neurotic disposition. Urine, blood Wassermann, blood sugar were negative. Roentgen-ray examination of the gastro-intestinal tract showed hypermotility and hyper-peristalsis. Skin tests were positive to chicken, cheese, peaches, banana, pneumococci and Staphylococci aurei. No sources of infection could be discovered. The articles of food to which the patient was sensitive were eliminated from the diet, with no improvement. Dr. Finlayson made a neurologic diagnosis of psychoneurosis

and stated that he had been able to produce hives in this patient while in his office by any excitement to the nervous system, as by anger, fright, emotions, etc.

Focal Infection. Tonsils, teeth, sinuses and gastro-intestinal . tract are most often the seat.

CASE V.—Miss H. was seen in May, 1920. Hives came on following rhinitis and sinusitis. Skin tests showed positive reaction to pneumococci and Staphylococci aurei. Operative measures to improve breathing space and sinus drainage were instituted, with relief of condition. The patient had had hives two weeks before being seen.. Two months have passed and no return has occurred.

Injection of Foreign Protein. The most common example of this manner of producing urticaria is from the injections of vaccines or horse serum. Such a case as this is the following:

CASE VI.—Seen in January, 1920. An exudate had appeared on the patient's tonsils a few days previous and his physician injected antidiphtheritic serum. The throat cultures later proved to be negative. Following the injection a severe urticaria developed. Adrenalin relieved the condition entirely, but it soon reappeared and lasted for several days.

Conclusions.—A study of urticaria along the lines outlined by various writers for asthma, hay fever, eczema by means of cutaneous tests, using food, bacterial, animal and pollen proteins, will be a helpful procedure. It will be a means of discovering the sensitive type of cases. The classification of types of urticaria will be of assistance. Some common examples have been shown. While the results have been satisfactory in these cases a much larger proportion of non-sensitive cases has been encountered. In a large number of those sensitive to foods the elimination has failed to relieve the condition. No statistics are presented, but views are expressed covering a study of cases encountered during the past two years.

THE VALUE OF BASAL METABOLISM STUDIES IN THE DIAGNOSIS AND TREATMENT OF THYROID DISEASES.[1]

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BASAL metabolism studies, particularly in thyroid disease, have occupied the attention of many investigators and clinicians especially in the last few years, and out of these studies have arisen several

practical methods of determination of basal metabolism as well as certain definite conclusions as to the deductions which one is able to draw from such experimental work.

By the basal metabolism of an individual is meant that minimum chemical change resulting from the continuous organic cellular functions of the body which are essential for life. These chemical changes require oxygen, and it is possible by measuring the oxygen consumption by the body at complete physical and alimentary rest to determine the minimum heat production or basal metabolic rate for the individual. Thus the basal metabolism can be measured by calorimetric estimations of the heat production resulting from the continuous chemical changes in the body, either by direct computations of the heat given off, as is made possible by the large Atwater Rosa-Benedict apparatus, or by indirect calculations of it from the oxygen consumption by the body.

How gradually through the work of Lavoisier about 1780, Liebig about 1842, Voit about 1857, Pettenkofer about 1866, Rubner about 1885, and finally Atwater and Rosa about 1897, the basis of our present knowledge of metabolism developed, is outlined in Lusk's *Science of Nutrition*. Since then, through the work of Sonden and Tigerstedt, Jacquet, Grafe, Speck Zuntz, Geppert, Tissot, Douglas, Rolly, Benedict and Carpenter and DuBois, several types of apparatus for estimating metabolism by measuring the respiratory exchange have been constructed and many metabolic studies of adults and children in health and disease by many other investigators have been carried out.

Du Bois recently reviewed the history of basal metabolic studies in thyroid disease. Some of the noteworthy contributions to this phase of metabolism in which we are interested will be mentioned. Magnus Levy, in 1895, was first to demonstrate an increase in metabolism in hyperthyroidism and a decrease in myxedema. In 1899 Hirschlaff reported a severe case of hyperthyroidism, with autopsy findings, in which the rate rose to 105 per cent. above normal. In 1909 Bergman found a decrease in metabolism in myxedema and an increase after thyroid administration. The most important recent articles have been those of Du Bois, Means, McCaskey, Plummer, Boothby and Rowntree.

All investigators agree that basal metabolism depends largely upon thyroid activity and that an increase in the activity of this gland raises the metabolic rate above normal, while a decrease in thyroid secretion depresses the rate below its normal level. Other ductless glands, especially the pituitary and ovary control metabolism to a lesser degree, though certain diseases such as fevers, lymphatic leukemia, hyperpituitarism, polychemia, severe diabetes, cancer and pernicious anemia also increase the basal metabolism rate and starvation, hypopituitarism and wasting diseases decrease

it, all these conditions can easily be ruled out in a careful diagnostic study. Thus, for proper investigation, basal metabolic rate determinations in thyroid disturbances are coming to be recognized as being as indispensable as is the Wassermann reaction in syphilis or temperature determinations in fever.

Because of this recent recognition of the value of metabolic rate determinations in the study of thyroid diseases, two types of apparatus, namely, the Benedict portable respiration apparatus and the modified Tissot respiratory valve apparatus, have been perfected for the clinical estimation of basal metabolism. The Benedict type is so constructed that pure oxygen is kept circulating through the patient's lungs, the CO_2 being extracted from the expired air by soda lime and the metabolic rate being determined from the oxygen consumption which is read off directly from the spirometer scale. The Tissot type necessitates the collection of the expired air during a definite short period of time in a large spirometer, samples of which are later analyzed by the Haldane gas analysis machine for oxygen and CO_2, from which the oxygen consumption and the respiratory quotient are computed.

This Benedict type has gained considerable recent recognition as an instrument suitable for office estimations of basal metabolism through the articles of McCaskey and advertisements in the journal which recommend it for clinical use. Only casual mention has been made, however, of the modified Tissot unit which has been the instrument most commonly used by clinical men. The Tissot type has certain advantages not enjoyed by the Benedict. These are fewer connections, no necessity for electric current, no necessity of providing oxygen, no possibility of motor difficulty, no necessity of daily cleansing of spirometer and motor and no replenishing of soda lime and calcium chloride mixtures. Benedict and Carpenter both repeatedly state that the Tissot would be preferred to the Benedict in all cases were it not for the time-consuming and difficult gas analysis.

In regard to this analysis it necessitates, of course, care and accuracy, and because of this phase of technic with the Tissot, about three-quarters of an hour more time is consumed in the test than is necessary in the use of the Benedict. However, the Tissot type furnishes an accurate measure of the respiratory quotient and the CO_2 excretion, which is comparable, as Carpenter has shown, with that obtained with the universal respiration apparatus and which cannot accurately be determined with the Benedict portable type. Moreover, it must be realized that this metabolic work cannot economically be carried out by many men in any community and that the actual work will probably be done in most cases, by a well-trained technician, under the supervision of the clinician, to whom an extra hour of time will mean little, providing more accurate

and complete data are obtainable.   The clinical applicability of the Tissot method is shown on a large scale at the Mayo Clinic, where several units are in operation all morning, and where the gas analyses are made by high-school girls under the supervision of Doctors Boothby and Sandeford.

The writer has been interested in basal metabolism in thyroid disease since 1915, when he came in intimate contact with the work of Means, Joslin, and Du Bois in Boston and New York.   This interest was intensified last October when he watched the work of Boothby and Plummer at the Mayo Clinic.   Since then the modified Tissot type of apparatus has been established in his office and it has been found to be most satisfactory for clinical use.   He has followed the instructions given by Boothby in his recent monograph, both in regard to the manufacture of the spirometer, the setting up of the Haldane and the actual experimentation and computations.

Through the able assistance of Margaret Eakin we have made careful clinical and metabolic studies of some 80 cases of actual and suspected thyroid disturbances and have become convinced of the value of basal metabolic rate determinations as a guide to both the diagnosis and treatment of these conditions.

In the first place, *mild or definite cases of hyperthyroidism can be differentiated from neuroses and early tuberculosis, by basal metabolic rate determinations.*   In a series of 49 cases referred to me, with the diagnosis of actual or suspected hyperthyroidism, only 16, or 39 per cent., had rates above the approximate normal limits of ± 10 per cent.   Clinically, all the cases showing rates higher than $+10$ per cent. were definitely hyperthyroid.   Moreover all the other cases, with the exception of case 23, that showed normal metabolic rates had one or more symptoms and signs which suggested hyperthyroidism, though a very careful scrutiny of their records in most cases would incline one to doubt the existence of too much thyroid secretion.   It is in these cases, especially where, as in Case 31, a decided exophthalmos was present, or in Case 1, where marked tachycardia, nervousness and sweating occurred, or in Case 22, where a tachycardia following a recent tuberculosis persisted, that a method of deciding on the responsibility or harmlessness of the thyroid gland is of great importance.   We all see tremulous, nervous, excitable, weak and thin individuals who may or may not be hyperthyroid in type, the definite determination of which state is impossible without such a test as this one we are considering. Clinicians especially interested in heart diseases and in tuberculosis are beginning to see the advantage of these determinations in their diagnostic work.   The basal rate determinations are being found of increased value in the analysis of tachycardias.   Peabody was able by metabolic studies to confirm his impression that the thyroid was not causative in the etiology of the "Irritable Hearts of Soldiers." McCaskey, moreover, emphasizes the importance of this use of the

metabolic rate as a diagnostic procedure in these types of disturbances.

Again, the *severity of an obvious case of hyperthyroidism can be more accurately determined through basal metabolism rate determinations, than by any other method of analysis.* Thus in our series Case 14 had symptoms which could easily suggest a very severe state of hyperthyroidism, whereas her metabolic study placed her in the mild group of cases. Case 27 impressed one as suffering with extreme hyperthyroidism, and it was with much satisfaction I found him to be only in the severe type of the disease. Case 36 had encephalitis lethargica develop on top of her hyperthyroidism, and the problem of how much the thyroid was to blame for the prolonged convalescence and weakness was greatly illuminated by the basal metabolic rate result. Case 56, who had exaggerated symptoms and signs of hyperthyroidism, did not suggest before our metabolic rate study the unusually high rate of +128 per cent. Finally, Case 73, who one year ago had a marked struma with tachycardia, exaggerated tremor and loss of weight and had her septic mouth cleaned up at that time, still has marked exophthalmos and some tremor. Though I thought her hyperthyroidism was nearly gone, I was distinctly surprised at the normal rate.

As a guide to the amount of roentgen-ray therapy needed in a case of hyperthyroidism due to hyperplasia of the thyroid gland, basal metabolism studies are indispensable and are necessary for scientific work. Case 10 when first seen was a severe type of true hyperthyroidism, and at that time we were not ready to make metabolic rate determinations. We had given her four rounds of roentgen-ray treatments when her first test was made, and in view of her increased weight, slower pulse, great improvement in her nervous condition and her increased strength, together with a rate of only +7 per cent., we discontinued roentgen-ray therapy for one month. By that time her clinical condition was not quite so favorable and her rate had risen to +12 per cent., because of which another round of roentgen ray was given. Case 17 has not been benefited, however, to the same extent, though five complete rounds of heavy therapy have been given. Case 27 had his rate reduced from +58 per cent. to +46 per cent. after two complete rounds of roentgen ray. Case 23, with a rate of +10 per cent. after eleven roentgen-ray exposures, had had marked hyperthyroidism before treatment. Case 36 has had definite clinical improvement and a reduction of rate from +33 per cent. to +21 per cent. after four rounds of roentgen-ray therapy and without absolute rest. Case 55 has had definite amelioration of symptoms and reduction in rate by the use of roentgen ray over several months. In Case 42, however, the condition became steadily worse, operation being contra-indicated with death in a few weeks, though roentgen ray was given in large doses on three different occasions. Our experience indicates a

definite beneficial effect of roentgen ray in cases of true exophthalmic goiter. The amount of therapy necessary to reduce the metabolic rate to normal limits certainly varies with the case. That there is a danger of too much roentgen ray is certain. Moreover, roentgen ray will probably be found ineffective in fulminating cases of the type of Case 42 in our series. With the increasingly low mortality after operative treatment in mind, we cannot at this time recommend roentgen ray as a substitute for surgery in all cases of hyperthyroidism. When it is used the effect must be carefully followed by metabolic rate determinations. This is especially emphasized by an experience of a colleague in another city whose patient remained well for two years after a thyroidectomy. Then he became weak, nervous and his condition suggested a return of his hyperthyroidism and he was sent for roentgen-ray therapy. Soon afterward it was found that he had a −35 per cent. rate and his condition immediately improved on thyroid gland administration. Here roentgen ray was being given where it was absolutely contraindicated and the error was discovered only through metabolic rate studies. All probable cases of mild hyperthyroidism should have their rates determined before roentgen-ray therapy, since many innocent thyroids are undoubtedly frequently roentgen rayed when they should be left entirely alone. By so doing not only will harm be prevented but false cures by the roentgen ray will not be obtained.

Another use of the metabolic test lies in the indication given as to the degree of the toxicity of adenomas of the thyroid. It is well known that adenomatous thyroids may produce no symptoms of hyperthyroidism or that all the symptoms of Graves' disease may occur. Thus the finding of rapid pulse, nervousness and tremor in an individual with an adenoma of the thyroid calls for a determination as to the responsibility of symptoms, whether the gland has taken on excessive secretory activity or whether a neurosis or sympathetic stimulation is causative. Seven cases (2, 11, 19, 24, 45, 67, and 76) with adenomas have been seen, all of which presented some symptoms indicative of at least mild hyperthyroidism. The first two cases had rates of +53 per cent. and +28 per cent., and case 45 had a rate of +74 per cent. The other cases showed normal rates, thus making the percentage of hyperthyroidism in these suspected adenomas only 43 per cent. Case 2, with a rate of +53 per cent. after very extensive roentgen-ray therapy, illustrates the opinion of roentgenologists today that hyperthyroidism due to adenomatous thyroids is not benefited by roentgen-ray treatment in the marked degree that hyperthyroidism due to hyperplasia of the gland is by such treatment. This woman, subjectively, feels a little better but her thyroid is still very active, as shown by her symptoms, and especially by her recent rate of +57 per cent. In spite of an accompanying diabetes and organic heart disease I shall recommend

her for surgery, to be done by local anesthesia. Case 67 had been diagnosticated as having a toxic adenoma, and before a metabolic study was done had received three rounds of roentgen ray with no amelioration of symptoms. The normal rate recently obtained probably indicates that the symptoms for which she was being treated by roentgen ray were neurotic in nature. Case 76 had an intrathoracic adenoma and recently had been told she was extremely toxic, as indicated by a marked tremor and subjective nervousness. Her rate was a normal one, again indicating a functional rather than a toxic nervousness.

As a guide for the surgical removal of hyperplastic, colloid, and adenomatous thyroids, metabolic rate studies have gained recognition from the leading goiter men of the country. Means emphasizes the importance of these tests before surgery, and with Boothby feels that when rates of over +70 per cent. are found, rest or ligation should be resorted to before thyroid removal. During the last two years the goiter surgery of the Mayo Clinic has been directed in a definite way by the results obtained in their metabolic laboratory. Crile is using this test routinely, moreover, in his preoperative studies. It is generally conceded by surgeons, however, that the metabolic rate is not an inflexible guide for surgery, and that even when the rate is high and the clinical condition favorable it is probably safe to operate. It has been suggested that in most cases it would be wise to lower the metabolic rate by roentgen-ray therapy before surgical removal of the thyroid. Indeed in view of the recent article of Means, in which metabolic and clinical studies two years after surgical or roentgen ray treatment showed equally low metabolic rates, with no mortality resulting from the roentgen-ray therapy, we feel that roentgen ray should be kept in mind in the treatment of true hyperthyroidism due to hyperplasia of the thyroid gland before surgery is decided on. As before stated, adenomatous thyroids must be treated surgically, since the metabolic rates are not easily reduced by roentgen ray.

As a method for the diagnosis of hypothyroidism and myxedema, metabolism tests, moreover, hold as an important position as in the diagnosis of hyperthyroid states. Clinicians are always presuming lack of thyroid secretion because of dry skin, thin hair, slow pulse and obesity. Analysis of such cases often shows a perfectly normal rate and indicates that the responsibility of the symptoms cannot be attributed to thyroid activity. Thus in 25 cases recently referred, with the possibility of hypothyroidism, only ten, or 40 per cent., had metabolic rates sufficiently low to indicate too little thyroid or possibly other ductless gland inactivity. Of these 25 cases, 3, 8, 12, 16, 30, 38, 41, 48, 58 and 60 had obesity as their main characteristic and could easily suggest the lack of sufficient thyroid secretion.

CHART I.—BASAL METABOLISM IN ACTUAL AND SUSPECTED HYPERTHYROIDISM.

Case No.	Name.	Date.	Age	Sex	Ht., in cm.	Wt., in kg.	Av. pulse.	Av. resp.	CO_2 given off c.c.	O_2 absorbed, c.c.	Respiratory quotient.	Cal. per hr. Per kg.	Cal. per hr. Per sq.m.	Metabolic rate, per cent.	Duration of symptoms.	Symptoms, because of which patient was referred for investigation.	Remarks.
1	G. B.	1920 Mar. 13	29	F	169.57	58.77	130	18	176.5	215.8	0.810	1.05	36.9	−1.6	7 yrs.	Nervousness; tachycardia	Quiet; drowsy.
2₁	E. A.	15	57	F	146.3	50.45	124	20	197.6	267.79	0.730	1.502	53.72	+53.5	2½ yrs. (adenoma of thyroid)	Typical symptoms of hyperthyroidism	Quiet.
2b	E. A.	Aug. 13	57	F	146.3	47.3	120	20	190.2	269.2	0.707	1.590	55.05	+57.2	. . . .	Has had five rounds of x-ray treatment	Quiet.
5	M. M.	Mar. 18	25	F	157.0	52.9	120	26	156.2	203.4	0.768	1.094	37.92	+1.12	1 yr.	Marked nervousness; slight tremor; loss of weight; tachycardia	Quiet.
6	K. M. R.	18	29	F	153.5	49.8	105	17	139.5	163.5	0.854	0.956	32.68	−12.8	3 yrs.	Marked nervousness; under weight; slight struma of thyroid	Restless.
7	J. F. J.	April 21	41	F	165.8	44.35	76	13	121.0	176.0	0.688	1.116	33.82	−6.06	7 mos.	Marked nervousness; sweating; tremor; slight exophthalmos; severe diabetes	Quiet.
10a	A. H.	Mar. 24	28	F	154.5	49.6	118	18	165.4	201.7	0.822	1.177	40.23	+7.28	1 yr.	Acute onset of all typical symptoms of hyperthyroidism; has had three x-ray treatments, the last being on Feb. 19, 1920, with marked improvement resulting	Quiet.
10b	A. H.	April 22	28	F	154.5	48.65	114	20	163.2	215.0	0.760	1.259	42.2	+12.5	1 mo.	Slight increase in nervousness	Quiet.
11	A. M.	Mar. 21	49	F	161.5	53.2	95	20	209.2	246.2	0.85	1.353	46.15	+28.2	2 yrs.	Tremor and eye signs; adenomatous thyroid of 17 yrs. duration, showing moderate toxic symptoms for 2 years	Quiet.
14	P. C.	27	21	F	160.0	54.55	128	20	227.4	288.2	0.789	1.519	53.15	+41.8	5 mos. (following influenza)	Marked nervousness; tremor; moderate eye signs; tachycardia; sweating	Quiet.
17	Mr. L.	April 2	39	M	166.5	56.6	88	15	246.7	296.5	0.832	1.545	53.2	+34.7	1 yr. (following influenza)	Marked nervousness; moderate eye signs; loss of weight; tremor, weakness	Quiet.
18	E. R.	6	19	F	162.5	49.4	65	18	150.2	179.2	0.839	1.054	34.51	−9.1	6 mos.	Symmetrical struma; slight nervousness	Quiet.
19	R. E. B.	7	33	F	161.0	52.7	74	16	146.3	171.9	0.837	0.968	32.85	−6.92	7 yrs.	Moderate nervousness, enlarged thyroid for six to seven years, increased in last year	Quiet.
20	B. H.	8	18	F	164.5	56.62	64	14	142.8	193.9	0.737	0.974	34.4	−7.1	2 yrs.	Symmetrical struma; slight nervousness	Quiet.
21	M. T.	9	34	F	151.0	46.62	75	15	127.3	163.9	0.777	1.007	33.55	−4.61	10 mos. (following influenza)	Nervousness; loss of weight; diarrhea	Quiet.

			Age	Sex	Ht.	Wt.									Duration	Remarks	Condition
22	G.H.	20	26	F	158.0	62.54	80	14	148.1	185.2	0.80	0.852	32.85	− 9.18	1 yr.	Tachycardia; moderate nervousness; recent tuberculosis	Quiet.
23	M.W.	15	23	F	161.0	48.4	135	15	165.3	211.2	0.784	1.250	40.4	+10.56	1 yr.	Had typical symptoms of hyperthyroidism, which have been diminished by 11 x-ray treatments	Quiet.
24	R.B.	14	38	F	170.5	64.3	72	18	193.7	243.4	0.796	0.620	39.99	+15.3	20 yrs.	Large adenomatous thyroid; nervousness; dyspnea; loss of weight	Quiet.
25a	C.N.L.	16	41	M	174.5	60.9	100	14	290.0	366.0	0.793	1.733	60.85	+66.5	8 mos.	Typical symptoms of hyperthyroidism; but able to do light work	Quiet.
27b	C.N.L.	May 18	41	M	174.5	61.6	100	11.5	283.1	337.2	0.84	1.592	56.45	+54.3	....	Has has two x-ray treatments, with marked improvement	Quiet; had one dish oatmeal.
31	B.G.	April 21	46	F	164.0	51.15	74	14	140.4	173.0	0.812	0.977	32.45	− 9.88	1 yr.	Marked nervousness; weakness; moderate exophthalmos	Quiet.
32	E.O.	23	19	F	156.0	51.83	92	16	140.9	204.9	0.688	1.133	38.8	+ 2.75	3 yrs.	Nervousness; tachycardia; symmetrical struma of thyroid	Quiet.
33	H.B.	26	34	F	159.0	51.2	79	15	156.2	196.2	0.795	1.103	37.65	+ 3.15	2 yrs.	Recent tuberculosis; nervousness; moderate tachycardia	Quiet.
34	H.S.B.	27	26	F	167.0	57.25	65	12	139.4	193.8	0.720	0.955	33.45	−10.8	1 yr.	Exophthalmos; moderate tremor and nervousness	Quiet.
35	F.B.	29	43	M	160.5	51.6	101	24	233.5	335.5	0.696	1.838	62.1	+61.3	1 yr. (following influenza)	Typical symptoms of hyperthyroidism; able to do light work; condition less severe in last two months	Quiet.
36	D.H.P.	May 1	58	F	158.0	54.45	99	22	183.3	255.0	0.719	1.322	46.6	+33.2	6 mos. (accompanying cholecystitis)	Typical symptoms of hyperthyroidism; has had six x-ray treatments	Quiet.
40	B.P.	17	42	F	174.0	52.95	65	12	121.2	157.7	0.769	0.852	27.67	−23.1	2 yrs. (following tonsillect.)	Marked nervousness; weakness; underweight	Quiet.
42	W.H.N.	24	47	F	157.0	53.22	92	17	194.7	248.0	0.786	1.336	46.76	+29.9	6 mos.	All typical symptoms of hyperthyroidism	Quiet.
43	G.F.	26	59	F	163.5	51.6	76	17	120.1	168.4	0.714	0.920	30.8	−12	1 yr.	Nervousness; slight exophthalmos.	Quiet.
45	V.G.	27	35	F	167.0	67.28	130	19	291.5	396.5	0.735	1.667	63.75	+74.6	4 yrs.	Typical symptoms of hyperthyroidism; adenoma	Quiet, very nervous.
47	G.L.	28	31	F	166.5	81.8	85	17	222.6	295.5	0.754	1.027	44.25	+21.2	1 yr.	Marked nervousness; recent tuberculosis; tremor	Very restless.
49	R.R.S.	June 2	32	F	161.0	55.72	71	14	139.3	179.2	0.778	0.922	32.46	−11.0	3 yrs.	Nervousness; long-continued mild temperature	Quiet.
50	T.C.B.	4	40	F	161.0	55.45	74	8	156.0	191.4	0.816	0.996	35.04	+ 2.6	6 mos.	Marked nervousness; tremor	Quiet.
51	F.E.B.	5	58	F	164.0	45.25	108	18	168.8	215.7	0.784	1.366	42.30	+20.9	8 mos.	Typical symptoms of hyperthyroidism	Quiet.
53	R.J.C.	9	24	M	168.5	58.7	92	10	202.8	256.0	0.793	1.252	44.05	+11.5	1 yr.	Nervousness; tremulousness; tachycardia	Quiet.
54	M.C.S.	11	48	F	159.0	61.55	115	19	216.8	274.0	0.792	1.278	48.45	+34.6	5 mos.	Moderate exophthalmos, tremor and nervousness; slightly enlarged thyroid	Quiet.

CHART 1—CONTINUED.

Case No.	Name	Date	Age	Sex	Ht., in cm.	Wt., in kg.	Av. pulse	Av. resp.	CO₂ given off c.c.	O₂ absorbed, c.c.	Respiratory quotient.	Cal. per hr. Per kg.	Cal. per hr. Per sq.m.	Metabolic rate, per cent.	Duration of symptoms.	Symptoms, because of which patient was referred for investigation.	Remarks.
55	E. T.	1920 June 12	23	F	173.0	58.7	118	20	228.3	286.0	0.799	1.403	48.47	+27.0	2 yrs.	Marked exophthalmos, nervousness; tachycardia and loss in weight; has had 7 x-ray treatments	Quiet.
56	P. A. E.	14	41	F	168.5	91.1	122	40	503.0	562.0	0.895	1.816	82.3	+128.6	1 yr.	Very marked nervousness, tremor, sweating and weakness; slight exophthalmos; loss of 60 pounds; marked dyspnea; enlarged thyroid; tachycardia; impossible to rise from a sitting posture	Quiet.
61	E. A.	29	20	F	166.8	49.4	79	20	137.5	202.6	0.680	1.152	37.2	− 0.8	2 yrs.	Small struma; tachycardia; loss of weight	Quiet.
62	N. C.	29	51	F	162.0	76.45	61	15	165.2	216.0	0.765	0.806	34.03	− 2.27	4 yrs.	Marked nervousness; weakness; dizziness	Quiet.
63	H. H. A.	July 9	23	F	161.0	66.6	86	8	146.2	238.7	0.613	1.038	40.72	+ 8.6	1 yr.	Has had skin eruption; thought by dermatologist to be due to thyroid disturbance	Quiet.
65	C. S.	10	42	M	175.0	67.3	50	8	179.3	273.1	0.662	1.142	40.7	+13.05	1 yr.	Tachycardia; sweating; nervousness	Quiet.
67	L. B.	31	26	F	158.5	48.02	86	19	148.7	193.7	0.769	1.151	37.7	+ 0.53	4 yrs.	Marked nervousness; slight tremor; small adenoma; has had right lobe of thyroid removed	Quiet.
68	E. H.	29	53	F	152.0	61.35	70	13	147.7	206.8	0.715	0.948	36.98	+ 5.66	1 yr.	Nervousness; increased perspiration	Quiet.
72	M. M.	Aug. 12	38	F	165.5	79.1	85	17	166.3	234.7	0.709	0.835	35.2	− 3.56	2 yrs.	Nervousness; tachycardia; loss of weight	Quiet.
73 75	L. McC. D. B.	16 28	42 19	F F	152.25 161.0	51.55 47.3	73 86	18 15	139.8 116.7	194.6 181.5	0.718 0.707	1.066 1.108	37.61 35.75	+ 4.48 + 5.94	1 yr. 4 yrs.	Nervousness; slight tremor / Marked nervousness	Quiet, Drowsy; quiet.
76	M. R. W.	26	58	F	164.0	59.7	84	15	146.0	210.0	0.696	0.991	35.8	+ 2.9	25 yrs.	Intrathoracic adenoma of 25 years' duration; recent nervousness, tachycardia and weakness	Quiet.
77	W. H. O.	31	22	F	164.5	65.9	53	16	152.3	213.3	0.715	0.909	34.88	− 7.0	1 yr.	Marked nervousness; emotional instability	Quiet.
79	N. H.	Sept. 4	36	F	162.5	56.4	68	16	162.3	224.9	0.723	1.125	39.8	+ 9.0	1 yr.	Colloid goiter; weakness; marked nervousness	Quiet.
80	H. McQ.	7	26	F	162.0	51.85	76	11	117.8	193.2	0.707	1.047	35.64	− 4.96	4 mos.	Nervousness; slight struma, gradually reducing since tonsillectomy one month ago	Quiet.

None of them showed too low rates. Cases 64, 66 and 78 had been taking thyroid just before the metabolic rate was determined. The slightly increased rates might indicate the ordinary response of a normal individual to thyroid medication, and to be sure these cases are hypothyroid in type, the rates should be determined again two or three weeks after the cessation of thyroid administration. Case 59 when first seen one year ago was a typical advanced case of myxedema with anemia, non-pitting edema and mental disturbances. At present she is taking thyroid very intermittently and feels well, though her rate is still −28 per cent. Case 48 is one of obesity with a collar of abnormal fatty deposits around the neck. His rate of +18 per cent. indicates no lack of thyroid secretion. He eats moderately and perspires freely, but still maintains his excessive fat in spite of his rather high rate.

Finally, as a guide to correct thyroid administration, metabolic rate determinations are of the greatest value. As already stated, hypothyroidism with consequent thyroid therapy is undoubtedly often misdiagnosed. Metabolic studies, moreover, as pointed out by Means, usually show it takes much less thyroid to keep that rate at normal than is often given, and equally important it is found that the rate can be elevated considerably above normal for some time without producing symptoms of hyperthyroidism. That such therapy does harm, moreover, even when symptoms are not present, is shown by a case recently seen in which thyroid administration in rather large dose for obesity suddenly produced a dilated thyrotoxic heart. This emphasizes the necessity of the use of the metabolic rate studies as a means of first being sure of your clinical diagnosis and second of gauging the amount of thyroid therapy. At present in the use of the dry thyroid gland we have little idea of the strength of the preparation. Kendall has shown that the amount of thyroxin in thyroids varies according to seasons. The active principle of the thyroid which Kendall recently has isolated in pure crystalline form will probably soon be used by many physicians for accurate thyroid administration. Plummer has shown that 1 mg. of this thyroxin raises the metabolic rate about 2 per cent. and that it takes about 1 mg. a day to keep the rate of a myxedematous patient up to the normal. However, he determines this dose by metabolic rate studies. The effect of administering desiccated thyroid gland is shown in Case 4, in which the rate was raised in one month from −13 per cent. to +7 per cent. by a dose of 1 grain twice daily. Possibly this dose, for this woman of good size, will, if continued, raise her rate above normal; but this can best be determined by other tests. We feel that thyroid administration to children should be guided, if possible, by metabolic studies, and that these studies should be the basis for the diagnosis of mild hypothyroid states that are so often assumed by clinicians in their young patients. No child should receive thyroid simply because he looks "a little hypothyroid in type."

CHART II.—BASAL METABOLISM IN ACTUAL AND SUSPECTED HYPERTHYROIDISM.

Case No.	Name	Date	Age	Sex	Ht., in cm.	Wt., in kg.	Av. pulse.	Av. resp.	CO₂ given off c.c.	O₂ absorbed, c.c.	Respiratory quotient.	Cal. per hr. Per kg.	Cal. per hr. Per sq.m.	Metabolic rate, per cent.	Duration of symptoms.	Symptoms, because of which patient was referred for investigation.	Remarks.
3	1920 J. E. L.	Mar. 17	40	F	167.5	103.8	90	14	232.0	284.2	0.817	0.792	38.79	+7.75	38 yrs.	Over weight	Quiet.
4a	A. K.	18	37	F	155.5	68.55	79	21	147.1	181.4	0.812	0.784	37.5	−13.7	6 mos. (following encephalitis lethargica)	Increased weight; apathy, weakness; moderate exophthalmos	Quiet.
4b	A. K.	May 3	37	F	155.5	68.55	79	21	172.2	231.5	0.744	0.96	39.12	+7.18	....	Has taken 1 gr. of desiccated thyroid twice daily for one month	Quiet.
8	J. S. R.	April 12	57	F	158.0	73.0	65	18	153.0	185.2	0.832	0.707	30.72	−12.2	5 yrs.	Obesity; sluggish mentality; thin hair	Quiet; sm. breakfast.
12	M. S.	Mar. 25	79	F	164.4	81.8	58	16	164.1	195.3	0.841	0.694	30.12	−8.7	2 yrs.	Dry skin; falling hair; slight mental dulness; no increase in weight	Quiet.
16	R. B.	April 1	31	F	172.0	98.9	64	11	200.6	252.8	0.794	0.735	34.42	−5.7	4 yrs.	Obesity; dry, inactive skin; thin hair	Quiet.
26	F. R.	15	26	F	163.5	68.4	84	14	196.1	231.8	0.846	0.986	38.44	+2.5	4 mos.	Slight increase in weight; pregnancy, with some suggestions of hypothyroidism	Quiet.
28	Mrs. M.	19	48	F	164.5	54.3	78	10	132.7	171.9	0.772	0.907	30.95	−14.0	20 yrs.	Secondary anemia; relative lymphocytosis; myxedematous facies	Quiet.
30	L. Y.	May 20	19	F	161.5	69.35	66	18	176.9	224.3	0.789	0.929	37.05	−2.5	3 yrs.	Obesity; inactive skin	Quiet.
37	E. E. M.	7	59	F	161.0	75.8	71	17	131.8	194.6	0.678	0.721	30.38	−13.2	4 yrs.	Nervousness; obesity; dyspnea	Quiet.
38	H. J. K.	12	31	F	160.5	96.77	72	17	204.8	283.6	0.723	0.827	40.01	+9.62	8 yrs.	Obesity; inactive skin	Quiet.

No.	Initials	Date	Day	Age	Sex	Height	Weight									Duration	Remarks	
39	J. A.		15	19	F	175.0	96.45	63	12	167.3	243.6	0.688	0.711	32.27	−15.1	4 yrs.	Obesity; apathy; slow pulse; thin hair	Quiet.
41	L. C. C.		22	52	F	162.0	89.15	68	16	155.4	225.0	0.692	0.710	32.55	− 7.0	20 yrs.	Obesity; lack of perspiration; thin hair	Quiet.
44	R. E. D.	June	2	36	F	169.5	95.3	64	15	176.2	239.4	0.742	0.710	32.68	−10.45	2 yrs.	Obesity; apathy; dry skin	Quiet.
48	M. T. C.	Aug.	12	48	M	162.75	77.3	73	15	216.5	296.5	0.730	1.083	45.77	+18.87	8 yrs.	Obesity; abnormal fat pads over shoulders	Quiet.
52	Mrs. C.	June	9	38	F	161.5	70.55	60	19	150.7	202.3	0.745	0.814	32.75	−10.27	4 yrs.	Had typical symptoms of hypothyroidism and has been greatly benefited by thyroid administration	Quiet.
58	S. A. M.		24	54	F	162.5	65.6	74	14	151.6	210.4	0.721	0.905	34.73	− 0.77	3 yrs.	Weakness; falling hair; general hypothyroid appearance	Quiet.
59	T. W. H.		24	55	F	164.0	56.4	54	12	101.2	143.0	0.708	0.712	25.12	−28.2	4 yrs.	Typical symptoms of myxedema; has taken thyroid intermittently for last year with great improvement	Quiet.
60	J. T. W.	July	28	72	F	162.5	76.55	63	16	154.1	216.5	0.713	0.796	33.48	+1.45	8 yrs.	Obesity; thin hair; apathy	Quiet.
64	L. H.		1	32	F	150.5	67.3	85	18	175.0	249.3	0.703	1.042	43.0	+17.8	2 yrs.	Has been taking thyroid for one year with marked improvement; 10 pounds loss in weight	Quiet.
66	E. A.	Aug.	6	52	F	165.5	83.72	64	16	188.4	249.4	0.756	0.855	37.15	+ 7.7	2 yrs.	Large and heavy; puffy facies; rather thin hair; active skin; slight nervousness	Quiet.
69	L. L.		2	42	F	154.0	66.65	67	13	133.8	173.4	0.772	0.745	30.07	−16.48	3 yrs.	Generalized non-pitting edema; thin hair; increased weight; apathy	Quiet.
71	G. K.		10	29	F	169.0	95.1	66	9	169.8	220.4	0.771	0.662	30.45	−18.8	3 yrs.	Obesity; apathy; dry skin; has taken 5 gr. thyroid daily for one month with great improvement	Quiet.
74	F. D. L.	Sept.	25	51	F	167.0	63.45	46	11	113.3	166.3	0.688	0.738	27.23	−22.2	2 yrs.	Non-pitting edema; slight apathy	Quiet.
78	L. S.		1	45	F	152.5	67.3	72	16	188.4	240.0	0.786	1.022	41.72	+15.9	30 yrs.	Overweight; dry skin; has been taking thyroid	Quiet.

Conclusions. The *importance* of basal metabolism studies in the handling of thyroid diseases must be recognized. By metabolic rate determinations we are greatly aided in our diagnosis of early and obscure cases of hyperthyroidism. Moreover the degree of severity of an obvious hyperthyroidism can be determined by this test. Again the presence or absence of toxicity of an adenomatous thyroid is made evident through these metabolic studies. As a guide for surgical removal of goiters, surgeons are recognizing the value of this test. Finally in the diagnosis of hypothyroidism and in directing and gauging thyroid administration metabolic rate determinations are of the greatest importance.

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BLOOD CHANGES IN A GASTRECTOMIZED PATIENT SIMULATING THOSE IN PERNICIOUS ANEMIA.

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Gastrectomy is a term often applied to an operation which is merely a resection of the major portion of the stomach. This statement coincides with Sir Berkeley Moynihan's opinion, who reviewed the history of gastrectomy in 1907 and added to the literature two cases of his own, bringing the number of reported cases to seventeen. Three doubtful cases are included in his series. Moynihan states that the first complete gastrectomy was performed by Conner in 1883. The patient died on the table. The next complete resection for carcinoma was performed by Schlatter in 1897. The patient lived fourteen months and died because of a recurrence. Moynihan's patient lived the longest after operation, three years and eight months.

My attention was first called to cases of this type by a man (Case 204441) who presented himself at the Clinic for examination on August 10, 1917. The patient was fifty-eight years of age. He had complained intermittently for the past fifteen or twenty years. His illness was characterized by exacerbations of months' duration and by a dull, heavy pain in the epigastrium immediately after meals. The pain subsided from three to four hours after meals and a sensation developed which the patient described as a hunger more distressing than the immediate after-meal pain; this was relieved by food or drink. A clinical diagnosis was made of peptic ulcer. Malignancy was suspected because of recent continued gastric distress, recent loss of fifteen pounds in weight and rapid decline in strength in the past four months.

The blood- ressure was normal. The hemoglobin was 80, erythrocytes 5,520,000 and leukocytes 8200; the index was 0.7+. No differential count was made. A single tubing of the stomach revealed 120 c.c. of gastric contents in one and one-half hours after a modified Ewald meal. No free hydrochloric acid was found; the total acidity was 4. The roentgenologist reported an indeterminate pyloric lesion. After careful dental examination four teeth were condemned because of apical abscesses and two were held under suspicion. The examination otherwise was of no special importance. The patient was operated on August 18, 1917 (W. J. Mayo). The dictated description of the operation reads as follows:

Operation. "A median incision was made which extended well up to the ensiform cartilage. A movable carcinomatous ulcer was found on the posterior wall of the stomach extending up to within almost 4 cm. of the esophagus. A total gastrectomy was performed

and about 1 cm. of the esophagus removed. The end of the esophagus was sutured to the lateral wall of the jejunum, about 45 cm. from its origin, with interrupted silk and continuous catgut. The line between the esophagus and cardia was visible and was removed. Fat and glands were removed up to the diaphragm. There was very little glandular involvement." The pathological report from tissue removed was "carcinoma of the cardiac end of the stomach with no glandular involvement." Specimen showed the transition of esophageal tissue into the gastric tissue and of gastric tissue into the duodenal tissue. This is interesting from an operative point of view.

The patient returned to the Clinic on June 29, 1918. He had been comparatively well after the operation but had lost seven pounds in weight. He complained of epigastric pain, heart-burn, a heavy
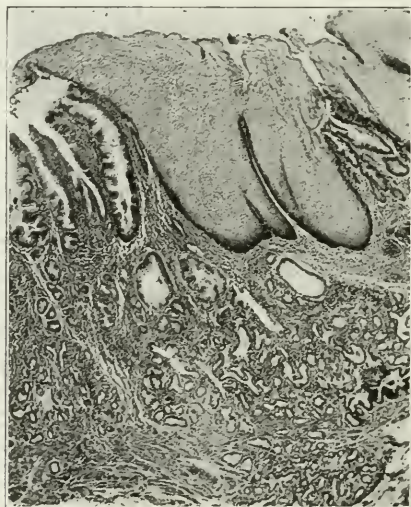
Fig. 1.—Case 204441. Photomicrograph, showing transition of the esophageal mucosa into the gastric mucosa.

sensation and excessive salivation after meals. He was, however, taking three fair-sized meals each day with a glass of milk between meals. The bowel movements were loose, one to three stools each day. The scar of the operation had healed by first intention. Palpation of the abdomen revealed no pathological condition. Because of the patient's apparently favorable condition, with the exception of his weight, no laboratory tests were made.

May 5, 1919, the patient again visited the Clinic. He had grown progressively weaker during the last year, more rapidly the last three months. His diet was general and fairly well balanced. He complained of regurgitation after meals which, if long continued, resulted in the regurgitation of bile; this was fairly well controlled

by salt-water, a prescription of his own. He was somewhat paler than on the previous examination, and his wife stated that he was "more yellow" at times. He weighed 100 pounds. There were no paresthesias or lightning pains; the mouth had not been sore; the mucous membrane of the tongue was somewhat smooth at the edges. The most interesting feature was disclosed by the laboratory study of the case, particularly of the blood. The urine showed a faint trace of sugar, even on a starch-free diet; it contained a faint trace of albumin, a few hyaline casts and pus cells and was slightly acid in reaction; the specific gravity ranged between 1012 and 1018.
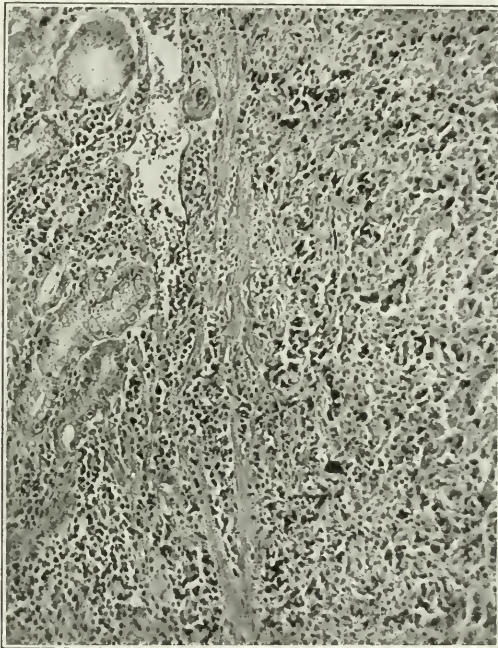
FIG. 2.—Case 204441.   Gastric carcinoma at the base of the ulcerated area.

The blood sugar by the Benedict method was 0.05 per cent. The patient declined further study of the nature of the glycosuria. The cytologic study of the blood revealed the picture of pernicious anemia. The hemoglobin ranged between 53 and 55; the erythrocytes were between 2,000,000 and 2,280,000; the white cells varied between 2200 and 7600, and the color index was constant at 1.2 +. The differential count read as follows: 200 cells counted; polymorphonuclear neutrophils, 59 per cent.; small lymphocytes, 35.5 per cent., large lymphocytes, 5.5 per cent. Slight anisocytosis and poikilocytosis were present. The Ribiere test revealed an increased resistance of the red cells. The blood Wassermann test was negative.

The blood was classed in Group IV. An analysis of the duodenal content estimated in Wilbur and Addis units showed an increase in bilirubin, urobilin and urobilinogen. A neurological examination did not reveal cord changes or other abnormalities. The pancreatic ferment test showed marked reduction of pancreatic activity. Roentgenograms of the chest and the esophageal-jejunal juncture were negative. In consultation it was decided that although the blood count was that of pernicious anemia several clinical features of pernicious anemia were lacking.

While it is realized that the study of one case is of no value in drawing conclusions, it may nevertheless give a possible clue to the cause of pernicious anemia. The case under discussion suggests that the absolute lack of gastric ferments might have something to do with an incomplete or abnormal food-splitting process, the results of which might themselves be hemolytic to the blood or detrimental to the blood-forming organs. Pernicious anemia is invariably associated with achylia. This patient was, of course, completely deprived of gastric juice by the operation, and in the course of time returned to the Clinic with a blood picture of pernicious anemia. Immediately the question arises—Why do not all patients with achylia develop pernicious anemia? a question which cannot at present be answered.

With this theory of the cause of pernicious anemia in mind a thorough review of the French, Italian, German and English literature was undertaken. Much has been written on the operative technic and the immediate postoperative results of complete gastrectomy but with one exception, Moynihan's second case, no report was found in which a patient's subsequent history had been followed for any length of time. Moynihan's patient was a man, aged forty-three years, who had a two-year history of delayed gastric distress one hour after the ingestion of food. The pain was relieved for about one hour by food and by vomiting, which was obstructive at the time of examination. The patient also complained of a dysphagia. May 31, 1907, a complete gastrectomy was performed for carcinoma of the stomach, situated high on the lesser curvature. The esophagus was sutured to the first jejunal loop by interrupted and continued sutures. The patient's immediate postoperative convalescence was rapid and satisfactory and he left the hospital in eighteen days. Moynihan again discussed this case in 1911, stating that the patient had been in normal health until 1910, when "he began to show evidences of profound anemia and was strikingly pale and breathless, and he lost weight." He improved under treatment so that he was able to return to the work he had done formerly. In August, 1910, he again failed in strength, although his appetite was good and he had no indigestion. In October the anemia reappeared and he was obliged to stop work. In the latter part of December the patient was confined to bed; he died January

31, 1911, having survived the operation three years and eight months. The following is the summary from the necropsy report by Goffery Steward: "All the organs exhibited an extreme anemia; the blood in the heart and great vessels was watery. The liver was pale and somewhat fatty. The spleen contained a large and very old infarct. The heart muscle was pale and flabby. No recurrence of the carcinoma was found. The chief points of interest were, (1) the complete absence of any recurrence or dissemination of the malignancy; (2) the profound anemia, and (3) the absence of any striking jejunal dilatation at or near the site of anastomosis."

In Moynihan's case, as in the one herewith reported, there were recurring anemia and weakness, with some of the pathological changes seen in pernicious anemia. Apparently pernicious anemia was not thought of in this case; otherwise a more complete necropsy report would have been made, together with reference to the pathology of the bone-marrow. However the history is suggestive of pernicious anemia and adds its bit to the evidence at hand.

June 1, 1920, our patient returned to the Clinic in a somewhat weaker condition. The recrudescences and remissions of his anemia were of shorter duration than are usually observed in pernicious anemia, while his health in general was in a steady decline.

The patient had had six severe attacks of abdominal pain lasting from one-half hour to five hours; they were sudden in onset, were associated with the vomiting of large quantities of bile and were terminated by the results of a purge. They were not accompanied with jaundice. Urinary symptoms were absent with the exception of slight frequency. The diet was liberal; the patient ate fish, liver, pork, cabbage, eggs, milk, potatoes, squash, carrots, lettuce, radishes, sauces, jellies, candies, fruits, peanuts, toast, waffles and so forth. Practically the only foods which distressed him were meat, which he craved, and fresh bread. These seemed to precipitate regurgitation. The general course of the anemia seemed to be a steady decline with short recrudescences and remissions rather than of marked remissions. The examination of the eyes, including the fundi, was negative. There was no glossitis and the atrophy at the edge of the tongue had not spread. The abdomen was pasty but nothing abnormal was palpable. There was moderate edema of the legs as far as the knees. The systolic blood-pressure was 120 and the diastolic was 80. The pulse-rate was 78. The specific gravity of the urine was 1016; it was slightly alkaline and, aside from a trace of albumin, was negative. The hemoglobin remained quite constantly at 48 per cent. and the erythrocytes varied between 1,420,000 and 1,880,000, the leukocytes between 4000 and 4700 and the color index between 1.2+ and 1.6+. The differential count showed polymorphonuclear neutrophils 64 per cent., small lymphocytes 33 per cent. and large lymphocytes 3 per cent. Anisocytosis was moderate, poikilocytosis and poly-

chromatophilia were slight. The platelet count was 126,000. The blood Wassermann test was again negative. The coagulation time (Lee method) and calcium time were eight minutes. There was an increased resistance of the red cells. A roentgen ray of the chest and of the esophageal-jejunal juncture was negative. The pancreatic test of the stool was less than 250 units (Wohlgemuth test). Schmidt's test of the stool for bile was positive. The stool was thick and white, containing undigested meat fibers, mucus and fat, but no parasites. The blood picture was again considered suggestive of pernicious anemia, but with several unusual features.

It is emphasized that no attempt has been made to drawn conclusions from these two cases; they do, however, open a field for investigation. Dr. Mann, of the Mayo Foundation now has begun as experimental study of the blood changes following gastrectomy.

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STREPTOCOCCUS HEMOLYTICUS EMPYEMA.[1]

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Since February of this present year we have been much impressed by the frequency of pleural effusions. During the pandemic of influenza of 1918 this feature in our experience was very infrequent, but common in this outbreak. Among our cases there were over 25 which could be classified as empyemata; 7 of these were due to the streptococcus hemolyticus. These 7 patients developed this feature as a complication and not a sequel of acute pulmonary infection; they were treated by frequent aspirations, which was followed by subsequent resection; the number of aspirations aver-

[1] The material upon which this article is based was presented at the monthly conference of the staff of the Mercy Hospital. The article itself was prepared for the Pennsylvania Section, Clinical Congress of the American College of Surgeons, at Pittsburgh, October 7, 8, 9, 1920.

aged seven in number; the length of time between aspirations was two or three days; the period before resection was done was between two and three weeks; no washing of the pleuræ was practised and all recovered, but over a prolonged period of time. Two of these cases required second resection despite the proper surgical procedure skilfully carried out.

Moschcowitz, in the Mütter Lecture of 1919, has written extensively on empyema, and from a surgical as well as from a pathologic aspect has done much to bring this old subject to a better understanding. One hesitates after the recent articles by Witenskey, Behrend and others to approach the subject, but the analysis of our work from the internist point of view during these few months has been instructive to us and is the basis upon which this brief record is presented. Before entering upon the consideration of this group, cognizance of certain general ideas seem pertinent. A limited questionnaire presented to certain surgeons among our colleagues upon the subject of empyemata and their results almost uniformly elicited the response that empyema was a simple surgical procedure, and the results of operations were uniformly good. This attitude of the surgeons which has long prevailed seems to us will have to be changed, particularly in dealing with those empyemata which are due to the Streptococcus hemolyticus. The results of former surgical practice in the early part of the war gave the army surgeons such a startling mortality as to compel them to reconsider the methods of dealing with empyemata. The diagnosis of pleural effusion, its pathology and end-results in Streptococcus hemolyticus empyema are of importance and worthy of the greatest concern both from the point of a life-saving procedure as well as for a problem of functional restoration to health. This type of empyema seems now to us, and probably to all surgeons, a different surgical problem from the empyemata due to the other causes. The entity may and probably will disappear in a short time from among our clinical work, but its significance at the present time must be appreciated, and we believe met by certain methods now well known and advised by internists and surgeons of wide opportunity. Again a certain idea must be emphasized, neglect of which makes the results in these cases hazardous, and that is that this is a complication of pneumonia rather than a sequel. While a result of pneumonia always, nevertheless it is an immediate complication, and as such must be met in a different way from other forms. Our work makes us believe, and this is in accord with others, that the effusion is a purulent one from the start and not an effusion, at least not in bulk, subsequently infected. While with the opinion expressed by certain writers that some of these empyemata are cured by simple aspirations, we are not in accord, nor are we in harmony, with delayed treatment. This simple fact of complication rather than sequel should be borne in mind, and we do not feel that it can be over-

emphasized, for it is this conviction upon which the recent methods of treatment and good results are based. The appreciation of the formation of the empyema from pneumonia admirably explained by Moschcowitz and others is acceptable and explains the pathology.

This complication comes on so rapidly and early, a fact recorded by others, that after a few failures of early recognitions we grew to suspect its frequency, and its recognition was subsequently rarely at fault. The patients were so ill that physical signs and exploration were depended upon, the fluoroscope studies being postponed until the case became one of surgical sequel rather than complicated pneumonia. The sign of increased, high-pitched, vocal resonance helped us more than any other sign in finding fluid present even when the amount was small. These patients improved at once after the first aspiration which seemed out of proportion to the amount of fluid withdrawn. The mechanical factor of cardiac displacement seemed of less importance than the presence of toxic effusions. The first aspiration showed the Streptococcus hemolyticus, and all subsequent aspirations were consistent from a bacteriologic study up to the time of resection. The number of aspirations averaged from five to seven, extending over a period of two weeks or more, when from a patient with a very high surgical risk the case became one for good surgical work and was considered safe from a prognostic point of view. Elliott also, with rather full plate work on the thoraces of his cases, stated that the number of aspirations on his patients were four or five and the length of time involved a period of two weeks. Our own more frequent aspirations and greater length of time seemed to us better, although, too, late resection has one drawback to which we find brief reference by others and which we encountered in three of our patients, namely, dense pleural adhesions. The character of the fluid withdrawn grossly inspected was a feature which attracted our attention and has been spoken of by others. The first fluid taken when the patient was in the midst of his infection or earlier was of an amber color, but not the clear, serous fluid of exudate usually encountered. By the time the second or third aspiration was performed the pus was frank and the later ones were of the same character but denser in quality. After five or six aspirations the pus assumed a chocolate appearance, and to us this appearance indicated the time for resection. At this time the clinical picture of the patient was that of convalescence from acute infection. This feature of sequence in the appearance of the pus was very constant, and we think is worthy of note, and has been so stated by others. With the opinion that the chocolate appearance of the pus is due to the traumata of frequent aspirations as suggested by one surgeon we cannot entirely concur. The day previous to the removing of the patient to the operating room the final aspiration was done. A very striking and consistent feature was the large amount of fluid sometimes withdrawn. In one instance

we withdraw about 3 liters from a large man during his second aspiration, when $1\frac{1}{2}$ liters had been withdrawn only a few days before. Such large amounts can easily be dangerous to life, because of the now known although not generally appreciated elasticity of the mediastinum which produces interference with the other side of the thorax.

We have practised preliminary tapping in all forms of empyemata at Mercy Hospital for many years, when cases were not too urgent, and believe strongly in it.

The problem of washing the pleural cavity after the resection and insertion of the tubes is worthy of great consideration, and we believe this may be the better plan, judging from the experience of other men, and shall consider it in the future should such cases come under our care. One case of a colleague not in this group did well under the Carrel-Dakin solution. This may shorten the time of cure.

Our own feeling was for costatectomy instead of thoracotomy, and this we had performed. Many other men are in favor of the latter and with a simpler procedure and earlier washing with the Carrel-Dakin solution this may suffice for cure in some cases. The fact that two of our patients required second resection to establish sufficient drainage, although well done at the primary operation, makes us in favor of the former at present.

There were 2 cases in this group of dense adhesions which presented a problem difficult of solution and are yet unsolved. The 7 cases due entirely to the Streptococcus hemolyticus treated as we have outlined, and with no deaths, seems to warrant this record. The disappointments were the long periods of convalescence and the dense adhesions which followed in 2 of the cases. The use of the Carrel-Dakin solution in the future may remove such disappointments.

INTERNAL HYDROCEPHALUS IN A SYPHILITIC, PROBABLY DUE TO INTRASPINAL TREATMENT.

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AND

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THE common dangers of the intraspinal treatment of neurosyphilis have been discussed by various writers and are now generally known. Among the most important are septic meningitis, due to faulty technic; death from respiratory paralysis; paraplegia; loss of bladder and rectal sphincter control; sensory changes about the

perineum and in the legs. So far as we have been able to determine, internal hydrocephalus has not been mentioned in this connection. We therefore wish to record a case presenting this interesting but distressing complication.

History. The patient is a young white man, an attorney by profession, aged thirty-two years. He has been married for five years, but there have been no pregnancies.

In 1907 he contracted a genital sore, which was painful, with a seropurulent discharge but no local adenopathy. The sore persisted for six months. One month after its appearance he developed a sore throat, followed in another month by rheumatic pains and by small sores in the mouth. Three months later a generalized macular rash, together with lesions at the anus, appeared. Treatment consisted of "powder" by mouth.

In 1912 he began to suffer with occasional mild headaches, worse in the late afternoon and night, and with shooting pains in the legs. The headaches persisted with increasing severity until 1915, when they became severe enough to cause him to consult a physician. The blood Wassermann at that time was positive. One intravenous injection, presumably arsphenamin, followed by a course of intramuscular mercury and potassium iodide, brought about a decided improvement.

During the next three years he developed loss of libido and potentia, girdle sensation, difficulty in mental concentration and a change in disposition manifested by heavy drinking. The headache did not recur until about July, 1918, and was then of only slight intensity; it followed his rejection by an Army Medical Examining Board because of a diagnosis of "cerebrospinal syphilis." He was told at this time that the Wassermann of the blood and spinal fluid were both positive, whereupon he placed himself under treatment, consisting of six intravenous injections of arsphenamin and one intraspinal injection of mercurialized serum. Following this the blood Wassermann was said to have become negative.

Several hours after the intraspinal treatment there was a severe reaction, consisting of excruciating headache and pains in the legs lasting for four days, during which time he remained in the hospital. When he went home on the fifth day he felt fairly well, but on the sixth day he was suddenly seized with a fresh, terrific headache and pains in the legs. For the next forty-eight hours he was said to have been delirious and to have had a high temperature. He had stiffness of the extremities and retraction of the head. With this late reaction he remained in bed ten days.

For the next six weeks he felt quite well, but gradually an entirely new sort of headache began. The old headache had been infrequent, mild and generalized. These new headaches were almost constant, occipital and of terrific intensity. To quote his own expression, he "nearly went crazy with the pain." On two occasions during this phase of his condition he attempted suicide.

Physical Status. In December, 1918, he consulted one of us. At that time the physical examination showed round, regular pupils of the Argyll-Robertson type, coarse tremor of the tongue, pain on pressure over the cervical spine, absent knee- and ankle-jerks and oral sepsis. Psychiatric examination showed none of the characteristic signs of general paralysis.

Serology. The blood Wassermann was negative; the cerebrospinal fluid examination showed fifty cells, a strongly positive globulin test, Wassermann positive with 0.1 c.c. and a paretic type gold curve.

Treatment. When first seen his headaches were thought to be due to cerebrospinal syphilis, and from December 23, 1918, until October, 1919, he was kept under continuous antisyphilitic treatment. During this time he received seven intraspinal injections of mercurialized serum according to a method described by us,[1] six spinal drainages followed by arsphenamin and eleven separate intravenous injections of arsphenamin products, a total of twenty-four intravenous arsphenamins. From the standpoint of serology the results obtained were gratifying. The blood Wassermann remained negative and on October 14, 1918, the cerebrospinal fluid showed six cells, a slightly positive globulin, Wassermann negative with 1.0 c.c. and a negative gold curve.

Progress. Clinically, however, it was noted that the patient improved but little. Reactions following the intraspinal treatments were exceptionally severe, consisting of unbearable headache and pains in the legs, rendering a continuation of intraspinal medication impossible.

From December, 1918, until July, 1919, the headache continued almost as severe as before. During the next three months, however, a very considerable improvement took place; but after an intraspinal treatment on November 3 the pain recurred and rapidly grew worse until, during December, headache was constant, sometimes requiring morphin for relief.

November 29, examination of the eye-grounds disclosed unilateral choked disk right, with some edema of the left disk, and a high degree of vascular sclerosis. Consultation with an ophthalmologist revealed in addition marked compound hypermetropic astigmatism. With the hope that the edema of the disk would subside spontaneously and that the refraction error might, at least partially, account for the headache the error was corrected with glasses, but without relief.

In reviewing the patient's course at this time we found as evidence of increased intracranial pressure the severe headache and the low-grade choked disks, but no nausea, vomiting, bradycardia or localizing symptoms. It was recalled that from May 2 until

[1] Keidel, A., and Moore, J. E.: Treatment of Neurosyphilis by the Intraspinal Route, Johns Hopkins Hosp. Bull., November, 1920, xxxiv, 404.

October 4 treatment had been intravenous only, no lumbar punctures having been done.   October 4, 11, 25 and November 3 spinal drainage was carried out.   On the first date (October 4) the pressure was markedly increased and the fluid spurted out in a steady stream to a distance of several inches.   When 70 c.c. had been rapidly removed the procedure was terminated for fear of reducing the intracranial pressure too quickly.   At the four succeeding drainages it was noted that the pressure seemed to grow progressively lower, so that at the time of the last treatment, on November 3, spinal fluid flowed only drop by drop, and ceased to flow at all after 40 c.c. had been obtained.

Laryngological consultation on September 20 had been completely negative for any sinus disease, either of the frontals, antra, sphenoids or ethmoids.

It being by this time obvious that we were dealing with some intracranial condition, careful review of the various symptoms just outlined prompted the suspicion of an internal hydrocephalus, perhaps due to an old meningitis, with adhesions in the floor of the fourth ventricle.

Stereoscopic Roentgenologic Examination of the Head on December 29 showed the following rather startling picture: "The parietal sutures on both sides, especially near the top of the head, are distinctly separated.   The lambdoidal sutures are also very decidedly separated.   The sella turcica is quite large, but this may be a normal variation.   There are no shadows to indicate a localized tumor in any place.   There is no evidence of a periostitis to indicate lues.   The condition suggested an intracranial pressure affair without being able to pick out the particular lesion.   The paranasal sinuses show an absence of both frontals.   The maxillary sinuses are small but clear."

Surgical Consultation.   This lent added weight to our tentative diagnosis.   December 31, 1919, Dr. George Heuer saw the patient in consultation and confirmed the presence of bilateral choked disk, more marked on the right.   There was also a questionable bitemporal hemianopsia.   Right subtemporal decompression was decided upon and was performed January 24, 1920.   At operation very troublesome bleeding was encountered from the posterior branch of the middle meningeal artery as well as from the other dural vessels, all of which were much larger than normal.   The dura was under slightly increased tension, and on pricking considerable fluid escaped.   The brain was not bulging and no evidence of tumor was found.   Two attempts at ventricular puncture failed.

During the patient's convalescence from this operation eight abscessed teeth were extracted and his oral hygiene considerably improved.   Two months later the choked disks had subsided and the headache was almost completely relieved.   He felt so well that he returned home and resumed his professional work.   The improve-

ment was only temporary, however, and in May, 1920, the same headaches recurred, usually after mental strain and in the early afternoon, always associated with tense bulging of the decompression area.

In July he returned to Baltimore, once more incapacitated by the severity of the headache. Serologic examination disclosed a negative blood Wassermann; in the cerebrospinal fluid there were eight cells, a weakly positive globulin reaction and a luetic zone gold curve. The spinal fluid Wassermann was negative with 0.2, 0.4 and 0.6 c.c., suggestive positive with 0.8 c.c. and positive with 1.0 c.c. In the absence of Dr. Heuer he was seen by Dr. Walter Dandy, who concurred in our diagnosis of internal hydrocephalus. According to the routine of study used for these cases by Dr. Dandy, intraventricular and intraspinal phthalein and roentgenograms after intraventricular and intraspinal air injections were proposed.

The patient refused all of these procedures except the intraspinal phthalein, which was carried out on July 16. Excretion of dye in the urine was as follows:

	Trace.	
First two hours	20	per cent.
First fourteen hours	5	"
Second twelve hours	2	"
Third twelve hours	1	"
Fourth twelve hours		
	28	"
Total (fifty hours)		

Intramuscular phthalein on July 19: 43 per cent. excreted in two hours.

A recent letter informs us that his progress has been much the same. He continues to be partially incapacitated by headaches, which are worse whenever he exerts himself mentally or physically.

Discussion. In a series of papers Dandy and Blackfan[2][3] and Dandy[4][5] have thoroughly presented the question of hydrocephalus. Briefly summed up their clinical conclusions are as follows: Internal hydrocephalus can be divided into two anatomically different types, depending on the patency or occlusion of communication between the ventricles and the subarachnoid space. If communication is completely blocked off the hydrocephalus is obstructive. Absorption of cerebrospinal fluid cannot take place from the ventricles though from the subarachnoid space, which the fluid cannot reach, it may be normal. Communicating hydrocephalus results if the obstruction between the ventricular and subarachnoid system is incomplete. Clinically it was shown to occur because of the forma-

[2] Internal Hydrocephalus, An Experimental, Clinical and Pathologic Study, Am. Jour. Dis. Children, December, 1914, viii, 406.
[3] Ibid., December, 1917, xiv, 424.
[4] Extirpation of the Choroid Plexus of the Lateral Ventricles in Communicating Hydrocephalus, Ann. Surg., December, 1918, p. 569.
[5] Experimental Hydrocephalus, Ann. Surg., August, 1919, p. 129.

tion of a barrier of dense adhesions (following meningitis) at the base of the brain, which, while sometimes permitting the passage of fluid from the ventricles to the spinal subarachnoid space, mechanically obstructed its flow to the cerebral subarachnoid space, where most of its absorption should take place. The communicating type of hydrocephalus has been produced in dogs by a perimesencephalic band of gauze, saturated in an irritant which induces adhesions.

The intraventricular introduction of phenolsulphonephthalein will conclusively demonstrate the classification of hydrocephalus. If phthalein is recoverable by spinal puncture within ten minutes thereafter the condition is communicating. Furthermore, absorption and excretion of phthalein injected intraspinally is usually normal, or nearly so, in the obstructive type of hydrocephalus, and is markedly reduced in the communicating type.

Dandy[6] [7] has also introduced the method of roentgenography of the air injected spinal and ventricular systems. This might be expected to show clearly any dilatation of the ventricles, which might be found in either type, as well as the failure of the air to reach the cerebral sulci or the ventricular system if blocked by a band of adhesions at the base as in communicating hydrocephalus.

In this case the diagnosis of internal hydrocephalus is, to our minds, fairly well established because of (1) the character of the headaches; (2) the presence of choked disk; (3) progressive decrease in the pressure and amount of cerebrospinal fluid during the successive punctures of October and November, 1919 (though a fair amount of fluid, somewhat less than normal, could always be recovered); (4) the temporary improvement after decompression; (5) the behavior of the excretion of phthalein injected intraspinally; (6) the striking roentgenoscopic picture.

It is, of course, essential to rule out cerebral or cerebellar neoplasm or cyst. The existence of such a lesion seems improbable because of the history of sudden onset, the lack of progress in the disease and the absence of localizing signs. It is probable that here the obstruction is only partial and that a certain amount of ventricular fluid is allowed to flow into the spinal system. It is unfortunate that roentgenoscopic studies of the air filled ventricles and spinal canal were not permitted. Such studies would have made the diagnosis more definite.

Unfortunately, also, the ventricular injection of phthalein was not permitted. This would have allowed a demonstration of the patency of the foramina between the ventricular and the subarachnoid systems. The intraspinal injection of phthalein did, however, afford the information that only a small part of the subarachnoid space was participating in the absorption of cerebrospinal

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[6] Ventriculography following the Injection of Air into the Cerebral Ventricles, Ann. Surg., July, 1918, p. 5.

[7] Roentgenography of the Brain after the Injection of Air into the Spinal Canal, Ann. Surg., October, 1919, p. 397.

fluid. Normally, after intraspinal phthalein 35 to 60 per cent. is excreted in two hours. In this patient there was but a trace in two hours and only 28 per cent. was excreted in forty-eight hours.

Having concluded that in all probability the patient's headaches are due to internal hydrocephalus of the communicating type, questions arise as to the etiologic factors which produced this condition. Syphilis has, of course, been suggested by various authors, and is particularly noteworthy as a cause of infantile hydrocephalus. A syphilitic process which will almost completely occlude the foramina of exit of the cerebrospinal fluid from the ventricular system, or which will so affect the meninges as to produce a dense band of adhesions around the base of the brain, must in the adult be relatively uncommon, as few such cases of hydrocephalus in adults are observed. The possibility of such a condition due to syphilis is, however, admittedly academic. On the other hand the time relation of the first intraspinal injection to the onset of the characteristic headache stands out very strikingly. It must be admitted that for some time we failed to be impressed by this possible relation of cause and effect; but later consideration has urged upon us the conclusion that the first intraspinal injection given the patient set up a severe meningitis, which, since he survived it, was probably aseptic. This in healing produced a mass of adhesions about the subarachnoid space, causing a partial occlusion of one or more of the three foramina of exit from the fourth ventricle. Such a phenomenon must, however, be extremely rare, since we have been unable to find similar cases in the literature and since our own fairly large experience affords no like example.

The hydrocephalus in this case is of the communicating type, since there are periods of freedom from both headache and the bulging of the decompression area and since a fair amount of spinal fluid was usually obtainable at the time of puncture. The phthalein absorption is characteristic in that it was markedly reduced.

So far as treatment is concerned there would seem to be little to be done. The operation of choroid plexectomy is hazardous; according to Dandy it is impossible to break up adhesions at the base because of their inaccessibility. One can hope for a spontaneous cure. To quote Dandy and Blackfan:[8] "It is not difficult to imagine recovery following the gradual disappearance of adhesions. It is also possible to imagine a sudden rupture of the thin wall of a large fourth ventricle cyst, producing a new foramen of exit to the subarachnoid space."

Summary. 1. There is presented a case of communicating internal hydrocephalus in a neurosyphilitic.

2. The hydrocephalus appears to stand in the relation of effect and cause to an intraspinal treatment with mercurialized serum.

3. A possible though remote danger of intraspinal therapy is pointed out.

[8] Loc. cit.

OZENA AND ITS RELATION TO TUBERCULOSIS.

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ALTHOUGH not an uncommon disease, ozena has been relegated so strictly to the sphere of the rhinologist and the laryngologist that it is but little known outside these specialties. For a great many years there have been scattered references in the literature pointing out the frequency with which ozena and tuberculosis are to be observed in the same patient. This fact has been recognized in a general way, but has by no means been accorded the attention it deserves. Recent work done along these lines emphasizes the necessity of a more general knowledge of the symptomatology and therapy of ozena on the part of the medical profession as a whole. The frequent incidence of tuberculosis in ozenatous patients makes it of as much importance for the internist to recognize and examine a case of ozena as a possible subject of pulmonary involvement as it is for the nose and throat specialist to be familar with the various systemic diseases, of which derangements in his own particular field of observation are only part and parcel.

It will be the object of the following paragraphs to set forth the evidence at hand concerning the coincidence of these two diseases, together with the results of some experimental work done on the subject in the department of laryngology of the Johns Hopkins Hospital.

The word "ozena" is derived from the Greek, and means literally a stench. The lesions are confined to the mucous membranes of the nose, pharynx and may extend to the larynx. It is characterized by the formation of greenish-black crusts, with a sickening odor. It usually begins in childhood and runs a progressive course, tending to become less severe as old age advances. A predilection for filth makes it more common among the lower classes. Children of ozenatous parents are often found to be suffering with the same malady, and there is considerable evidence to show that it is contagious. The appearance of a well-developed case is often one of marked cachexia and malnutrition.

In the first stages there is a transient hypertrophy of the turbinates. Eventually the mucous membrane lining of the whole nose undergoes atrophy and all lymphoid and secretory structure disappear completely. Ulceration is not the rule. An idea of the profound changes that take place in the histological picture may be gained from the accompanying photomicrographs. Fig. 1 shows a section through the mucous membrane of a comparatively normal

Fig. 1.—Section through the mucous membrane of a comparatively normal middle turbinate, showing columnar epithelium and glandular structures.

Fig. 2.—Section through the mucous membrane of the middle turbinate taken from a case of ozena, showing the stratified epithelium and entire absence of glandular structure.   There is no evidence of tubercle.

middle turbinate. Note the stratiform ciliated cylindrical colum-
nar epithelium with goblet cells interspersed. Beneath is the
basement membrane and finally the tunica propria of fibro-elastic
tissue with its venous plexuses and tubo-alveolar glands. Con-
trast this with Fig. 2. One can scarcely realize they are from
the same anatomical locality. The stratiform columnar epithelium
has been entirely replaced by a layer of stratified epithelium des-
quamating on the surface. Polymorphonuclears and small round
cells are fairly abundant in this layer and in the one immediately
below it, which corresponds to the submucosa. In the deeper
structures, plasma cells, fibroblasts and eosinophils are found.
There are numerous bloodvessels and venous plexuses. The
striking feature is the complete absence of all glandular and secre-
tory structure so abundant in the normal nose. Note will also
be made of the complete absence of any structure resembling
tubercle.

Many organisms have been mentioned in connection with the
etiology of ozena. Among the better known are (1) the
Abel-Löwenberg[1] bacillus, described by Abel in 1893, and (2)
the cocco-bacillus fetidus ozenæ discovered by Perez,[2] and with
which he claimed to have reproduced in rabbits lesions character-
istic of ozena. The third organism identified with the disease is
an acid-fast bacillus, and it is concerning the significance of this
organism in the nasal secretions of ozena that a great deal of the
controversy of recent years has had to do. Although it has long
been known that such bacteria are found in the secretions of the
ozenatous nose, they have in general been looked upon as acci-
dental, just as similar flora with acid-staining properties are fre-
quently present in sebaceous secretions, in the discharge from
chronic ears, etc. Not everyone, however, admits this to be the
case. There are those who hold that the acid-retaining proper-
ties of this particular bacillus have a more sinister meaning; that
if it is not the tubercle bacillus it bears such a resemblance to
that organism as to demand more than a casual notice. And,
indeed, there is considerable ground for their contention, both
clinically and bacteriologically.

As early as 1882 Fränkel[3] collected from the literature records of
6 cases of ozena which had come to section. Five of these were
found to have definite tuberculosis. In Alexander's[4] series of 22
cases 15 were found to have died of tuberculosis. On the clinical

[1] Bakteriologische Studien über Ozaena Simplex, Centralblatt für Bakteriologie,
1893, xiii, p. 161.
[2] Recherches sur la bacteriologie de l'ozena, Annals de l'Institut Pasteur, 1899,
xiii, p. 937.
[3] Pathologische Mittheilungen, ii Beiträge zur Rhinopathologie, Virchows Arch.,
1882, lxxxvii, p. 285.
[4] Die Bezeihungen der Ozaena zur Lungentuberculose nebst Bemerkungen über
die Diagnose der Ozaena, Arch. f. Laryngol. u. Rhinol., 1903, xiv, p. 1.

side there is even more significant evidence. Alexander in the paper quoted above found a family history of tuberculosis in 16 of 22 cases. Wingrave[5] found a similar history in 37 out of 60 cases. Caboche[6] found a family history of phthisis in 16 of his 39 cases. In our own series 4 of the 8 cases in which a family history was obtained were found to have tuberculous antecedents.

The incidence of tuberculosis in people suffering with ozena is just as striking. Alexander in the same monograph records 50 cases of ozena in which definite pulmonary tuberculosis was found in 22, suspicious tuberculosis in 7 and pulmonary lesions of a different character in 4. Theisen[7] found phthisis in 7 out of 20 cases of ozena. McKenzie[8] in 34 cases found 5 with pulmonary tuberculosis and 3 with other tuberculous manifestations. Mackeith[9] found "phthisis pulmonalis" in 4 out of 13 cases. In our own series of 9 cases 3 showed frank pulmonary tuberculosis and 3 evidence of less active lesions. In other words, 40.4 per cent. of the cases cited above showed a more or less definite clinical tuberculosis and 56.6 per cent. gave a family history of phthisis.

These figures would certainly indicate something more than a mere accidental association of the two diseases. What then is this relationship? Before attempting an answer let us return to a consideration of the acid-fast organisms found in the crusts in ozena.

The tinctorial qualities of these bacilli can be demonstrated in almost all true cases of ozena. We have not found them in other diseases simulating ozena, such as syphilis of the nose. When found they are most abundant in the thick black crusts of a fully developed case. The best preparations are obtained by taking a bit of the crust, dissolving it in sterile salt solution and spreading it on a slide with a platinum loop. Fix by passing several times through a flame. Overheating will cause the organisms to swell and become distorted. Stain in the usual manner by the Ziehl-Neelsen method.

Owing to the fact that many of these bacilli are not alcohol-fast, it is best to decolorize only in an acid bath, using 25 per cent. sulphuric acid. The preparation is counterstained with methylene blue. The acid-fasts will be found to stand forth a bright red in contrast to the blue of the other organisms. They vary greatly in their morphology, ranging all the way from streptothrix-like clumps

[5] Atrophic Rhinitis, Journal of Laryngology, Rhinology and Otology, 1894.

[6] L'ozéne forme larvée de la tuberculose, Ann. d. mal. d. l'orielle, du larynx (etc.), 1917, xxxiii, pt. ii, p. 260.

[7] Etiology and Diagnosis of Ozena and its Relation to Pulmonary Tuberculosis, Albany Medical Annals, 1904, xxv, p. 140.

[8] Atrophic Rhinitis (Ozaena) and Tuberculosis, Journal of Laryngology, Rhinology and Otology, 1916, xxxi, p. 176.

[9] Atrophic Rhinitis (Ozaena) and Tuberculosis, Pt. ii, Tuberculin in Atrophic Rhinitis, Journal of Laryngology, Rhinology and Otology, 1916, xxxi, p. 232.

to short, thick rods. They frequently occur as thin, curved, beaded rods, identical in appearance with the tubercle bacillus.

With the assistance of Dr. Esau Greenspon, of the pathological department, an attempt was made early in the year 1918 to culti- vate these organisms. Crusts were washed several times in sterile saline solution and implanted on Dorset egg medium, sheep serum agar, blood agar and other media. Unfortunately for our work Dr. Greenspon was called to the colors at this time, and this fact, coupled with other exigencies brought on by the war, forced us to abandon this phase of the work. However, the organisms in question have been isolated and grown by Wingrave,[10] using Dorset egg medium reinforced with ozena crusts.

Animal Experiments. In the paper last quoted there is, further- more, recorded an account of guinea-pig inoculations. Six ani- mals were injected, using a reinforced emulsion made from ozena crusts. At section the 3 animals which had been injected intra- peritoneally were found to have escaped all infection. The 3 which had been inoculated subcutaneously showed definite tuber- culosis, with caseation of glands, giant-cell formation and "tubercle bacilli in and around the giant cells."

Our experiments along these lines have not been so successful. Crusts were collected from 5 cases of ozena in which we had first demonstrated the presence of acid-fast bacilli. An emulsion of the crusts was made from each case and 3 c.c. of this injected into guinea-pigs, using 2 animals to each patient. The intraperitoneal method was used. At the end of four weeks several animals had died of intercurrent infections—no gross signs of tubercle were found at autopsy. Smears and sections from various organs were stained with similar results. The remaining animals were sacri- ficed at the end of six weeks. No signs of tuberculosis were found. A second group was inoculated, with the same disappointing results. Recently a third series of animals was injected, using material from one new and two old cases. This time the emulsion was introduced subcutaneously. The regional lymph glands became swollen within a week. The animals died during the fourth and fifth weeks. They were carefully examined, but no histological evidence of tubercle was found in the glands or viscera.

As before mentioned we first ascertained the presence of the acid-fast organisms in the material used. Arguing from the well- known susceptibility of the guinea-pig to the tubercle bacillus we are forced to conclude, from our experiments, that the acid-fast bacillus found in the nasal secretions of ozena is not identical with the tubercle bacillus.

Tuberculin Therapy.—It would entail too much space to go into the many methods advocated in the treatment of ozena. Their

[10] Atrophic Rhinitis (Ozaena) and Tuberculosis, Pt. iii, The pathological Aspect, Journal of Laryngology, Rhinology and Otology, 1916, xxxi, p. 276.

very number and diversity are an indication of our lack of true information on the subject. In general there are two classes of therapy employed. Local measures in the form of irrigations, suppositories, instillations and paraffin injections. In the second group fall the various forms of vaccinotherapy. The first class of remedial agents acts apparently in a purely mechanical manner and are efficacious only so long as one persists in their use.

Results of a more lasting character are claimed from the use of vaccines. Hofer and Kofler,[11] using a vaccine made from the Perez bacillus, reported favorable results. Subsequent reports on the use of this vaccine conflict. Golgau[12] experimented with seven different varieties of vaccines, and from his results concludes that all such forms of therapy are of little or no value. Mackeith,[13] starting with the premise that ozena is a tuberculous manifestation, has treated a series of 13 cases with tuberculin. His results have been very good. Some of these patients have been under observation as long as two and a half years after treatment was inaugurated. Of these 7 showed great improvement, 3 improvement, 2 suffered relapse and 1 case was not benefited.

In January, 1918, we mailed cards to about 100 names indexed in the nose and throat dispensary under the headings "Ozena" and "Atrophic Rhinitis." Of this number about 40 reported for examination. Our task was to pick out only those which we considered to be genuine cases of ozena. We chose as our more important criteria the characteristic fetor, atrophy of the mucous membranes and the presence of the greenish-black crusts in the nose. When possible smears were made to determine the presence of acid-fast bacilli. From this group we have been able to obtain fairly complete records of 9 cases of what we consider to be true ozena. As the patients reported they were given the routine nose and throat examination, including roentgen ray of the sinuses and Wassermann test. Of the 9 cases, 7 consented to undertake the tuberculin treatment, for the administration of which as well as for the chest examinations we are indebted to the Phipps Tuberculosis Dispensary.

The tuberculin used was the human bouillon filtrate. An initial dose of from $\frac{1}{100000}$ to $\frac{3}{100000}$ mg. was given and the dosage increased gradually until at the end of a year the patient received 1000 mg. each month. A glance at the following abstracts will give an idea of the success that has attended our treatment of ozena with tuberculin:[14]

[11] Bisherige Ergebnisse einer neuen Vakzinationstherapie bei Ozena (Cocco bacillus fetidus ozena Perez), 1913, xxvi, No. 42, p. 1698.

[12] Vaccine Treatment of Ozena, Laryngoscope, 1918, xxviii, p. 380.

[13] Loc. cit.

[14] These observations were carried up to September, 1920.

CASE I.—H. K., male, white. Birthplace, United States. Laborer. Aged twenty-nine years. Complaint: "Pimple in the nose." Admitted January 3, 1918.

Family History. Negative.

Past History. Negative, except for chronic nasal discharge.

Personal Examination. Temperature, 99.2°. *Roentgen-ray sinuses*, negative. *Wassermann*, negative. *Glands*, not enlarged. *Nose*, inferior turbinates atrophied; both sides filled with foul-smelling discharge and greenish crusts. *Smear* from nose showed numerous acid-fast bacilli. *Chest Examination:* slight impairment to the third rib on the right and left and throughout the back. Breath sounds diminished. *Von Pirquet test* slightly positive. *Roentgen ray of chest:* spotty infiltration of both lungs, especially on the right side, tuberculous in origin. *Diagnosis:* possibly some fibrosis of both uppers.

Course. At the end of three months, during which time he was seen weekly, this patient showed a marked improvement. The discharge disappeared almost entirely and lost its disagreeable odor. His general health became better, with improvement in appetite and a gain of ten pounds in weight. From this time to the present his condition has remained about stationary. He now receives the maximum dose of 1000 mg. each month. He has discontinued all irrigations and other treatment.

CASE II.—A. L., male, white. Birthplace, United States. Schoolboy. Aged thirteen years. Patient referred for consultation from the Phipps Tuberculosis Dispensary December 27, 1917.

Family History. Mother has tuberculosis. One sister died of tuberculosis.

Personal History. Scarlet fever and diphtheria in infancy. Profuse discharge in nose for some time.

Personal Examination. Temperature, 99.2°. *Wassermann*, negative. *Glands*, not enlarged. *Nose*, middle turbinates atrophied; dry, foul-smelling discharge throughout the nose. *Tonsils*, not enlarged. *Chest Examination:* manubrial dulness; impairment to second rib and to the lower angle of the scapula behind. *Impression*, mediastinitis. *Von Pirquet*, positive. *Roentgen ray chest*, marked fibroid infiltration of the right lung; probable thickening of the pleura. *Diagnosis:* changes probably tuberculous in origin.

Course. Patient has been under tuberculin treatment for a year. The odor has disappeared and the discharge has practically ceased. He has gained in weight. At present is receiving 1000 mg. of tuberculin each month.

CASE III.—M. F., female, negress. Birthplace, United States. Aged eighteen years. *Complaint*, nasal discharge.

Family History. None obtainable.

Personal History. Nasal trouble for past year.

Personal Examination. Wassermann, negative. *Roentgen-ray sinuses,* clouding both antra. *Glands,* not enlarged. *Nose,* inferior turbinates atrophied; thick, greenish crusts with typical fetor. *Tonsils,* atrophic. *Nasopharynx,* walls covered with greenish crusts. *Smear* from the nose showed acid-fast bacilli in large numbers. *Chest Examination:* possible minimal left apical tuberculosis; rales heard.

Course. After an irregular course of treatment for three months the patient returned and volunteered the information that her subjective symptoms had disappeared. Examination of the nose showed practically no discharge and no odor. The patient could not be prevailed upon to continue treatment.

Case IV.—M. V., female, white. Birthplace, United States. Schoolgirl. Aged fourteen years. *Complaint,* sunken nose. Admitted June 25, 1919.

Family History. One sister has nose trouble (ozena).

Personal History. Nose has been "sinking for several years;" offensive discharge; complete anosmia.

Personal Examination. Temperature, 98.8°. *Wassermann,* negative. *Roentgen-ray sinuses,* infection of right frontal, ethmoids and antrum. *Glands,* just palpable in anterior and posterior triangles. *Nose,* external deformity; interior filled with thick, black crusts with a disagreeable odor; atrophy of both inferior turbinates; antra irrigated and fluid returned clear. *Smear* from nose showed numerous acid-fast bacilli. *Chest examination,* negative. *Von Pirquet,* slightly positive.

Course. There was an apparent flare-up of the nasal condition and some local reaction after the first seven injections of tuberculin. At the end of six months the discharge had practically disappeared together with the odor.

About one year from the time the treatment was commenced the patient suffered a relapse, with a return of the discharge and odor. She is still under treatment.

Case V.—C. G., female. Birthplace, United States. Occupation, housework. Aged twenty-three years. *Complaint,* trouble with nose and throat. Admitted March 5, 1918.

Family History. Negative.

Personal History. Occasional headache. Post-nasal discharge for two years.

Personal Examination. Temperature, 97.8°. *Wassermann,* negative. *Roentgen-ray sinuses,* negative. *Glands* are just palpable in the posterior triangles of the neck and at the angles of the jaw.

Nose, atrophy of both inferior turbinates; profuse purulent discharge on both sides, with odor. *Tonsils,* atrophic. *Chest Examination,* negative for tuberculosis.

Course. After five months' treatment with tuberculin the patient reports that she thinks the discharge is considerably less. Examination shows a slight amount of discharge on the left side. *It is worthy of note that nine months after first being seen this patient developed pulmonary tuberculosis while under observation.*

Case VI.—M. C., female. Birthplace, United States. School-girl. Aged ten years. *Complaint*, nasal odor and nasal discharge. Admitted October 25, 1919.

Family History. Mother has pulmonary tuberculosis.

Personal Examination. Wassermann, negative. *Roentgen-ray sinuses*, negative. *Glands*, not enlarged. *Nose*, foul, greenish crusts in the posterior nares and in the nasopharynx. All turbinates atrophied. *Smear* showed numerous acid-fasts. *Chest examination*, negative. *Von Pirquet*, negative.

Course. After five months' treatment with tuberculin, the nose shows only a small amount of discharge on the right side. Odor not marked. From this time until the present date the patient has suffered several remissions. At no time, however, has her condition been as bad as when first seen.

Case VII.—J. R., male. Birthplace, United States. Clerk. Aged twenty-eight years. *Complaint*, atrophic rhinitis.

Family History. Mother died of pulmonary tuberculosis.

Personal History. Had attacks of chills and fever for eight years. Cough and pain in chest. Formation of foul-smelling crusts in the nose since childhood. Anosmia.

Personal Examination. Glands are just palpable at the angles of the jaws. *Nose*, septum deflected to the right; left side filled with typical foul-smelling discharge. *Pharynx*, purulent discharge on the posterior wall. *Sinuses* are clear. *Smear* from nose showed acid-fast bacilli in large numbers. *Chest examination*, breath sounds and percussion note impaired at both apices. (Examination made outside the hospital.)

Course. After three months' treatment with tuberculin the patient reported for examination. He says that those with whom he is in daily contact no longer complain of the odor. Examination of the nose showed about half the amount of discharge first noted.

Case VIII.—F. K., white. Birthplace, Bohemia. Occupation, farmer. Aged forty-seven years. *Complaint*, throat trouble. Admitted November 6, 1918.

Family History. Negative.

Personal History. Cough for one year.

Personal Examination. Glands not palpable. *Nose*, turbinates atrophied; discharge, with fetid odor.

Chest Examination. Impairment of the upper right and left; rales on the left side. *Tubercle bacilli* present in the sputum. *Roentgen ray chest,* spotty infiltration of left upper and right apex. *Diagnosis,* pulmonary tuberculosis. In this patient the onset of tuberculosis and ozena were apparently simultaneous.

Course. Not treated for nasal condition.

CASE IX.—E. S., male, white. Birthplace, United States. Aged sixty-nine years. *Complaint,* catarrh and deafness. Admitted May 10, 1920.

Family History. Probable history of tuberculosis and ozena in family.

Personal History. Nasal discharge since early adult life.

Personal Examination. Temperature, 98.4°. *Wassermann,* negative. *Roentgen-ray sinuses,* clouding of left frontal and ethmoids. *Glands,* not enlarged. *Nose,* inferior turbinates atrophied; middle turbinates, covered with thick, greenish crusts, with foul odor. *Nasopharynx* shows same picture as nose.

Chest Examination. Fibroid changes over uppers; marked on right side; few persistent rales above right clavicle. *Roentgen ray,* old fibroid tuberculosis of left upper.

Course. Not treated.

To summarize:

Cases I and II show great improvement two and a half years after treatment was started.

Cases III and VII show improvement after three months' treatment.

Case V showed an initial improvement after five months' treatment. Four months after stopping treatment she developed pulmonary tuberculosis.

Cases IV and VI showed an initial improvement followed by relapse—No. IV after one year's treatment and No. VI after five months' treatment.

By improvement we mean cessation of discharge and a better condition of health in general. In none of the cases was the atrophy in the nose affected. In some the sense of smell returned to a certain extent.

The good results reported from the use of other vaccines make us wary of attributing to the tuberculin any specific action on the nasal condition. At any rate whether the amelioration of symptoms following the use of tuberculin be due to a general tonic action or is the result of the introduction of a foreign protein into the blood or whether there is some direct action on the nasal disease is beside the question. The fact remains that of the various remedies we have heretofore tried in the treatment of ozena by far the best results have been obtained with the use of tuberculin.

Our results and those of Mackeith certainly warrant a more extensive trial of this form of therapy.

As intimated before, our main object has been to point out and insist upon the relation that exists between the disease ozena and tuberculosis.

We offer as evidence from our own and cases collected from the literature:

28 cases that have come to autopsy, tuberculosis was found in 20 and was the cause of death in 15 of these.

129 cases in which a family history of tuberculosis was demonstrated in 73.

126 cases in which definite clinical tuberculosis was found in 52.

It is true our laboratory tests argue against any etiological identity. On the other hand the clinical evidence cannot be dismissed as falling within the realm of coincidence. The question of the etiology of ozena has yet to be settled. That the disease is very frequently associated with tuberculosis is a fact—a fact that it behooves every practising physician to bear in mind and one that should cause him to investigate every case of ozena coming under his notice as a possible instance of tuberculosis.

DIABETES MELLITUS, SYPHILIS AND THE NEGRO.

By I. I. LEMANN, M.D.,

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IN view of Warthin's report that he has found syphilitic pancreatitis in all of the diabetic cases at the University of Michigan coming to autopsy, it has seemed worth while to examine from this point of view a material rich in syphilis. Warthin's[1] statement is "that diabetes may be associated with the more marked degrees of syphilitic pancreatitis, and in our autopsy series all of our diabetic cases have been so associated, but that a number of syphilitic pancreatitis of similar degree of severity have not presented the clinical symptoms of diabetes. It seems very probable, therefore, that latent syphilis is the chief factor in the forms of pancreatitis most frequently associated with diabetes, but that diabetes is not always associated with severe degrees of this type of pancreatitis." Since this report was made there has been very little discussion of the matter in the literature, though Warthin's contention has not gone altogether unchallenged. Thus, J. R. Williams[2] reported that only 4 out of 143 cases of diabetes mellitus gave a positive Wassermann and the

[1] AM. JOUR. MED. Sc., 1916, clii, 157.
[2] Jour. Am. Med. Assn., 1918, lxx, 365.

physical examination of 126 out of the total 143 patients did not lend support to the view that syphilis is a common causal factor in diabetes. Jacob Rosenbloom[3] reported that in 62 cases of diabetes he found positive evidence (including positive Wassermanns) in 7, or only 10.3 per cent. Five of the 7 patients were persuaded to take syphilitic treatment. There was no increase in the carbohydrate tolerance in any of these cases after treatment. Anna I. Van Saun[4] investigated the blood from 72 known diabetics. Only 1 gave a positive Wassermann reaction; 52 gave a negative reaction, 2 a doubtful reaction and in 19 cases the controls failed to hemolyze, so that no readings could be made. The one serum giving a positive reaction was that of a patient giving a history of syphilis. Of the 2 doubtful reactions 1 was a patient with a history of chancre twenty-six years previously; the other patient gave no history of syphilis.

My own experience in private practice has given me the same impression that syphilis is seldom the cause of diabetes mellitus. In such cases where lues does certainly exist we must consider whether it is present simply as a concomitant affection or as the real cause of the diabetes. Only once in my series did antisyphilitic treatment have any effect upon the carbohydrate tolerance, which is in agreement with the experience of Rosenbloom already quoted. It is perfectly apparent that a diabetic may have or may acquire syphilis just as he may acquire tuberculosis or typhoid fever, but that is quite different from the situation of the syphilitic who because of his syphilitic pancreatitis presents the phenomena of diabetes mellitus. It is not denied that syphilitic pancreatitis may present the clinical picture of diabetes mellitus; but my present thesis is that such cases represent the exception and not the great body of diabetic patients. It is in support of this contention that the results of this statistical study are presented.

The syphilization of the negro is a matter of common knowledge to all practitioners in the South. They present a material enormously rich in every aspect of the disease, because, owing to their ignorance and poverty, they go frequently untreated or inadequately treated. They are more liable even than other patients to disappear from view when their immediate pressing symptoms have been relieved to reappear when the disease has later made vast inroads. If therefore syphilitic pancreatitis is the common cause of diabetes mellitus we should find the latter disease more prevalent among them than among the whites. This, however, is not the case. Indeed, it was formerly thought that diabetes mellitus was relatively rare in the negro. While this disease is not rare in the negro, still the incidence is not as great among them as among the whites. This I showed ten years ago from a study of the reports of the

[3] Jour. Am. Med. Assn., 1917, lxviii, 1232.
[4] Jour. Med. Research, 1917, xxxvii, 205.

Charity Hospital at New Orleans covering twelve years (1898–1909). There were 45 white diabetics and 19 negro diabetics in 61,298 admissions. The negroes furnished 40 per cent. of the admissions and only 30 per cent. of the diabetics. The total incidence was 0.63 per thousand. The incidence among the whites was 0.72 per thousand while among the negroes it was only 0.47 per thousand.

TABLE I.—DIABETES MELLITUS IN CHARITY HOSPITAL, 1898–1909.

Year.	White cases.	Negro cases.	White admissions.	Negro admissions.	Total. admitted.
1898	2	5	4,738	2,996	7,734
1899	5	0	5,068	3,412	8,480
1900	4	0	4,614	3,114	7,728
1901	7	3	4,657	3,068	7,725
1902	7	2	4,928	3,248	8,176
1903	6	3	4,767	3,434	8,201
1904	2	0	5,300	3,299	8,689
1905	2	1	5,091	3,221	8,412
1906	1	0	5,027	3,425	8,452
1907	4	3	5,294	3,556	8,950
1908	3	2	5,874	3,666	9,540
1909	2	2	5,850	3,726	9,576
	45	19	61,298	40,265	101,565

0.72 per 1000.   0.47 per 1000.   White and negro, 0.63 per 1000.
Percentage of diabetics: White, 70 per cent.; negro, 30 per cent.
Percentage of admissions: White, 60 per cent.; negro, 40 per cent.

A review of the figures for the years 1910–1919 confirms the impression obtained for the earlier period in a remarkably accurate way. In 160,044 admissions there were 135 white diabetics and 59 negro diabetics. The negroes furnished 43 per cent. of the admissions and only 30 per cent. of the diabetics, practically the same relation as in the former period.

TABLE II.—DIABETES MELLITUS IN CHARITY HOSPITAL, 1910–1919.

Year.	White cases.	Negro cases.	White admissions.	Negro. admissions.	Total admitted.
1910	11	0	6,719	4,594	11,313
1911	20	7	7,314	4,906	12,220
1912	15	5	7,838	5,145	12,983
1913	5	3	8,405	5,944	14,349
1914	19	9	9,700	7,042	16,742
1915	8	7	9,897	7,926	17,823
1916	21	11	10,111	8,540	18,651
1917	13	9	10,908	8,686	19,651
1918	15	4	11,359	7,862	19,221
1919	8	4	9,789	7,359	17,148
	135	59	92,040	68,004	160,044

1.4 per 1000.   0.86 per 1000.   White and negro, 1.2 per 1000.
Percentage of diabetics: White, 70 per cent.; negro, 30 per cent.
Percentage of admissions: White, 57 per cent.; negro, 43 per cent.

TABLE III.—INCREASE IN DIABETES MELLITUS AT CHARITY HOSPITAL.

		Total incidence, 1898–1909
0.63 per M.		" 1910–1919
90 per cent. increase 1.20 "	White	" 1898–1909
0.72 "	"	" 1910–1919
94 per cent. increase 1.40 "	Negro	" 1898–1909
0.46 "	"	" 1910–1919
83 per cent. increase 0.83 "		

TABLE IV.—CHARITY HOSPITAL, 1910–1919.

	92,040 whites; 57 per cent.		68,004 negroes; 43 per cent.	
Admissions . . .				
Diabetes . . .	135	" 70 "	59	" 30 "
Aneurysm of aorta .	107	" 30 "	244	" 70 "
Acquired syphilis .	2,785	" 44 "	3,484	" 56 "
Congenital syphilis .	175	" 48 "	183	" 52 "
Gumma of brain .	82	" 41 "	115	" 59 "
Gumma of liver .	11	" 40 "	16	" 60 "
Syphilitic iritis .	50	" 35 "	93	" 65 "
Locomotor ataxia .	129	" 80 "	31	" 20 "

A striking fact is well illustrated in Table III. The incidence of diabetes mellitus has risen here as it has elsewhere, as has been reported by Joslin and others. The burden of the increase has been borne fairly equally by the whites and the negroes, and whatever cause is operating to produce this increase has affected both races alike. The total incidence has risen from 0.63 per thousand to 1.2 per thousand (90 per cent.); the white incidence from 0.72 per thousand to 1.4 per thousand (94 per cent.) and the negro incidence from 0.47 to 0.86 per thousand (83 per cent.). It can hardly be fairly contended that syphilis has been a more potent factor in the production of diabetes in the last decennium than in the preceding one. Moreover if it were, the heavier burden should have fallen upon the more intensely syphilized race. Since it fell upon both races approximately alike, it would be most plausible to seek the explanation in some factor affecting both alike and operating in increasing intensity. Syphilis hardly complies with these conditions.

That it does not comply with these conditions may be made evident from a study of the ravages produced by syphilis in other parts of the body in the white and negro respectively. Although the negroes form about 40 per cent. of the admissions to our hospital and furnish only 30 per cent. of the diabetics, they furnish more than 50 per cent. of all the syphilitic diseases. This I have tried to show graphically in Table IV.

The only exception to the rule that the negro furnishes more than his relative share of any syphilitic disease is locomotor ataxia. Dr. R. M. Van Wart (personal communication) informs me that this is in accordance with his clinical experience and that of other neurologists of the South. While the negro by no means shows even a relative immunity to luetic infection of the central nervous system, still he does show a relative decreased incidence of locomotor ataxia. It would appear, therefore, that we must accept one of two explanations of the smaller incidence of diabetes among the negroes and its possible relation to the theory of syphilitic pancreatitis as a common cause of diabetes mellitus:

1. There is no relation between the incidence of diabetes mellitus and syphilis; hence there is no probable etiologic relation between the two.

2. There is an unexplained immunity of the negro race to the production of spirochetal pancreatitis just as there is an unexplained immunity of the race to the production of locomotor ataxia.

I am convinced of the validity of the former alternative for the reasons set forth in this communication. The assumption of the second alternative would leave unexplained the increased incidence of diabetes mellitus in both whites and negroes and the fact that this incidence has increased equally in both races.

STUDIES ON THE DOSAGE OF DIGITALIS IN CHILDREN.

By Hugh McCulloch, M.D.,

AND

Wayne A. Rupe, M.D.

(From the Department of Pediatrics, Washington University, School of Medicine.)

Purpose. We have attempted to determine the amount of tincture of digitalis that is necessary to produce certain effects on the heart of children in order to establish whether the relation between body weight and dosage that has been recently established for adults is directly applicable to children, or if not, what modifications are necessary in order to base the dosage of the tincture of digitalis on the body weight of children of various ages and weights. As a result of our observations in thirty-six children, we have noticed certain effects that are worthy of mention and emphasis.

Introduction. Since the introduction of accurate methods of standardization of digitalis, it has been found that by the careful administration of large doses of the drug, effects on the human heart can be obtained within a very short time. Very typical and definite physiologic effects may be observed after two to five hours. It has been found necessary and advisable to use standard amounts of the drug, otherwise unsatisfactory and even unfortunate results might result when large doses are given. Eggleston[1] has advocated the use of formulæ from which the dose of standardized preparations of dried leaves, tincture or infusion may be estimated. The dose of the tincture is estimated according to body weight, 0.15 of a cat unit being given for each pound. The effects of the drug can be determined through its toxic action, which produces vomiting and alterations in the electrocardiogram. These alterations are notable delay in conduction from auricles to ventricles, alteration in the form of the T wave and the appearance of premature ectopic beats. The estimation of the dose is based on findings made in the pharmacologic laboratory on cats after intravenous administration of the drug. To apply the method to human beings and to change the method of administration of the drug from intravenous injections to oral administration may involve some alteration in the amount necessary to produce an effect. The dosage should be the amount of drug sufficient to produce an optimum therapeutic effect and just below the amount that would produce toxic effects. In the methods mentioned no account is taken of the possibility of any variation in the response to digitalis, with variations in age or body weight, over such wide limits as in children and adults. It has not been shown that hearts show appreciable variation in the

[1] Arch. Int. Med., 1915, xvi, 1.; Jour. Am. Med. Assn., 1920, lxxiv, 733.

character of their response to digitalis even though the hearts be from species widely separated; for example, frogs, cats or human beings.   It is quite possible that the method of administration may lead to some variation.   The theoretic dosage for children has been the same for adults, due allowance being made for difference in body weight.

Method.   The drug employed has been the tincture of digitalis obtained in the open commercial market and kept for general use. It has been standardized according to the cat method of Hatcher and Brodie,[2] has been kept under conditions that prevent an appreciable depreciation in its potency and has been standardized at intervals.   Only small amounts sufficient to last a few days were dispensed to the wards for use.   The cat standardization of the tincture has shown that one cat unit averaged 1 c.c.

The patients selected were in the St. Louis Children's Hospital for various complaints, none of which were of such a nature at the time of the administration of digitalis to confine the patient to bed. None of the patients were suffering from recognizable heart disease nor from any condition that might have any effect on the heart. As far as could be determined the hearts were normal.

For the purpose of observation the patients were confined to bed or allowed very limited periods in a wheel chair or sitting about the wards.   The children were all somewhat below normal weight for their age, though not to such an extent as to influence the action of the drug; nor was there any abnormality or disturbance in the gastro-intestinal tract.   Electrocardiograms for control were made before any of the drug had been given, and subsequently every twenty-four hours.   Weights in kilos were obtained in the beginning of the experiment.   The children were all under similar circumstances.   No element was present which might have induced tachycardia, such as fever, excitement or emotion.   The drug was given in small amounts of water, at times with small quantities of saccharin, four times daily, when the stomach was more or less empty. The estimated total dose was divided so that an interval of six days was required for the administration of the total amount.   The drug was measured out in individual doses in minims, using a minim glass, not a dropping pipette; but the total amount of the drug and all estimations were made in cubic centimeters.

Evidence of the action of the drug was indicated by vomiting or such alterations of the electrocardiograms as have been previously recognized as digitalis effects.   The appearance of any of these phenomena was taken as the end-point of the observation and the drug was discontinued.   The amount of the drug which had been taken up to this time was estimated to be the dose necessary to produce a therapeutic effect.   Vomiting was often associated with

malaise and discomfort, but the difficulty in interpreting these latter two symptoms in children made them unsatisfactory to rely upon as positive evidence. The vomiting was considered to be an effect only when it occurred at times other than immediately after the drug was administered and when it could not be attributed to some other cause.

Case No.	Age in months.	Weight in kilos.	No. of c.c. every 4 hrs.	No. of doses received.	Initial and subsequent effects noted.	Total c.c. of drug received.	C.c. per kilo received.
1	13	8.5	1.06	5	Vomiting; partial $A-V$ block; increased inversion of T III	5.30	0.62
2	25	8.9	0.33	6	Sinus arrhythmia; decrease in ventricular rate	2.00	0.22
3	16	9.1	1.14	7	Vomiting; increase in $P-R$ time	8.00	0.88
4	12	9.6	0.80	24	No effects produced	19.20	2.00
5	20	9.6	0.80	12	Sinus arrhythmia; decrease in ventricular rate	9.60	1.00
6	21	9.6	0.80	24	None	19.20	2.00
7	24	9.6	0.67	16	Sinus arrhythmia; decrease in ventricular rate	10.00	1.05
8	28	10.0	1.20	14	Partial $A-V$ block; later sino-auricular block; vomiting	16.00	1.60
9	23	11.1	0.90	8	Sinus arrhythmia; decrease in ventricular rate; vomiting	7.20	0.65
10	30	11.2	0.60	10	Decrease in ventricular rate	6.00	0.53
11	24	11.7	0.71	14	Sinus arrhythmia; decrease in ventricular rate; increase in $P-R$ time	10.00	0.85
12	34	12.8	1.60	4	Vomiting; sinus arrhythmia	6.40	0.59
13	27	13.3	1.67	12	Vomiting	20.00	1.50
14	49	13.9	1.73	12	Vomiting; sinus arrhythmia	20.80	1.50
15	42	14.4	1.80	14	Vomiting	25.20	1.74
16	48	14.7	0.93	16	Vomiting; increase in $P-R$ time	15.00	1.06
17	66	14.7	1.57	7	Sinus arrhythmia; vomiting	11.00	0.75
18	35	15.0	0.53	6	Sinus arrhythmia	3.20	0.21
19	36	16.0	1.33	8	Vomiting; partial $A-V$ block	10.70	0.66
20	46	16.0	1.34	5	Vomiting	6.70	0.41
21	62	16.8	1.40	18	Decrease in rate	25.20	1.50
22	72	17.1	2.15	4	Vomiting	8.60	0.50
23	51	17.6	1.47	9	Increase in $P-R$ time; vomiting; increased inversion of T III	13.20	0.75
24	72	19.0	2.00	8	Sinus arrhythmia	16.00	0.84
25	60	21.0	0.83	23	No effect produced	19.00	0.90
26	96	21.8	0.83	23	No effect produced	19.00	0.87
27	79	23.4	2.98	13	Vomiting; decrease in ventricular rate	38.80	1.66
28	132	26.8	1.67	20	Vomiting; increased inversion of T III	33.30	1.25
29	132	27.7	2.16	20	Vomiting; decrease in ventricular rate	45.20	1.50
30	144	27.7	2.00	24	Increased inversion of T III	48.00	1.74
31	120	29.0	0.81	22	No effect produced	18.00	0.62
32	120	30.8	0.81	22	No effect produced	18.00	0.58
33	132	33.0	1.00	24	No effect produced	24.00	0.73
34	156	40.0	1.67	24	No effect produced	40.00	1.00
35	156	40.5	1.13	24	No effect produced	27.00	0.66
36	180	50.0	2.00	24	No effect produced	48.00	0.96

Alterations of the normal electrocardiogram, which were recognized as digitalis effects, are decrease in rate and sinus arrhythmia; prolongation of the auriculoventricular conduction time, sinoauricular and auriculoventricular heart-block, premature ectopic contractions and alterations in the form of the T wave.

In this group of cases we have considered a persistent decrease in the rate of fifteen or more beats per minute as counted on the electrocardiogram as positive evidence of digitalis effect. Many of the control curves showed slight variations of the cardiac rhythm, but certain cases developed a very exaggerated sinus arrhythmia which was independent of respiration and which was attributed to digitalis. A few of the cases showed a well-marked sinus arrhythmia in the control curves, and in these cases any further alteration in rate or of this arrhythmia was not considered a digitalis effect. Sino-auricular heart-block was noted. Further changes were prolongation of the P–R interval of 0.040 second or more up to partial auriculoventricular block. Diminution in size or reversal of direction of the T wave were also observed and attributed to the action of the digitalis.

Discussion. Vomiting was observed as the first sign in 13 cases. When it occurred it seemed to be an early symptom and came after the administration of smaller quantities of the drug than were required to produce the other effects.

The rate was decreased more than fifteen beats per minute in 9 cases. Of these 9 cases, 5 showed a definite sinus arrythmia. The appearance of the sinus arrythmia in these children also seemed to be an early symptom, occurring before other changes in the electrocardiogram took place. The decrease in the rate without a sinus arrhythmia was not an early symptom.

Sinus arrhythmia which had not been present in the control curves appeared in 9 cases, and was well marked in all. In the curves of the sinus arrhythmia it was found that the P–R interval showed considerable variation. It was always shortest after the long diastolic pauses and longest during the periods when the rate was increased. When the P–R interval was prolonged in these periods of increased rate it was increased beyond the normal P–R time as observed in the control curves. An example of this effect is shown in Figs. 1 and 2 from Case 36. They show a sinus arrhythmia not related to respiration. Digitalis effect. Q–R–S complex normal, T wave upright. Ventricular rate varies, being 55.5 per minute in the periods of retardation, 93.8 per minute in the periods of acceleration. The P–R time varies from about 0.120 second after the long diastolic pauses; when the rate increases to 90 the P–R time is 0.160 second. The normal ventricular rate in this case was 93.5 per minute. The normal P–R time was 0.160 second.

Interpretation. Sinus Arrhythmia. Otherwise Normal Curves. An electrocardiogram similar to No. 3911 (Fig. 1) was obtained.

At 2 P.M. the patient was given 0.001 gram of atropin sulphate intramuscularly. Record No. 3916 was obtained at 2.45 P.M. It shows a normal cardiac mechanism. No evidence of any arrhyth-
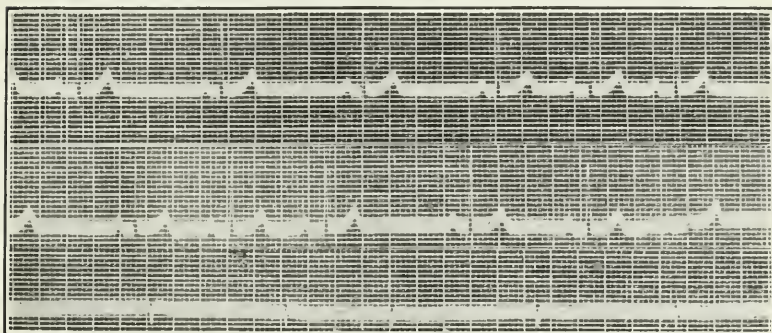
Fig. 1.—Electrocardiogram No. 3911.   Made April 8, 1920.[3]

mia. $Q-R-S$ complex is normal. The T wave is diphasic in Lead I and II, inverted in Lead III. Ventricular rate, 150.0 per minute. $P-R$ time, 0.120 second.

Interpretation.   Normal cardiac mechanism.   Tachycardia due to removal of vagus inhibitory influences. T wave inverted.
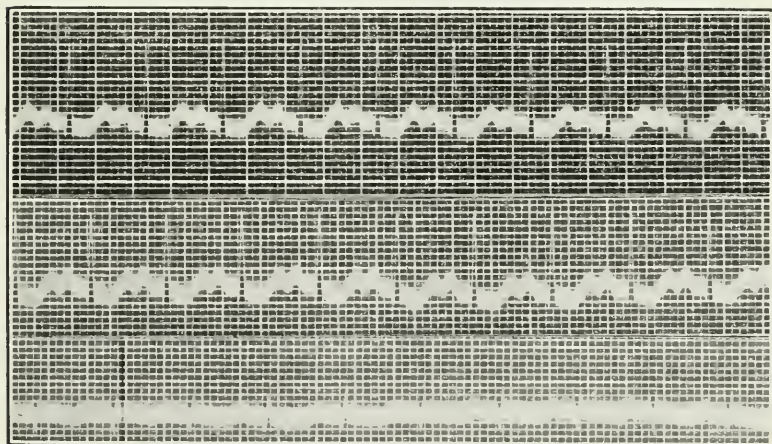
Fig. 2.—Electrocardiogram No. 3916.   Made March 9, 1920.

The variation of the $P-R$ time in these cases may be explained in two ways: There may be a digitalis effect of the conducting tissue, causing a delay in the passage of the impulse, which may be apparent only when the rate is faster and the conducting tissue has not the

[3] Lead I, II and III from above downward and from left to right.   The three usual leads made under standard conditions.

same length of time in which to recover from the fatigue produced by the spread of the preceding impulse. Under such circumstances the $P–R$ interval will be longer in the periods of faster rate and will be short in the periods of slowing when the conducting tissue has had sufficient time to recover. Or the variation in the $P–R$ interval may be evidence of variations in vagus action in association with fatigue in the conducting tissue, as the vagus nerve on stimulation delays the conduction of the impulse from auricles to ventricles.[4] Removing the vagus influence on the heart by injection of atropin in our cases showed a complete release of the heart from vagus inhibition and a coincident disappearance of the sinus arrhythmia, the $P–R$ interval being constant and not prolonged.

Depression of the impulse conduction from the sinus node to the auricles was shown in one case by sino-auricular heart-block.

The $P–R$ interval was delayed 0.040 second or more in 4 cases and partial auriculoventricular heart-block occurred in 3 cases.

Alteration in the form of the T wave was observed 4 times.

Ten cases showed no sign of digitalis effect. Of these 10 cases 8 were under observation in the beginning of the study when the dose given was too small to produce an effect. The remaining 2, for reasons not apparent to us, showed no reaction after very large doses. It is possible that certain individuals may be unusually tolerant to digitalis given by mouth or may fail to absorb the drug.

In children weighing twenty kilos or less a response was noted in 14 patients with doses below 1 c.c. per kilo, while in only 8 patients was the dose necessary to produce an effect above 1 c.c. per kilo. In children whose weight was above twenty kilos 8 did not respond when the dose of digitalis was below 1 c.c. and 4 responded only when the dose was considerably above 1 c.c. It would seem, then, that children up to the body weight of twenty kilos are somewhat more sensitive to digitalis than children above that weight.

Considering the group as a whole, however, in only 3 patients were digitalis effects noted on doses corresponding to the dosage described by Eggleston as sufficient to produce an optimum therapeutic effect on adults. No effect was noted in 8 patients after doses of 2 or 3 or more times the amount prescribed by Eggleston. Effects were obtained in 13 patients only after administration of doses 2 or 3 times as great and in 10 only with doses at least five times as great. It must be considered that Eggleston's formulæ have been applied to patients with heart disease and not to patients with normal hearts. Administration of quite large amounts to these children was never attended by other than very minor evidences of digitalis action.

Conclusions. 1. Our results show that between eight and twenty kilos of body weight, or up to the approximate age of four years,

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[4] Robinson and Draper: Jour. Exper. Med., 1912, xv, 14.

children respond more readily to digitalis than do children above this weight and age. It would seem that older children with normal hearts require a larger amount per unit of body weight than is necessary to produce an effect in adults with heart disease.

2. There is considerable variation in the amount of digitalis necessary to bring about a response in the hearts of children.

3. We have noticed vomiting to be one of the early signs of the effect from digitalis administration, often occurring before there were any alterations in the electrocardiogram. Changes in the electrocardiogram were not constantly found in all the cases in which a digitalis effect was obtained. The most common change observed in this group of children was the appearance of a sinus arrhythmia. Alteration in the size and direction of the T wave occurred in a small number of all the cases.

PEDUNCULATED TUBERCULOSIS OF THE PERITONEUM: PERLSUCHT: EXTREME INFREQUENCY OF THE CONDITION IN THE HUMAN: REPORT OF A CASE WITH DISCUSSION OF BOVINE INFECTION.

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In contrast to the types of tuberculosis of the peritoneum and pleura observed in the human, peritoneal and pleural tuberculosis in cattle manifests itself in the production of caseous or calcified masses of variable size, surrounded by a fibrous capsule and embedded in a rather loose proliferating connective tissue distinct from the subperitoneal connective tissue; frequently these masses attain considerable dimensions and by their weight draw out the underlying connective tissue, thus acquiring a pedicle. Practically always there are associated bands of adhesions studded with rows of caseous sessile nodules, suggesting the appearance of a string of pearls, whence the name "Perlsucht." While this type of tuberculosis can be observed *par excellence* in the sheep, it is the form in which tuberculosis of the serous membranes of all cattle most frequently manifests itself.

It is interesting to note that this type of tuberculosis is an exceedingly rare occurrence in the human, there being recorded in the literature the description of but two cases, the first by Bizzozero in 1867 and the second by McCallum in 1901. Bizzozero was unable to find recorded a similar condition, and later McCallum, who included in his thorough investigation of the literature the excellent reviews of the more recent literature of Brunn, failed to find any reference to a similar condition.

The case reported by Bizzozero occurred in a twenty-four-year-old peasant who died with the symptoms of pulmonary tuberculosis. The autopsy revealed conglomerated tubercles in the lungs with cavities in the apices. The peritoneal cavity contained about a liter of seropurulent fluid and the loops of intestine were firmly adherent to one another by a yellowish exudate. Removal of the exudate revealed innumerable whitish, tuberculous nodules of the size of the finest grain of millet seed to that of a pea, scattered throughout the visceral and mesenteric peritoneum. Sometimes the tubercles united to form a plate the size of a five lira piece. The nature of the peritoneal tubercles, especially those of the mesentery, was very varied. Some amounted to mere white spots embedded in the tumefied peritoneum, others projected by their whole height above the level of the peritoneum, while still others were not attached by their point of origin except by a peduncle of a length which varied from 1 mm. to 1 cm. and varying in diameter from 1 to 1.25 mm.; often the peduncle was flattened together, amounting to a thickness of but 0.125 mm. The histologic constitution of the tubercles immersed in the peritoneum and those with the peduncles was the same, and, as usual, had outside a layer of connective tissue in active proliferation and internally the elements in detritus and fatty degeneration. The mucosa of the ileum was pigmented and showed numerous tuberculous ulcers, corresponding with which were especially numerous tubercles on the peritoneum.

"The microscopic examination of the peritoneum," he says, "shows me the probable reason why, while in other cases of tuberculosis the small neoplasms are adherent to the peritoneum, in mine they were for the most part pedunculated. The preparations show that the connective tissues of the membranes were separated by an abundant hyaline fundamental substance in which were numerous new-formed cells, of which some were spherical or oval and others fusiform or stellate; naturally the peritoneum, tumefied and softened by the presence of superfluous fundamental substance and of numerous new-formed cells, could not support the weight of the tubercles, and yielding, formed of necessity a peduncle. The layers of muscle fibers have taken no part in the new formation.

"This case leads me to believe that in all probability tubercles might also produce a kind of free body in the peritoneum, as is the case with fibromata, lipomata, etc., and even sclerosed appendices epiploicæ."

McCallum's case occurred in a white woman, aged thirty-eight years, who died with the symptoms of pulmonary tuberculosis. At autopsy the peritoneal cavity contained no excess of fluid; the peritoneal surfaces were free and glistening, but lying just under the serous surface of both visceral and parietal peritoneum were numerous nodules which had a most extraordinary arrangement. The

diameters varied from 1 mm. to 2 cm., and while some were only slightly elevated above the level of the peritoneum, most of the nodules hung free, each in a sort of long, blind tube, formed apparently by the drawing out of the peritoneum into a tubular pedicle. Some of the pedicles reached a length of 12 cm. and most of them took their origin from a wide uplifting of the peritoneum. All of the pedicles contained a clear reddish-yellow fluid which could readily be made to gravitate to either extremity by inverting or elevating the distal nodule; in many, the fluid could be made to run back and spread out under the peritoneum of the intestine and perhaps even to enter another tubular pedicle. In a few instances the tubular prolongations showed no caseous mass at the end, and, indeed, one elongated sac with thin delicate walls and clear yellow fluid contents was found entirely free in the peritoneal cavity. In some cases small caseous nodules were found hanging by a stalk inside the elevated peritoneum.

Sections of the nodules showed them to be necrotic except peripherally, where the structure exhibited the characters of tubercosis. Tubercle bacilli were found in great numbers, especially in the zone between the living and necrotic tissue.

The spleen and liver exhibited tubercle-like nodules which proved to have all the histologic features of tuberculosis. The lungs were studded throughout with miliary tubercles, and finally there was a tuberculous leptomeningitis, the pia over the pons, cerebellum and cerebrum showing a yellowish exudate with tubercles along the vessels.

The case which occurred in this hospital was that of a twenty-four-year-old white man, a Polish laborer, who was admitted to the South Side Hospital November 21, 1919, complaining of pain in the chest and abdomen, cough, general weakness and loss of weight. Both the family and previous history were negative. The patient stated that he was apparently well until about five years ago, when he began to suffer with constipation, anorexia and intermittent colicky pains of great severity. Two years ago he began to complain of a hacking cough which persisted to the time of admission. One week before admission he fainted on the street.

Physical examination revealed an emaciated young man, acutely ill and showing marked pallor of the skin with cyanosis of the visible mucous membrane. The thighs were acutely flexed on the abdomen. The chest was of the phthisical type and auscultation revealed many fine and coarse moist rales coming in showers and present all over the chest. Percussion revealed areas of hyperresonance, alternating with areas of dulness. The abdomen was tender and presented a diffuse board-like rigidity. Both ankles were edematous and pitted on pressure. Temperature on admission was 99.6°, rising later to 104°. The pulse registered 140 and was very shallow.

Respirations were 42. Death ensued thirty-six hours after admission.

Autopsy was performed five hours after death, with the following findings:

Anatomic Diagnosis. *Lungs.* Acute hemorrhagic tuberculous bronchopneumonia; chronic ulcerative tuberculosis; chronic productive and adhesive pleuritis (tuberculous).

Heart. Hydropericardium; cardiac hypertrophy and dilatation; acute parenchymatous myocarditis.

Abdomen. Chronic deforming peritonitis with extensive matting together of the viscera.

Gastro-intestinal Tract. Multiple subserous pedunculated nodules of the small and large intestine (approximately 1200 nodules).

Liver. Chronic productive tuberculous perihepatitis; multiple miliary tubercles.

Spleen. Chronic productive tuberculous perisplenitis; multiple miliary tubercles.

Kidneys. Chronic diffuse nephritis (large white kidneys); multiple cortical miliary tubercles.

Résumé of Protocol. The body is that of a poorly developed white male of poor musculature and nutrition, measuring 63 inches long and weighing about 100 pounds. A frothy blood-tinged fluid exudes from both nostrils. The neck is long and narrow and the inferior angle acute. Visible mucous membranes are deeply cyanosed.

The under surface of the recti muscles is intimately adherent to an underlying mass, from which it has to be separated by dissection. This mass is composed of a diffusely thickened and fused peritoneum and omentum, which give rise to an irregularly nodular, grayish yellow and in places caseous material, the whole forming a layer with an average thickness of 2 cm. The nodules in this mass are conglomerated, vary in size, some attaining the dimensions of a hazelnut; they are firm, yellowish gray and apparently free from caseation. This mass fuses with the capsules of the liver and spleen. The intestines present innumerable subserous, pedunculated, whitish yellow, firm nodules which vary in size from a pea to a large hazelnut, and are irregularly globular. In view of the extensive adhesions which wall together all the viscera, it is necessary to dissect out the abdominal and pelvic contents *en bloc*. There is no fluid in the abdominal cavity.

The right pleural cavity presents a few dense adhesions posteriorly; the left pleural cavity is practically obliterated by dense fibrous adhesions. The lungs are voluminous and completely fill the chest cavity. There are multiple irregularly scattered subpleural hemorrhages, some of which attain the size of a quarter. The lungs have a firm, finely nodular feel, cut more readily than normal and pieces sink only slightly below the surface of water. The cut surface is literally peppered with innumerable, regularly disseminated, pin-

head-sized grayish elevations which give to the surface a coarsely granular feel. These are surrounded by a concentric elevated deep reddish zone and then by a depressed brownish-red area. Bases of both lungs are intimately adherent to the domes of the diaphragm, from which they must be cut away. The right lower lobe presents an area of caseation about the size of a quarter. There are no areas of cavitation. Bronchi show a congested and swollen mucosa, to which is adherent a thick, tenacious, bloody mucus. Peribronchial lymph nodes are swollen, juicy and anthracotic.

The liver is intimately adherent to all the adjacent structures and has to be dissected out. Glisson's capsule is greatly thickened, attaining in places 12 mm.; it is grayish yellow in color and firm. The organ, except for its capsule, cuts normally, and the cut surface presents a nutmeg appearance from dilatation and congestion of the central veins. Right lobe superiorly shows on section a small circular pea-sized cavity distended with pus and located about 2 cm. below the surface. There are no tubercles apparent to the naked eye.

The spleen is bound to the adjacent viscera and posterior abdominal wall by dense adhesions; it is enlarged and measures 15 cm. long by 9 cm. wide by 6 cm. thick. The capsule is greatly thickened, attaining in places 9 mm. The substance is soft but non-grumous. The cut surface shows an excess of blood, the Malpighian follicles swollen, and there are numerous reddish-gray, irregularly scattered nodules, the largest the size of a dime and not elevated.

Both kidneys are equally enlarged, measuring 15 cm. long by 8.5 cm. transverse by 6.5 thick. Capsules strip easily, leaving behind a smooth pale cortex in which the stellate veins are congested. There are apparent the persistent shallow grooves of fetal lobulations. The cut surface is distinctly pale, the cortex swollen and the markings indistinct. There are multiple, irregularly scattered, pinhead sized tubercles, all of which are confined to the cortex.

Gastro-intestinal Tract. The coils of the small and large intestine are intimately adherent to each other and to the adjacent viscera. The serosa of both small and large intestine is literally showered with multiple pedunculated, irregularly globular tumor masses, which vary in size, the smaller ones the size of a pea and the largest ones attaining the size of a hazelnut. The pedicles average 3 or 4 mm., are reflected over the nodules and merge into the serosa of the intestine. The nodules proper are grayish yellow, firm and cut with resistance; they are apparently perfectly preserved in the gross and show no central caseation. The cut surfaces are suggestive of fibroma or fibromyoma. The mucosa was carefully examined for evidence of ulceration but was everywhere perfectly intact.

Histopathology. The multiple nodules of the intestine. Numerous sections of these were studied, twenty-four in all. Some of the sections were made through the nodule so as to pass through the

pedicle and underlying tissue. The central portions of the nodules reveal a pale, bluish pink, for the most part homogeneous and in places finely granular substance, which has no definite structure and corresponds to caseous necrosis, notwithstanding the fact that there was no naked eye evidence of caseation. Toward the periphery of the nodules the structure becomes more distinct, presenting the characters of tuberculous granulation tissue, consisting of irregularly arranged epithelioid cells with some multinucleated giant cells and numerous small spheroidal cells; more externally the capsular layer
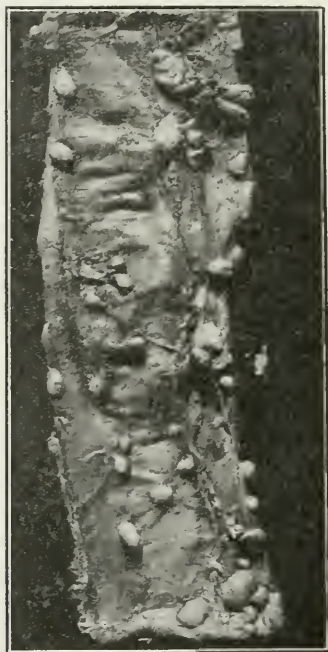
Fig. 1.—Photograph of intestinal serosa, showing multiple "pedunculated tuberculomas." These were universally distributed over the serosa commencing at the beginning of the jejunum and terminating at the rectum, numbering at least 1200 in all.

is formed by elongated connective-tissue cells over which can be seen in some sections the peritoneal endothelium. There is a distinct demarcation between the tuberculous process in the nodules and the underlying structure of the intestine. The interposed pedicle is composed of a loose, rather vascular connective tissue, showing a sprinkling of small round cells.

Lungs, liver, spleen and kidneys reveal upon microscopic examination numerous irregularly scattered perfectly typical epithelioid tubercles, with areas of caseous necrosis. The parietal peritoneum

shows tuberculous granulation tissue with large areas of caseation, and in places the structure is sufficiently preserved to show the conglomeration of epithelioid tubercles.

Comment.—The type of lesion described in the visceral peritoneum of the foregoing case together with the peritoneal pathology described by Bizzozero and McCallum in their own cases may be explained on a basis of a peculiar and in fact specific reaction of the host to an infection with a tubercle bacillus possessed of a relatively very low grade virulence. The literature on the subject is practically limited to a discussion of the frequency of bovine infection in the

Fig. 2.—Photograph of mucosa of small intestine, showing an entire lack of any evidence of ulceration.

human, its contribution to human mortality and methods of differentiation of the human bacilli from the bovine type. Except for some brief discussion of the human response to bovine infection in the report of the British Commission in 1911, there could not be found in the literature any mention or description of the nature of the pathology in the human resulting from infection with bovine bacilli.

Indeed, the importance of bovine infection in the human, more particularly in children, has been emphasized by Park and Krumwiede, who made an admirable study of 1042 cases with the following

conclusion: "Bovine tuberculosis is practically a negligible factor in adults. It very rarely causes pulmonary tuberculosis or phthisis, which causes the vast majority of deaths in man and is the type of disease responsible for the spread of the virus from man to man. In children, however, the bovine type of tubercle bacillus causes a marked percentage of the cases of cervical adenitis, leading to operation and disfigurement. It causes a larger percentage of the rarer types of alimentary tuberculosis requiring operative interference or, causing the death of the child directly or as a contributing
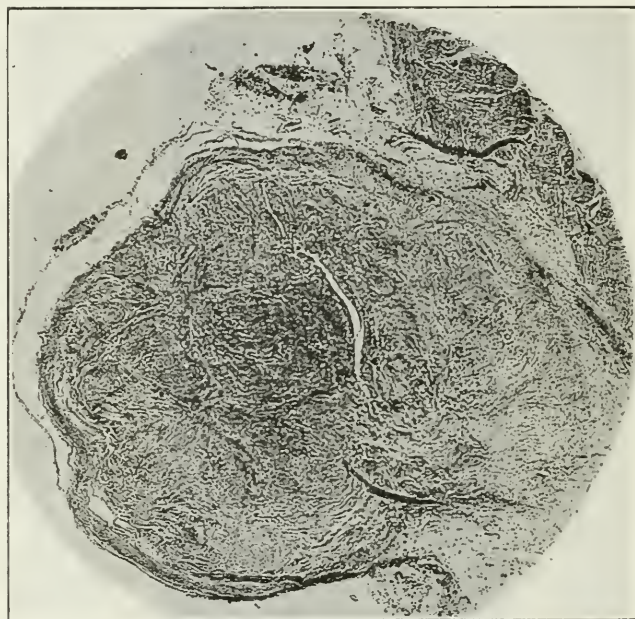
Fig. 3.—Low power photomicrograph of a nodule, showing complete encapsulation with peritoneal endothelium over the capsular layer. Note above and to the right, the muscularis of the intestine separated from the tuberculous process by healthy tissue.

cause in other diseases. In young children it becomes a menace to life and causes from 6 to 8 per cent. of the total fatalities from this disease."

Bacteriologically the differentiation between human and bovine bacilli can be definitely and readily accomplished. Briefly the types are differentiated culturally and by virulence tests as follows: All cultures growing luxuriantly on glycerin egg from the start are of the human type, while those growing sparsely or not at all in the first few generations are of the bovine type. The rabbit or calf virulence test is conclusive; bovine bacilli in every instance when

injected in doses of 0.01 mg. intravenously cause a generalized tuberculosis which is progressive and causes the death of the animal. Human viruses injected in the same amount produce no disease at all or at the most a local tuberculosis somewhere in the body.

It is unfortunate that virulence tests were not carried out with emulsions prepared from the nodules in our case. The immediate impression gained from the gross picture was that of tumor, and, in fact, the subserous nodules were regarded as the intestinal analogy of von Recklinghausen's multiple fibromatosis of the skin, so that
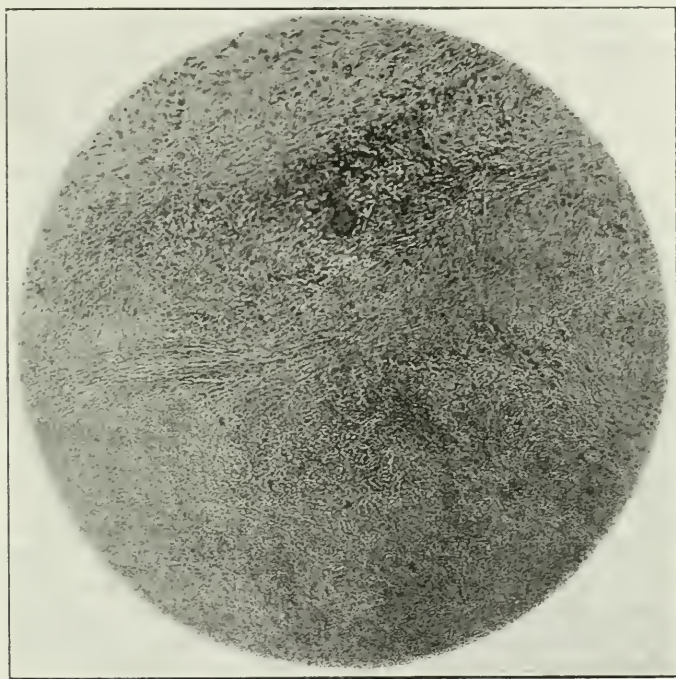
Fig. 4.—High-power photomicrograph taken from low power (Fig. 3), showing caseous necrosis, an epithelioid tubercle and tuberculous granulation tissue.

the specimens were placed in formalin and the tuberculous nature not suspected until revealed by routine histologic examination. The gross pathology of the lesion of our case as well as that of the peritoneum of the other human cases reviewed in this report is in every way identical with the tuberculous lesion of the peritoneum of cattle and designated as Perlsucht. This together with the fact that a very similar pathology has been produced by experimental inoculation of numerous Rhesus monkeys with bovine tubercle bacilli makes it reasonable to assume that the infectious organism in these human cases is very likely of the bovine type. The low-

grade virulence possessed by bovine bacilli for the human, and the established fact that transmutation of one type into another cannot occur, lead to the conclusion that the terminal generalized miliary tuberculosis in the last case was due to a superimposed infection with human bacilli. The British Commission reports two instances in which both human and bovine bacilli were isolated from the same patient, one from a caseous retroperitoneal gland in a seventy-year-old man and the other from a caseous bronchial gland of a four-and-a-half-year-old child dying with generalized tuberculosis. Out of 10 cases of alimentary tuberculosis in children, bovine bacilli were isolated from 4.

Finally it is interesting to call attention to the striking similarity of the pathology in pendulous tuberculosis of the peritoneum and that of the multiple, so-called "sarcoid growths" of the skin, which are grouped by Darier into four types of nodular skin lesions; in three of these the process is almost certainly tuberculous, while the fourth represents probably a form of cutaneous lymphosarcomatosis. As a rule the multiple benign sarcoid growths are characterized by the appearance of rounded, painless nodules which vary in size from a pea to a hazelnut or larger.   Histologically the picture is strikingly like that of tuberculosis, variable numbers of giant cells of the Langhans type lying in a stroma of epithelioid and small round cells. While in the group of Boeck ulceration never occurs, the nodules in the second group ulcerate occasionally and are located almost exclusively on the extensor surfaces of the extremities, bearing a clinical resemblance to erythema induratum.   In a third group of cases, described by Darier and Roussy as the rarest of all varieties of so-called sarcoid growths, the nodules are rounded or oval, painless, the overlying skin not ulcerated, the individual enlargements vary in size from a pea to a walnut and are occasionally connected with one another by a cordon of easily palpated sub-cutaneous shot-like bodies. The histologic features as depicted by Darier are indistinguishable from those of tuberculosis.

In many of the reported cases of multiple sarcoids the authors report an associated tuberculosis most commonly of the lungs and lymph nodes.   In a second set of cases positive reactions to tuber-culin were secured. In still other cases injections into guinea-pigs of emulsified nodules produced typical tuberculous lesions.   While at times the reaction in guinea-pigs was prompt, the animal dying in a few weeks, in other instances life was prolonged to the extent of a year or more until sacrifice of the animal resulted in the finding of nodules revealing on histologic examination changes indicative of indolent or even healed tuberculosis, the virulence of the tubercle bacillus thus varying greatly. This latter type of case, together with the cases in which no organisms were found, represent in all likelihood cases of bovine infection which could easily be differen-

tiated by virulence tests in rabbits. Bovine bacilli, while exceedingly virulent for rabbits, practically never cause death in guinea-pigs even when injected in large doses. In this connection it is interesting to note that the British Commission appointed to inquire into the relations of human and animal tuberculosis investigated 54 cases of lupus vulgaris, and in at least 25 per cent. of the cases they isolated tubercle bacilli which corresponded to the bovine type culturally and possessed the characteristic bovine virulence for rabbits.

Summary. 1. A case of pendulous tuberculosis of the peritoneum is reported, preceded by a brief review of the only other two cases of human pedunculated peritoneal tuberculosis recorded in the literature.

2. The condition is compared to the lesion in tuberculosis of the serous membranes of cattle designated as Perlsucht, with which it is pathologically identical.

3. An attempt is made to associate with the process the bovine type of tubercle bacillus and there follows a discussion of the relative virulence and importance of the bovine and human types of tubercle bacilli, in different forms of human tuberculosis, together with a brief review of the methods for differentiation of the two types of bacilli.

4. The pathology is discussed from the standpoint of representing the intestinal equivalent of the multiple benign sarcoids of the skin; in reality, low-grade tuberculous infections, better termed nodular cutaneous tuberculomas.

I wish to express my indebtedness to Dr. Samuel Haythorn, Director of the Singer Memorial Laboratories, for his interest and kindness in making the photographs and photomicrographs.

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THE SEQUELÆ OF EPIDEMIC ENCEPHALITIS.[1]

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At the height of an epidemic the attention of the medical world is focussed on immediate results rather than on after-effects. "Will the patient recover or die?" is the prognostic question above all others. When, however, the fire of the epidemic has burnt itself out and we begin to take stock of the condition of the survivors, other questions press for an answer. "Are certain disabilities to be regarded as temporary or permanent?" "When the patient has made an apparently complete recovery, is all well with him or is anything more to be feared?"

The answer to such questions can already be given in the case of influenza. Many a patient recovers from the disease only to be left a weakling for the rest of his life, open to the attacks of the tubercle bacillus and other invaders of the respiratory tract. What can be said of the recent outbreak of epidemic encephalitis?

In estimating the permanence of the damage done by the virus of epidemic encephalitis it is often difficult to separate what may with justice be called an after-effect from merely a long-continued manifestation of the disease. Sometimes symptoms may persist so long that we may with reason class them as sequelæ. Other after-effects succeed the illness only after an interval of varying duration.

The first cases of the disease appeared in Winnipeg in October, 1919. An analysis of 75 cases personally investigated together with the autopsy findings in 16 cases has been published in previous papers.[1] The worst of the epidemic was over by the end of January, 1920. Sufficient time, therefore, has elapsed to enable some estimate to be made as to the degree of completeness of recovery and to determine whether any untoward after-effects may be expected.

It may be said at once that in our experience complete and rapid recovery is uncommon except in really mild cases, that many patients continue to suffer from some of the symptoms in modified form, and that in a few there appear new symptoms which must be regarded as true after-effects. Of 31 patients who have been communicated with, 20 complained of symptoms after all the acute manifestations of the disease had disappeared.

For convenience of description the symptoms may be divided into four main groups: (1) General; (2) paretic (cranial nerves); (3) irritation; (4) parkinsonian.

[1] Boyd, W.: The Winnipeg Epidemic of Encephalitis Lethargica, Can. Med. Assn. Jour., February, 1920. Epidemic Encephalitis: A Study of Seventy-five Cases with Sixteen Autopsies, Ann. Med., July, 1920.

1. *General Symptoms.* In those recovering from encephalitis perhaps the most common complaint is marked general asthenia, which may last for many months. There is the same lack of energy and initiative so characteristic of the convalescence from influenza, but it is even more marked in degree. A large proportion of the patients reached by our "follow-up" system complained of this asthenia. In some cases it was many months before the patient began to recover strength. One patient was still very weak six months after the onset of the illness.

The explanation of the asthenia is open to doubt. If lethargic encephalitis is regarded as purely an affection of the central nervous system the asthenia may be due to exhaustion of the nerve cells. If, on the other hand, it is a true, systemic infection, with special localization in the central nervous system, as in the writer's opinion is the case, the asthenia may be similar in nature to that following such general infections as influenza and typhoid fever.

Headache, or a sense of fulness or discomfort in the head, has been a common after-effect. It is most frequently occipital in type, but it may involve any region.

Alteration in the temperament has been observed in a number of our cases, sometimes with definite evidence of mental disturbance. One girl, aged six years, after a typical attack of lethargic encephalitis, made a good recovery. Three months later her parents reported that her disposition had undergone a complete change. From being a bright, playful child she had become dull and apathetic and would sit for hours motionless in a chair, almost like one suffering from myxedema. A peculiar feature was an occasional loss of bladder control, more especially at night.

At least three of the cases have developed mental symptoms. In two of these delusions were the most prominent feature. In the third there was a general mental deterioration, accompanied by loss of memory and inability to focus the attention.

One patient, after spending three weeks in the hospital, during which he presented a typical picture of the disease, was discharged as improved. Two weeks later he developed an erythematous rash on the neck, arms and body, which was intensely itchy and lasted for about a week. His subsequent recovery was unusually delayed, and even now, nine months later, he has by no means completely recovered his strength.

Occasionally the apathy and torpor characteristic of the acute stage of the disease establish themselves as apparently permanent features of the patient's mental constitution and the flash and speed of the mind are lost forever. One such case reminds one irresistibly of the description given by the Arab physician Karshish in Browning's poem:

> "He listened not except I spoke to him,
> But folded his two hands and let them talk,
> Watching the flies that buzzed."

Whether the mental processes of such a patient will ever return to normal it is at present impossible to say. It appears not unlikely that he will gradually sink into a state of dementia.

An interesting example of what may be considered as the general after-effects of encephalitis is the following:

Mr. W. K., aged sixty-six years, suffered from a characteristic attack of epidemic encephalitis in November and December, 1919. The outlook for some time was extremely grave, but eventually he made a wonderfully good recovery and was discharged from the hospital just before Christmas. An account of the case, with a photograph of the patient, has already been published. For some time he remained perfectly well and was able to take part in the work of a farm. About a month later, however, he began to experience a weakness which gradually increased until he was no longer able to work. He would wake up in the morning feeling fresh and fit for work, but in the course of half an hour he would be quite exhausted and fit for nothing but to lie down. From being quite alert mentally he again lapsed into an apathetic and sleepy condition, dropping off to sleep at a moment's notice. About the same time he began to suffer from stiffness and "rheumatic pains" in many of his joints. The stiffness of the arms was so pronounced that he was unable to put on his coat. His hands became swollen and puffy and later desquamated. At the time of the original illness diplopia was a prominent symptom. It disappeared with recovery, but with the onset of these fresh symptoms it reappeared, although only at occasional intervals. A humming noise in the ears was also noticed.

When seen by me for the second time, on August 10, 1920, I was at once struck by his dull, heavy, bucolic look, which was much more marked than at the time of discharge. It was not the mask-like face of Parkinson's disease, seen so frequently in these cases. Rather did it remind one of the appearance in myxedema; there was the same yellow tint, the same broad, heavy look, the same puffiness of the face—a condition, indeed, to which the patient himself made reference. Slight weakness and tremors of the left side of the face recalled the facial paralysis on that side from which he had suffered during the initial illness. All the reflexes were normal. There was some desquamation on the chest and on the back of both hands. He was able to converse perfectly rationally, but cerebration was very slow and the memory was defective. He complained of copious salivation and severe constipation.

The general impression produced on the observer was that of a person in whom both the physical and mental peculiarities were due to hypofunctioning of the thyroid. I know of no case recorded in which definite thyroid disease could be attributed to epidemic encephalitis. That such may occur, however, was shown by one case in my own experience. A young woman had previously suffered

from exophthalmic goiter, but for four years she had shown no signs of hyperthyroidism, although presenting a slight degree of exophthalmos. Following an attack of encephalitis, however, the symptoms of hyperthyroidism returned in full force, and she now presents a typical picture of Graves's disease. I greatly regret that in a series of eighteen autopsies on cases of epidemic encephalitis I omitted to examine the condition of the thyroid in every instance.

The case of Mr. K., just recorded, affords a good example of true sequelæ, the consequences of the disease. Occasionally, however, one meets with what appears to be a relapse or recrudescence of the original trouble. Economo[2] reports a remarkably interesting case of this description in which there were several severe attacks, separated by periods of remission. He died two years after the onset of the illness. The brain showed numerous lesions, both recent and old, characteristic of epidemic encephalitis.

One case of this description has occurred in our experience.

Mr. D., aged twenty-seven years, was admitted to the hospital on June 15, 1920. Three days before he was overcome by weakness while at work and the next day was confined to bed. On admission he was in a drowsy, stuporous condition, although restless and excited at night. He was unable to answer questions and did not appear to be conscious of his surroundings. The temperature fluctuated between 101° and 103° for eighteen days, when it returned to normal. About the same time there was marked improvement in both his physical and mental condition. By July 24 he was sitting up in bed and on August 6 he was out on the sun-balcony, bright and cheerful, and apparently well on the road to recovery. About August 16, however, he again began to show signs of physical lethargy and mental torpor. Fever returned, the temperature varying between 100° and 101°. Speech became increasingly difficult and finally he was unable to open his mouth.

When I saw him on August 20 he was lying like a log in bed, flat on his back, with his hands folded across his chest like an effigy on a tomb. Apart from following one about the room with his eyes he showed no sign of life. He was unable to open his mouth or to make any movements except to raise or lower the hand a little way, by means of which he was able to signify yes or no to a question. Cerebration, as judged by such response, was markedly delayed. There was slight facial weakness on the right and distinct ptosis on the left side. The right pupil was larger than the left. Both fundi showed a low grade of neuroretinitis. This process, in the opinion of the ophthalmologist, was early. The most painful stimuli produced no change in the facial expression, but when asked if he felt pain he signified in the affirmative. Both knee-jerks were increased and on the left there was persistent ankle-clonus and a

[2] Economo: Subacute lethargic encephalitis, Wien. Arch. f. inn. Med., June, 1920.

positive Babinski sign.   The urine was normal and the cerebrospinal fluid showed a slight increase of globulin.   A couple of days later the temperature fell to normal, the ptosis disappeared and he was able to make monosyllabic replies.   Apart from this, however, there has been no improvement.

The interest of this case lies in the fact that it is apparently an example of a true relapse.   The return of fever, the ptosis, the Babinski sign and the lethargy all suggest a recrudescence of the disease rather than an epiphenomenon developing as a consequence of vascular or other derangement.

A few brief summaries from the "follow-up" records may be given as illustrating the subsequent history of some not unusual cases:

Mr. N. suffered from a severe attack of epidemic encephalitis in December, 1919.   It was remarkable for extremely violent myoclonic spasms of the rectus and other abdominal muscles, which continued over a period of several weeks.   He made a good recovery. In June, 1920, he says that he feels well except for tiredness, which is worse in the morning and passes off toward the evening.   Works in a store about three hours a day and spends the rest of the day lying down.   Tremors have all gone.   His weight, which before his illness was 145 pounds, is 158 pounds.

Mr. R. Recovered from a severe attack at the beginning of January, 1920.   In May he says that he feels "Not too bad and not too good."   Complains of "soreness" on the top of the head, in the stomach region and in left thigh.   He is now back at work.

Miss L. was discharged from the hospital as "improved" at the end of February, 1920.   In June she was still listless and apathetic, with vacant expression and unable to read for more than a few minutes at a time.

Miss K. was discharged from the hospital on December 18, 1919. At first she had presented a picture of acute paralysis agitans, followed later by lethargy and somnolence.   In September, 1920, she says that she has never felt well since leaving the hospital. Complains of general weakness, headache, "rheumatic pains" in hip and shoulder and stiffness in ankles and feet.   Occasional attacks of well-marked diplopia.

2. *Paretic (Cranial Nerves)*.   Evidence of prolonged cranial nerve involvement has been observed in a number of cases.   In several instances in which facial paralysis was a feature of the disease proper a lingering weakness has been detected many months later.   In none of our cases, however, has the paralysis been complete or even pronounced.

Diplopia has been a more common symptom.   In some cases it was a feature from the beginning of the illness; in others it came on after an interval of apparent recovery.   The mechanism of such recurrence will be discussed later in this paper.

Weakness of accommodation is perhaps the most frequent indication of cranial nerve weakness. For many months patients have been unable to read except with the aid of glasses, and there may be permanent impairment of vision. A marked example of this condition is the following:

A. M., a returned soldier, suffered from a typical attack of epidemic encephalitis in the beginning of December, 1919. When he began to recover from the illness toward the end of the month he found that he was unable to read. With the aid of $+3D$ glasses he could read with perfect ease. A subsequent examination made in August, 1920, showed that no improvement had taken place in the eye condition and that paralysis of accommodation was still complete.

Of the cranial nerves involved the most important is the optic. During the acute stage of the illness optic neuritis is very uncommon. There has not been a single instance in our series, although careful ophthalmoscopic examinations were made in nearly all the cases. In several cases congestion of the vessels and slight haziness of the edges of the disk were noticed. Notwithstanding this absence of evidence of acute inflammation there were at least two cases of undoubted optic atrophy. In one of these there was marked dimness of vision two months after recovery from the acute attack and the patient was unable to distinguish colors at two feet. A marked secondary optic atrophy was found on ophthalmoscopic examination. The second case, seen six months after the onset of the illness, was also marked by great dimness of vision, and the ophthalmologist's report was as follows: "On the right side the pupil is widely dilated, with complete loss of reaction to light. There is a marked degree of optic atrophy. The retina around the disk shows considerable degeneration. Evidently a low-grade inflammatory condition. In the left eye the pupil reacts very slightly to light. There is commencing optic atrophy. The retina around the disk shows the same condition of progressive low-grade chronic inflammation as is seen on the right side. One patch about 1 mm. in diameter just below the disk shows complete degeneration, but the retina all around the disk is partially degenerated and grayish in appearance."

3. *Irritation Group.* The most remarkable of the sequelæ of epidemic encephalitis in the experience both of such observers as of Farquhar Buzzard[3] and of ourselves have been motor disorders of the nature of spasms, automatic, athetoid and choreiform movements. These may merely form a continuation of the clonic movements so frequently observed in encephalitis, and especially affecting the abdominal muscles, or they may arise *de novo* in a patient never previously exhibiting such phenomena.

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[3] Encephalitis Lethargica, Proc. Roy. Soc. Med., 1919, No. 9, vol. xii.

The following case is an example remarkable for its extremely long duration and for the fact that there were no intervals or intermissions.

Mr. N., aged twenty-five years, was admitted to the hospital at the beginning of January in a dull and apathetic condition. The temperature was 102°. He lay in bed, staring at the ceiling in a stupid, cow-like fashion. The cerebrospinal fluid was under high pressure, 80 c.c. being withdrawn. The cells and globulin were normal. He soon lost the power of speech, there being actual difficulty in articulation. Although extremely emaciated he exhibited a ravenous appetite and suffered from intense thirst. Despite a marked degree of polyuria, sugar was never present on any occasion. Toward the middle of March tremors began to appear. These were well marked on both sides of the face and about the mouth, and also in the hands and arms, but the left leg only showed slight tremors. The abdominal muscles were not affected. The corners of the mouth were retracted about seventy-five times per minute. The twitchings of the hands were rhythmic, being faster on the left side than on the right. On one day those on the left were 240 and on another 188 per minute. The thumb and fingers of the left hand showed typical cigarette-rolling movements. There were periods of complete rest. The face was frequently bathed in profuse perspiration. The twitchings continued unabated until the patient's death which occurred early in July, six months after the onset of the disease. I did not have an opportunity to examine the brain.

In such a case it is difficult to speak of sequelæ, for the patient never appeared to emerge from the mental stupor characteristic of the onset of his illness. At the same time an interval of ten weeks elapsed before the development of the tremors.

There have been no cases in our series which have developed involuntary movements after an interval of perfect health, as in the many striking cases described by Buzzard. The following case, however, for a description of which I am indebted to Dr. Gordon Bell, affords an interesting example of an automatic action from an imperative idea developing during convalescence.

Mr. M., aged forty-five years, walked into the laboratory, sat down and crossed his right leg over his left. There were a number of people in the room at the time and he was not attended to at once. After sitting perfectly still for a minute he suddenly arose and walked around the room, from left to right, with a gait so peculiar that it is difficult to describe. It had the stiff, automaton-like character of the sentry-go, but in an almost grotesque degree. Having completed the circle he sat down and crossed the right leg over the left, all the time with a face expressionless and inscrutable as the sphinx, save for a peculiar twitching of both upper eyelids. A minute later he repeated the performance, nor did it differ from

the preceding one by a hair's breadth. When taken into an adjoining room and examined he was afraid of being laughed at and explained that he was utterly unable to help himself. He gave a typical history of epidemic encephalitis. Nearly a month ago he was seized one day with weakness in the legs, and on getting up the next morning found that he was unable to shave, as he saw two faces and two razors. The diplopia lasted for a few days and was then replaced by the double facial paralysis, which was still so much in evidence. The entire face was immobile, except for marked tremors and twitchings of the upper lids. A peculiar and interesting symptom was marked parosmia: he was constantly aware of disagreeable smells, and this proved to be the most lasting of his symptoms. At this stage in his recital he jumped to his feet and went through his customary evolution. He then explained that this distressing complication had developed during the period of convalescence, that he was wholly unable to control the impulse and that it was not to relieve any peculiar sensation in the legs, but because of something he felt inside his head, that he was compelled to behave in a manner he felt to be so ridiculous. He put his feet up on the table and vowed that he would stick to his chair, but the flesh proved too weak. The subsequent history was that the patient gradually improved, and in the course of a few months he was free both of his facial paralysis and his distressing automatism. The parosmia, however, still persists.

In a recent paper by Buzzard several examples are given of involuntary movements coming on many months after the initial illness. This illness occurred in one case in May, 1918. In September of the same year the patient noticed involuntary twitching of the right toe, which spread until it affected the greater part of the right leg and right shoulder. In December the right arm displayed spasmodic contractions every one or two seconds, which caused it to be thrown behind the trunk or slightly elevated. Clonic contractions occurred in the muscles of both buttocks and in the right thigh and leg. There were irregular rotatory movements of the abdominal wall and umbilicus. In another case constant movements of both shoulders appeared six months after an attack of epidemic encephalitis; the movements are described as being "trouser hitching" in character. Contractions of several groups of muscles in the legs were observed, and there were also forced movements of the head.

4. *Parkinsonian Group.* Many groups and subdivisions of epidemic encephalitis have been suggested. A long list of these is given in Tilney and Howe's recent monograph.[4] They may all be collected into three great classes, depending upon the brain level mainly involved. These are the upper cerebral or cortical group,

[4] Tilney and Howe: Epidemic Encephalitis, New York, 1920.

comprising a comparatively small number of cases manifesting such symptoms as hemiplegia, hemianopia, spasms and convulsions; the thalamic group with symptoms suggestive of Parkinson's disease; and the brain-stem group in which involvement of such cranial nerves as the oculomotor and facial is often associated with varying degress of somnolence. It is true that the disease process refuses to be confined to water-tight compartments, but for descriptive purposes such a classification is convenient.

In any considerable group of cases of encephalitis many examples of what may be called the Parkinsonian type will be encountered. Our series has provided some striking pictures of paralysis agitans, although without the characteristic tremor. A case described by Russel[5] bore a close resemblance to progressive lenticular degeneration, including the peculiar emotional disturbances. We have observed that such cases are slower in clearing up than are those of any other group. Not only are the symptoms persistent, but it almost appears as if in these cases the lesion were progressive.

A case in point is the following:

Mr. Z., aged twenty-three years, was under observation for nearly a month in the Winnipeg General Hospital suffering from epidemic encephalitis. At the commencement of his illness the chief features were restlessness and insomnia, but these were soon replaced by marked lethargy and drowsiness. The face acquired the mask-like appearance of Parkinson's disease, and when he was able to be up the posture and gait were also suggestive of that condition. He made a fairly good recovery, but even on discharge his face lacked that play of emotional light and shade which distinguishes the normal individual. When seen eight months later he was markedly worse. Some progressive lesion had apparently been at work. He sat leaning forward in his chair with the blank, expressionless face of a mask. He walked with a shuffling gait, the back bent forward, the arms flexed at the elbow and the hands at the wrist, the rigid gaze fixed on the ground. He had been unable to work for some months and there was a considerable degree of mental impairment. The pupils did not react to light, and the optic atrophy and retinal degeneration already described in an earlier section were observed on ophthalmoscopic examination. The picture presented was one of Parkinson's disease without the tremor.

In the next case the patient never completely recovered his health. At the same time the Parkinsonian features did not develop for some months, so that they may with justice be regarded as true sequelæ. For the details of this case I am indebted to Dr. A. T. Mathers.

Mr. M., aged sixty-two years of age, at the beginning of January, 1920, began to see double and suffered from insomnia, but later

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[5] A Study on Epidemic Encephalitis, Based on the Study of Seventeen Cases with Two Autopsies, Canada Med. Assn. Jour., August, 1920.

became very lethargic and drowsy. He was in bed for three weeks and has not been well since. At the present time (September, 1920) he complains of constant headache, of a feeling of dizziness or light-headedness, of clumsiness of the right side of the body and of an increased secretion of saliva. The face is immobile and expressionless. The gait is clumsy and he sways slightly as he walks. The right arm hangs as if useless and can only be used clumsily, but is not deficient in power. The right leg shares in the clumsiness. There is slight rigidity of the muscles on the right side of the body and the deep reflexes on that side are distinctly exaggerated. Adiadokokinesia and asynergia are marked on the right side. Vision is failing rapidly and ophthalmoscopic examination shows indistinctness of the margins of both disks, which are redder than they should be and are covered with numerous small vessels. The cerebrospinal fluid shows a slight increase in globulin, but is otherwise normal.

Tilney and Howe describe a case very similar to the above: Ten months previously their patient had suffered from an acute illness associated with dulness, stupidity and somnolence. A few weeks later paralysis of accommodation developed, together with weakness of the right side of the face and tongue, and the right arm and leg. On examination marked clumsiness and stiffness of the right arm and hand were observed, and to a lesser degree of the right leg. There was paresis of the right side of the face and tongue. The condition is described as hemilateral paralysis agitans without tremor.

In our own case two elements may be distinguished, the thalamic and the cerebellar. A lesion in the hypothalamus involving nerve paths running from the red nucleus through the superior cerebellar peduncle to the dentate nucleus of the cerebellum might account for all the symptoms.

The mechanism by which the sequelæ are produced may now be considered briefly: In order to form a conception of what may occur it is essential to have a clear picture of the condition of the brain when the acute attack is over. The brain substance has been the seat of an inflammatory process, the brunt of which has fallen not on the nerve cells but on the interstitial tissue. An inflammatory exudate has been formed, mainly perivascular in type, but also extending into the surrounding brain substance, and in the more severe cases hemorrhage and thrombosis are present, accompanied by a corresponding degree of tissue disintegration and degeneration. Such a condition in any other part of the body would be followed by organization and repair, with fibrosis, and in the brain fibrosis when once started is by no means a self-limited process.

The net result of all this is interference with nerve paths. Positive symptoms, as Hughlings Jackson long ago pointed out, cannot be produced merely by negative or destructive lesions, and must be attributed to the uncontrolled action of nervous impulses normally

held in check.   It is probable that many of the involuntary and spasmodic movements may be traced to the overaction of primitive motor paths arising in the thalamic region, just as similar movements in progressive lenticular degeneration are due to lesions in the lenticular nucleus.

To one familiar with the microscopic picture in any large series of cases of epidemic encephalitis the wonder is not that after-effects are common, but that, to any marked degree at least, they are comparatively rare.   We cannot leave the uncertain ground of hypothesis until more observations have been made on the condition of the brain in encephalitis after a considerable interval has elapsed. Greenfield[6] has described extensive calcification of the vessels in a case which died four months after the acute illness.   Should such an occurrence be shown to be frequent, it is an observation of great importance.

Little is to be gained, however, by idle speculation until a greater mass of pathologic evidence is available, and the future will no doubt shed fresh light both on the clinical manifestations of the disease and on the pathological changes which form their substratum.

I am greatly indebted to Dr. F. C. Bell, director of records in the Winnipeg General Hospital, for assistance in tracing the after-history of many of the patients in that institution.

MECHANISM OF LOWERED RESISTANCE FOLLOWING EXPOSURE TO LOWERED TEMPERATURE.

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The following study was undertaken for the purpose of ascertaining if possible the functional and structural changes which follow chilling of the body surface and which lead directly or indirectly to disease.   The belief has long been held by clinicians and investigators that when the surface of the body is chilled, certain of the internal organs, particularly the respiratory organs, become more susceptible to bacterial invasion.   Other authors, after careful investigation, have reached the conclusion that exposure to lowered temperature, of and by itself, may be a complete cause of disease without the intermediation of bacteria.   It was therefore planned to subject an animal to sudden and severe lowered temperature and to take note of alterations of function or structure, with special reference to the possibility of increased susceptibility to zymotic disease.

[6] Buzzard, E. Farquhar, and Greenfield, J. G.: Lethargic Encephalitis; its Sequelæ and Morbid Anatomy, Brain, 1919, xlii, 305.

Ruheman[1] recapitulated the various theories accounting for the deleterious effects of exposure to lowered temperature while he advocated the view that the lowered temperature in some way favored the growth of germs in the body. Lassar,[2] Rosenthal,[3] Fodor,[4] Edelheit[5] and Siegel[6] maintained that lowered temperature itself may cause disease without the participation of bacteria. Siegel presented forceful arguments in favor of this view. Descriptions of the specific changes in function and structure brought about in the different organs by exposure to lowered temperature have been published by various authors. Herz[7] described a local rise in blood-pressure following chilling of a part. Van Oarat[8] noted a rise of 10 mm. Hg in blood-pressure of chilled men. Mudd and Grant[9] refer to a general rise of blood-pressure in chilled animals. Their experiments prove that chilling of the body surface causes constriction of the vessels in skin and mucous membrane. They give a good discussion of the entire subject from the modern standpoint. Rossbach and Aschenbrandt[10] reported that cracked ice applied to the belly of cats caused first a pallor and then a redness of the tracheal mucosa.

Tirelli[11] found in the human subject a leukopenia which lasted seven hours after chilling, but he never found a subsequent hyperleukocytosis. Baecchi[12] working with rabbits found that death from cold was not due to changes in the blood, which he stated were relatively unimportant. Lassar[2] and Siegel,[6] working with rabbits, found that albuminuria followed chilling. Fria[13] and Picci[14] found a similar state of affairs in man. Congestion and petechiæ in internal organs of animals were described by Beck,[15] Lassar,[2] Zillessen,[16] Della Rovere[17] and Siegel.[6] Baro[18] and Stonesco[19] described similar changes as a postmortem finding in persons frozen to death. Stonesco states that gastric petechiæ constitute the most constant and characteristic sign of death from freezing.

In the present series of experiments, rabbits were subjected to generalized lowered temperature in the form of the ice bath at 1° C. For localized applications CO_2 snow was used over certain portions of the surface of the body. During the progress of the experiments, blood-pressure tracings were made by means of a mercury manometer connected up with the carotid under cocain anesthesia. The red and white blood cells were counted before, during and after the cold applications. The urine was examined before, immediately after and at varying intervals after the chilling. Finally, the sixty-eight animals constituting the series were killed and autopsied either immediately after the chilling or at varying intervals thereafter and the gross and microscopic changes noted. For various reasons, principally because the scope of the experiments was modified from time to time, not all the data were collected from all the animals.

The skin of rabbits in the ice bath is first pale and later red.

During the first fifteen minutes of the ice bath the ear veins are so contracted that blood for examination is obtained with difficulty. An hour after the cessation of the ice bath the ear veins are relaxed almost to the point of paralysis, but blood does not even then flow freely from a needle puncture, apparently because tonus is practically absent and intravenous pressure almost zero.

The blood-pressure of the rabbits is usually about 100 mm. Hg, but when suspended in the upright position the rabbit may suffer from a mild degree of shock accompanied by an arterial blood-pressure of 40 to 80 mm. Hg. When the animals are immersed in cold water the blood-pressure rises and remains consistently higher than normal until the animals' vital powers begin to become exhausted, then gradually declines.

Table I shows the blood-pressure in 6 cases. In these cases the average rise in blood-pressure occasioned by the ice bath was 63 per cent. Local applications of CO_2 snow did not cause a rise in blood-pressure.

TABLE I.

Figures represent blood-pressure in millimeters of mercury. The number of minutes refers to the time elapsed since the animal was immersed in the ice bath.

No. of rabbits.	Before ice bath, mm.	After 2 minutes, mm.	After 15 minutes, mm.	After 30 minutes, mm.	After 45 minutes, mm.
79	80	120			
82	80	100	90	88	90
83	55	100	106		
86	43	72	80	80	
88	32	84	100	80	
91	110	130	138		
99	66	100	100	95	

The leukocytes were counted in seventeen animals chilled by the ice bath. Of these all showed a leukopenia at some time within the first hour after the ice bath, which lasted usually about twenty minutes. The leukopenia was extreme in about half the cases, the white cells numbering less than 3000 per cubic millimeter. In seven of seventeen animals, the number of leukocytes in the shed peripheral blood was increased temporarily during the ice bath. The increase was not marked, averaging 40 per cent. The blood in these cases was taken from the ear vein in all but one case in which the blood was taken from the carotid. The results in that case indicated that a uniform method is preferable.

The red cells were counted in six chilled animals and the count was found to be unaffected by the chilling.

In this series all the six animals chilled and kept overnight showed marked albuminuria, but the result was partly vitiated by the fact that of 35 normal animals, 14 showed albuminuria (ignoring "trace" of albumin cases). Of the 6 animals exposed to the ice bath 4 showed

normal urine, free of albumin, before the ice bath, and these as well as the remaining 2 showed either a profuse amount of albumin or a "heavy cloud" of albumin after the ice bath.

This corroborates the current view that external cold exerts an irritating influence on the kidneys. Haidenhain[20] had reported renal ischemia as a result of cold applications to the body surface. It appears likely that vasomotor effects constitute one of the early signs of renal irritation from cold.

Grossly and microscopically the kidneys of the rabbits in this series of experiments failed to manifest any signs of damage recognizable by the methods employed.

Either immediately after the ice bath or at chosen intervals thereafter the animals were sacrificed by a blow on the head and immediately autopsied. The brain and its coverings was examined only once, with negative results. The trachea and abdominal and thoracic organs were examined grossly in all 69 animals. Sections were usually made of liver, lung, spleen, kidney and trachea. Two colons were sectioned for microscopic examination. Pronounced alterations were observed in the lung, stomach and spleen, while the heart, liver, kidney, bowels and other organs were apparently unaffected by chilling. The trachea was variable in its behavior.

Owing to the interesting experiments reported by Rossbach and Aschenbrandt[10] and referred to above, the trachea was examined with much interest. In rabbits subjected to the ice bath and autopsied soon afterward the trachea showed marked variations in different cases. It appears plain that the blood supply of the trachea fluctuates on slight provocation. Table II shows the number of cases presenting congestion of the tracheal mucosa at autopsy. There is marked variability both in chilled animals and in control animals.

In view of the detailed description given by Rossbach and Aschenbrandt it appears altogether likely that under proper conditions the pallor followed by redness which they reported could be produced. The present writer tried to repeat their experiments (with cats) but found that the violence inflicted upon the trachea while slitting it open for inspection was sufficient without hot or cold applications to cause early marked congestion.

An interesting experiment was performed by taking two apparently similar rabbits of the same litter: To the belly of one ice was applied; the other was not handled, and hence was a normal control. After twenty-five minutes the animals were killed in turn, and the trachea of each removed within two and a half minutes. The trachea of the one whose belly was chilled showed marked congestion of the tracheal mucosa; the control animal showed normal tracheal mucosa. Unquestionably the tracheal circulation has a most delicate susceptibility to external influences.

TABLE II.—TRACHEA.

	Trachea congested or cyanotic.	Trachea not congested or cyanotic.	Total.
Experimental treatment accorded animal:			
Chilled in ice bath	12	14	26
Applications of CO_2 to skin . .	2	2	4
Transfused	2	5	7
Normal animals	1	5	6
Miscellaneous conditions, adrenalin, pilocarpin, injuries, diarrhea, etc.	5	3	8

EFFECT OF POSTMORTEM CHANGES.

Animals autopsied more than one hour after death	9	2	11

In the present series of experiments the frequent occurrence of ecchymoses, not only beneath the pleural surfaces but permeating the entire substance of the lung, occasioned surprise by their striking appearance and by their early advent, they having occurred within fifteen minutes after the beginning of the ice bath. The splotches were of the color of oxyhemoglobin, and often the background, constituted by relatively unaffected lung tissue, appeared almost milk white. The splotches of ecchymosis or suggillation occasionally occupied one lobe or part of a lobe of one lung. More often the bases of both lungs were affected, while in one case both lungs were the seat (throughout their entire extent) of multiple small hemorrhagic areas which marked off on the surface the outline of the ribs but which scattered throughout the deeper substance of the lungs after an indiscriminate fashion.

Table III shows the frequency of ecchymosis of lungs in chilled and unchilled animals.

TABLE III.—LUNGS.

	Lungs ecchymosed.	Lungs not ecchymosed.	Total.
Animals chilled in ice bath . . .	20	13	33
Animals receiving CO_2 snow applications	..	10	10
Animals transfused	2	4	6
Miscellaneous group, consisting of normal controls; animals found dead in cage; animals dying before experimental chilling was effected; animals receiving adrenalin and pilocarpin; animals depilated with BaS and not otherwise handled .	3	16	19
			—
			68

It will be observed that ecchymosis of the lungs may occur from causes other than chilling and that the application of CO_2 snow to the abdomen and hindermost portion of the body did not cause lung changes in any of the ten rabbits studied.

Microscopically the ecchymosed tissue shows many interstitial hemorrhages of capillary dimensions. Usually the hemorrhage does not penetrate the lumen of the alveoli but remains imprisoned in the alveolar wall. Certain areas can be found, however, where the blood has burst into the lumina of the alveoli and trickled into the smaller bronchi. A striking feature is the great number of apparently independent small hemorrhages. Desquamated epithelial cells in the alveoli are rare, and there is little desquamation even in the bronchi.

In the lungs of animals chilled in the ice bath and surviving eighteen hours or more a moderate infiltration of polymorphonuclear leukocytes is seen in the alveolar wall. Lungs of freshly chilled animals do not manifest this.

The stomach was of all organs the seat of the most characteristic changes in the rabbits autopsied. Those animals killed immediately after the ice bath, which usually lasted from twenty to thirty minutes, showed practically no changes in the stomach, but those which survived more than six hours generally showed at autopsy multiple petechiæ just beneath the stomach mucosa. Usually there were from 12 to 100 of these petechiæ.

Table IV shows the relative frequency of occurrence of gastric petechiæ in animals subjected to the ice bath as compared with animals subjected to CO_2 snow applications and unchilled animals.

TABLE IV.—STOMACH.

	Petechiæ in stomach.	No pechiæ in stomach.	Total.
Experimental treatment accorded animal:			
Chilled in ice bath, death within one hour afterward	1	8	9
Chilled in ice bath, death within six to twelve hours afterward	5	0	5
Chilled in ice bath, death within twenty-four hours afterward	4	1	5
Chilled with CO_2 snow, death within one hour afterward	1	2	3
Chilled with CO_2 snow, death within forty-eight hours afterward	6	..	6
Unchilled, death from whatever cause	0	17	17
Chilled and kept over six hours before death	15	1	16
Unchilled, or if chilled, killed within an hour (recapitulation)	2	27	29

Table IV shows that gastric petechiæ occur almost uniformly after applications of CO_2 snow, but this is to be discounted on account of the local effect of the CO_2 snow acting directly through the abdominal wall upon the underlying stomach. No experiments were tried to ascertain whether applying CO_2 snow to remote parts of the body would cause gastric petechiæ.

Table VI emphasizes the fact that several hours had usually elapsed between the ice bath and the animal's death, in all cases

showing gastric petechiæ; and conversely, that normal stomachs were usually found in animals autopsied immediately after the ice bath.

No microscopic studies were made of the stomach. The petechiæ often had the appearance of little globes of blood so near the surface that it seemed almost possible to wipe them off with gauze. They were slightly larger than mustard seeds and withstood gentle friction under the hydrant. In animals kept overnight some of the petechiæ seemed to have been digested away, leaving small punched-out ulcers surrounded by a rosy areola.

The application of CO_2 snow to the surface of the abdomen caused hemorrhagic necrotic areas in the underlying coils of the colon, with ulceration of the mucosa. Vascular injection occurred in the serous coat of the colon. In some instances the gastric mucosa also exhibited areas of diffuse hemorrhage into the mucosa of that part of the stomach lying immediately beneath the point where the CO_2 snow was applied. The serous surface of the stomach lying between the chilling agent and the lesion in the mucosa appeared normal in some of these instances.

The spleen appeared contracted and pale in 8 of 9 animals autopsied just after the ice bath, while in 5 of 9 animals surviving several hours after the ice bath it was swollen and cyanotic. Table V shows the number of cases in which contracted or swollen spleen was observed.

TABLE V.—SPLEEN.

	Spleen contracted, pale.	Spleen normal.	Spleen swollen, cyanotic.	Total.
Experimental treatment accorded rabbit:				
Ice bath, death within one hour afterward	8	1	..	9
Ice bath, death six to ten hours afterward	1	1	2	4
Ice bath, death next day	..	2	3	5
CO_2 snow applied locally, death immediately afterward	..	1	1	2
CO_2 snow applied locally, death next day	..	4	2	6
Normal animal	..	7	1	8
Diarrheic animal	1	1	1	3
Transfused animal	..	2	1	3
Adrenalin administered	1	..	..	1
	11	19	11	41

Discussion. The outstanding fact pervading the results reported above is the intensity of the vasomotor reactions set up by the ice bath and their universal spread over the body. The hemorrhages in the lungs and in the stomach have been explained as infarcts, but infarcts are themselves of such an elusive character that in all probability no profit is to be derived from introducing them into the discussion. Moreover, simple asynchronism of the different

component parts of the blood channels is sufficient to explain these hemorrhages. It seems probable that a delicate adjustment is necessary in order that the blood may pass from the strong-walled arteries into the delicate capillaries without rupturing the latter. Whenever a powerful stimulus is applied to certain blood channels, either their immediate contraction or their subsequent relaxation may so alter the relations between artery, capillary and vein that excessive pressure is brought to bear on certain weak points and rupture results. Undoubtedly the possibility of thrombi must be admitted, but it is not only unnecessary to invoke thrombi and infarction to explain the lesions, but the rapid development of the lesions and the deliberate nature of platelet deposition render such a view difficult to accept.

Blood distribution was found altered in the lungs, the skin, tracheal mucosa, the stomach and the spleen, while others have reported anemia of the kidneys. The alteration in the number of leukocytes in the peripheral blood is probably based to some extent on vaso-motor changes.

In order to explain the increased susceptibility to bacterial invasion which follows exposure to lowered temperature the follow-ing hypothesis is advanced:

1. That vasomotor tone and organ function are maintained by the successive functionation of different shifts or relays of cells, each having its own threshold of susceptibility to stimulation, and rehearsing its stereotyped function according to the laws of fatigue and its own individual needs.

2. That vasomotor changes exert a provocative or stimulating influence on tissue cells, causing an increase in function.

3. That early though fully developed inflammation with all the classic symptoms is to be explained as excessive liberation of cell function, and that this may lead later to exhaustion, lack of coördi-nation and the consequence of these.

4. That the cell tends to summate the various similar and dis-similar stimuli playing upon it at each given instant and react to its environment as a whole.

5. That the vasomotor changes set up by lowered temperature can be summated with the stimulation from relatively harmless bacteria so as to bring on an excessive liberation of function con-stituting an inflammation of the affected part.

The reversible nature of the vasomotor changes observed in these animals is worthy of consideration. The skin is at first pale, later red; the tracheal mucosa was found pale or red and the observations of Mudd and Grant[9] indicate that the pallor precedes the redness. Since they contemplate inflammation of the mucosa as a possible result of their experiments, they by implication infer that a red stage is to follow the pale, although they do not confirm Rossbach and Aschenbrandt's[10] observation that the pallor rapidly gives way to

redness. After chilling the spleen is first pale and contracted; later, swollen and presumably congested. Haidenhain[20] observed that the kidney becomes pale during chilling, and while his experiments did not extend to the red stage, still it is likely that this organ, like others, undergoes a reversal.

A similar reversal was found by the author[21] in all of a series of several hundred skin injuries of the proper degree, and it is well known that Raynaud's disease and dermographism are characterized by such a reversal of color.

The universal distribution of this phenomenon is apparently based on the nature of the vasomotor mechanism. The author has recently published the result of experiments supporting the view that the specialized cells of the body tend to react in one stereotyped fashion to all forms of stimuli.[21] The contractile elements of the vasomotor system react by contraction when disturbed—that is, stimulated in any way. This accounts for the first or pale stage referred to above. There is only a certain amount of contractile energy available for each unit of time (with a uniform rate of stimulation), and if a sharp stimulus is applied in such a manner as to make an overdraft on the contractile mechanism during one unit of time, then the supply of contractile energy will fail in some subsequent unit of time after the extra stimulation has subsided. This will bring on the reversed or red stage referred to above.

It seems that not a great deal of attention has been given to the question whether arterial tonus is maintained by the simultaneous contraction of all the smooth muscle fibers concerned or by the successive contraction of different relays or shifts of fibers. The bulk of the evidence favors the latter view. In the case of an arteriole too small to pulsate the practically uniform tonus kept up throughout the day (if not during the night also) could not be maintained by all the cells contracting continuously unless repair and work could proceed in a cell at one and the same time. If it be supposed that the smooth muscle fibers contract successively by shifts this difficulty would be obviated. Pratt[22] has shown that neighboring individual striped muscle fibers do not have thresholds of the same level, but each fiber has its own level of susceptibility to stimulation, and therefore all the fibers do not participate in each contraction of the muscle. Such a state of affairs seems probable in smooth muscle and provides for the individual biologic needs of the fiber as well as for the organic needs of the organism as a whole.

Certain rhythmic and vermicular movements, best illustrated by the heart or the intestine, indicate that contraction of one muscle fiber tends to provoke contraction of its neighbor. Howell described a kind of primitive conductivity which characterizes all protoplasm. This quality tends to cause the transmission of any disturbance in cell life. It may well be supposed that the frank vasomotor fluctuations described in the foregoing experiments would

have an influence on all the cells of the given tissue, and this influence would be of a stimulating nature, for the cells tend to react toward any foreign influence by rehearsing their stereotyped function. The fact that cells tend thus to react has been referred to above. It is true that some cells are subject to inhibition when affected by certain outside influences, but the agents producing inhibition are relatively rare and of a highly specialized nature. (Sherrington has recorded that certain inhibitory reflexes affecting voluntary muscle are reversed by strychnin. This fact is noted to show that the process of inhibition is a highly specialized one.)

The rehearsal of its full stereotyped function on the part of any cell exerts a certain provocative influence on neighboring or related cells, and this influence need not be limited to the same type of cell, but muscle fibers could apparently affect secretory cells, and *vice versa*.

It is well known that depriving the highly specialized cells of blood very soon produces serious damage. It is not to be supposed that ischemia, even of short duration, would be without effect on the cells of the part. Repeated vasomotor spasms in Raynaud's disease eventually lead to death of the part, even though the affected regions, such as the extremities, possess a high degree of resistance.

As further evidence of the provocative effect of vasomotor abnormalities, it may be stated that hyperemia of the mucous membrane is generally accompanied by catarrh. Even angioneurotic edema is often associated with itching, showing that the disturbed circulation of the part provokes hyperesthesia.

Jankowsky[23] pointed out the fact that in the dermographic lesion the smooth muscle fibers have a lower threshold than the secretory cells, and hence a mild stimulus may provoke a response from the local vasomotor apparatus while not affecting the secretory apparatus. The experiments previously referred to have shown that the dermographic lesion is in all respects analogous to the reaction of normal skin toward various irritants and that it shows the same sequence and arrangement of pallor and redness. That is to say, any irritant, mechanical, chemical or electric when of the proper grade tends to provoke the equivalent of dermographism.

The dermographic lesion is inflammation of the purest type, because almost uncomplicated by any injury to the tissues from without. Consequently the dermographic lesion illustrates plainly the stereotyped nature of inflammation, the fact that it begins as a rehearsal of function up to the full capacity of the tissue, the fact that it tends to spread beyond the extent of the actual offending agent. In short that inflammation is really a liberation of functional energy leading quickly to exhaustion. While inflammation is often inaugurated by a foreign agent it may spread by the provocative action of one body cell toward another.

The fully developed early stages of inflammation, including all the classic symptoms, can be explained as simultaneous or synchronized function on the part of all the cells of the part. Inflammation has long been defined as "the reaction to injury." An injury would apparently be any stimulus of sufficient intensity to provoke the five symptoms which in the aggregate we term inflammation. This conception clearly implies that an injury and a stimulus differ only in degree, and since the whole is greater than any of its parts it follows that an injury must be a kind of super-stimulus.

If chemical stimulation alone were the only kind of stimulation causing inflammation it might seem that actual structural alteration of the cells took place in each instance over and above discharge of function, and that these alterations characterized inflammation. It seems highly improbable, however, that all varieties of chemical irritation should give rise to the same structural alteration, or that heat, cold, mechanical violence and electricity should also bring about the same structural alterations. It appears more probable that any structural alterations caused by the various injurious agents would be in each instance characteristic of the agent applied. Consequently they would vary one from another and would not form a part of the constant and uniform picture which we call inflammation. This makes it probable that the essential characteristic of inflammation is simply the state of excessive functionation.

It should be noted that neural stimulation is highly selective and does not ordinarily have the power to provoke full function on the part of both parenchymatous and stroma cells.

The phrase "summation of stimuli" is usually employed to designate a series of similar stimuli, but it is here applied to the similar or dissimilar stimuli, which affect a cell at any moment. Many physiologic phenomena appear to be based on the summation of dissimilar stimuli; among others, the knee-jerk. Without the tonic nerve impulses passing constantly from the cord, mechanical stimulation of the patellar tendon fails to provoke a response. Another example is the explosion of contractile energy set off in the strychninized animal by mechanic stimulation. The irritant effect of the strychnin apparently shows itself in two ways: (1) By causing a series of individual motor impulses, thereby increasing muscle tone, and (2) by stimulating a great number of motor cells subminimally, so they discharge their motor impulses only when an additional (mechanical) stimulus is applied. A third example of summation of dissimilar stimuli is seen when the muscles of a swimmer undergo cramp. In this instance the stimulation due to fright and lowered temperature when summated with the voluntary nerve impulses is sufficient to provoke spasm.

In short the cell seems to be a unit constructed so as to receive stimulation in various ways and to respond in a single way, that is, by a rehearsal of its stereotyped function.

Whatever the normal defences of the tissues against germs may consist of, it seems probable that they would be disorganized by the vasomotor fluctuation brought about by chilling the surface of the body. The deleterious effects of bacteria depend on their mechanical and chemical effect on the tissues. The foregoing paragraphs relating to the provocative effect of vasomotor fluctuations, together with those paragraphs relating to the process of summation of stimuli, suffice to show how chilling the body surface tends to favor bacterial disease.

We know that the bacteria are capable of thriving in inflamed tissues. The connective-tissue cells of the body seem to respond to stimulation by propagation. It is possible that bacteria have the quality of altering their behavior in response to changes in their environment and their response might take the form of propagation, but this subject has not been investigated.

Summary and Conclusions. 1. The changes provoked in rabbits by the ice bath are as follows:

Multiple minute hemorrhages in the lungs.
Multiple minute hemorrhages in the stomach.
Changes in blood content of tracheal mucosa.
Contraction followed by congestion of the spleen.
Pallor followed by redness of the skin.
Albuminuria.
Leukopenia followed by leukocytosis in the peripheral blood.

2. The first five of these changes are apparently caused by vasomotor variation. The remaining two are closely related to vasomotor function.

3. The following hypothesis is offered in explanation of the increased susceptibility to bacterial invasion brought about by chilling the body surface;

a. That vasomotor tone and organ function are maintained by the successive functionation of different shifts or relays of cells, each having its own threshold of susceptibility to stimulation and rehearsing its stereotyped function according to the laws of fatigue and its own individual needs;

b. That vasomotor changes exert a provocative or stimulating effect on tissue cells, causing an increased discharge of function;

c. That early though fully developed inflammation with all the classic symptoms is to be explained as excessive liberation of cell function, and this may lead later to exhaustion, incoördination and the consequences of these;

d. That the cell tends to summate the various similar and dissimilar stimuli playing upon it at each given instant and react to its environment as a whole;

e. That the vasomotor changes set up by lowered temperature can be summated with the stimulation from relatively harmless bacteria, so as to bring on an excessive liberation of function constituting an inflammation of the affected part.

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THERAPEUTIC PNEUMOTHORAX COMPLICATED BY HYDRO-PNEUMOTHORAX AND PLEURISY, WITH EFFUSION ON THE UNTREATED SIDE. REPORT OF A CASE.

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The coexistence of bilateral pleurisy with effusion is one of the rarest complications in pulmonary tuberculosis. The literature on the subject discloses so few authentic instances that when bilateral effusions are detected their tuberculous origin is seriously questioned. We are still in the dark as to the probable explanation of this phenomenon, but the fact remains that when a patient has a pleural effusion of tuberculous origin on one side he is immune, for a time at least, to pleurisy with effusion on the other.

It is not different in the case of therapeutic pneumothorax whether or not complicated by hydropneumothorax. Once a pneumothorax is induced the patient acquires an immunity f om pleurisy with effusion on the untreated side. Forlanini, who has probably had the widest experience with therapeutic pneumothorax, has never met with a case of hydropneumothorax complicated by pleurisy with effusion on the untreated side. Brauer and Spengler,[1] in their

[1] Handbuch der Tuberculose, 1919, iii, 227.

recent study of pneumothorax, state that there is no record of such a case in medical literature. Among the many hundreds of cases he has treated with therapeutic pneumothorax, Saugman did not encounter a single case of this description, and all recent text-books on tuberculosis fail to disclose a description of or reference to a case of this kind. Very recently, however, Als[2] reported a case, stating that it was the only one so far reported in medical literature. Fishberg[3] described the second case, the first one in the English language.

In this connection the following case may prove of interest. Here we observed an effusion with multiple fluid levels on the side treated with pneumothorax and another effusion on the untreated side.

FIG. 1.—Note extent of right pneumothorax after third inflation and clear left base

G. F., aged twenty-six years, housewife, was admitted to the sanatorium on May 5, 1919. She was in perfect health until February, 1919, when she began to cough and expectorate, and occasionally noted elevation of temperature in the afternoon hours. Loss of weight and strength soon ensued and her condition was diagnosticated as pulmonary tuberculosis. On admission, physical exploration of her chest disclosed extensive infiltration of the greater part of the right lung and the left upper lobe, together with

[2] Ein Fall von Rechtsseitigen Pneumothorax Artificialis mit Linksseitigen Pleurisy Exudat, Ztschr. f. Tuberculose. 1920, xxxi, 333.
[3] A Case of Pneumothorax Complicated by Hydropneumothorax and Pleurisy, with Effusion on the Untreated Side, Am. Rev. Tuberculosis, November, 1920.

definite evidence of cavity formation at the right upper lobe. The moisture, however, was confined to the lesion on the right. Roentgenologic examination confirmed the physical findings. On account of the fever, which ranged between 101° and 103°, cough and expectoration she was put to bed at absolute rest for six weeks. No improvement followed and her general condition grew worse daily. A pneumothorax was therefore induced on the right side on June 19, 1919. · The first puncture was made at the sixth interspace midaxillary line. Excellent negative pressure oscillations were found. Inflations were subsequently given at regular intervals. Fig. 1 shows the degree of collapse of right lung after the third inflation.
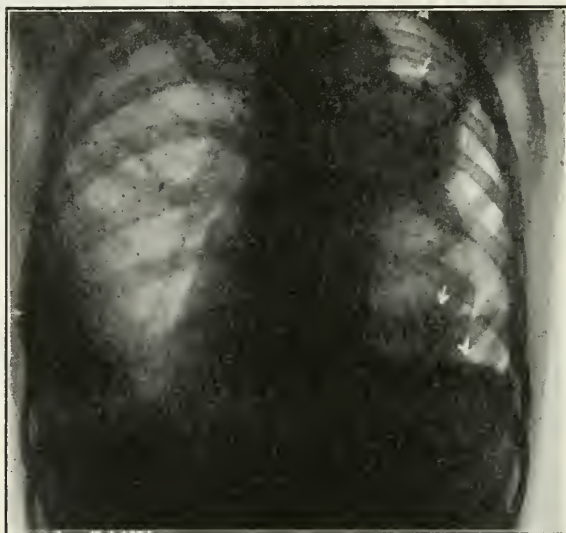
Fig. 2.—Note effusion and multiple fluid levels on right and pleural effusion at left base.

There was almost a miraculous change in the patient's condition. The fever abated after the third inflation. The cough and expectoration disappeared. Her appetite improved and with it an increase in strength and weight was soon noted. Her condition continued to improve until July 25, 1919, when she began to complain of headache, pain in the chest, distressing cough and nausea. Her temperature rose to 102°, but dyspnea and cyanosis were not noticeable. Two days later signs of fluid, i. e., shifting flatness and succussion, were discerned on the right side, and on exploratory puncture clear fluid was aspirated. Within ten days all the constitutional symptoms of toxemia disappeared and at the end of three weeks she was again enjoying good health and was none the worse for her experience.

On September 15, 1919, she complained of severe stabbing pain in the left lower chest posteriorly, distressing cough, headache and backache, and her temperature rose to 102° F., and two days later to 104° F. There was slight dyspnea on exertion but no cyanosis was noticeable, although the prostration was unusually marked. Physical exploration of the chest disclosed in addition to the preexisting right hydropneumothorax a pleurisy with effusion on the left side. Fig. 2 shows effusion on both sides. Within five days her temperature began to decline and general improvement was noted, and by the end of three weeks all the symptoms disappeared and the left pleural effusion was absorbed. She has been in perfect health since and is now able to take care of herself and perform a fair amount of assigned exercise without untoward results.

Comment. It is noteworthy that in all the three cases thus far recorded the artificial pneumothorax was induced on the right side and that the first effusion occurred on the side of the pneumothorax. What relation this may have to the subsequent left pleural effusion is difficult to presume, but it is interesting, nevertheless.

It would be expected that with one lung completely collapsed by a pneumothorax and the other compressed by a pleural effusion the danger of respiratory embarrassment would be immense, but, as a matter of fact, dyspnea and cyanosis were not the outstanding symptoms in our case nor in the cases referred to above. The respiration at the height of the fever and both effusions never rose above 32; nor was the heart action much interfered with, for the pulse was always of a good quality and never rose above 120, regardless of the height of the fever and bilateral effusion. For these reasons it was thought advisable not to aspirate the fluid from either side. The regular inflations of the right pleural cavity were not interrupted, but greater caution was exercised in keeping the intra-pleural pressure from rising too much above zero. The absorption of the left pleural effusion had no appreciable effect on the rate of absorption of the effusion on the right. The latter effusion was absorbed but slowly, undoubtedly due to the altered condition of the pleural surface resulting from the preëxisting pneumothorax. Her prognosis was not altered by the occurrence of these effusions, and she is now able to do a few hours' work without untoward effects.

EDEMA OF THE GLOTTIS IN OBSCURE DEATHS.

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THE causes of death in the international list which nearly every physician has constant need for deal with *systems involved, actual infections, poisons, external causes*, the *puerperal state, malforma-*

tions and *diseases of early infancy* and *old age.* Except for the old-age group, the respiratory system list of causes is the smallest, though probably it yields a major number in the number of deaths per year if tuberculosis, pneumonia, etc., are included. The face and neck have apparently yielded the least number of deaths if one would judge from the fine print under which "nasal fossæ, larynx, thyroid body" appear: In a fairly active autopsy service[1] in which medicolegal cases are sprinkled, the same "fine print" would be applicable.

This pathological service covers the sudden and unexpected deaths that occur in the Massachusetts State hospitals: The causes of these deaths have been analyzed in a series of 262 cases with autopsy, and a list is here appended.

ANALYSIS, AUTOPSIED CASES (SUDDEN DEATHS).

	1913 –14	1914 –15	1915 –16	1916 –17	1917 –18	1918 –19	Total.
Heart lesions	4	9	13	13	16	5	60
Acute infections,	11	13	8	4	9	7	52
Foreign bodies in larynx	3	2	7	2	2	..	16
Epilepsy	1	6	..	5	4	..	16
General paresis	3	1	2	6	1	3	16
Homicides	3	3	3	1	2	..	12
Suicides	3	3	1	3	3	5	18
Tuberculosis	1	2	2	3	2	3	13
Fractures	1	3	1	1	2	7*	15
Cerebral hemorrhages	..	..	5	..	1	..	6
Thrombosis	2	..	..	2	..	..	4
After tube feeding	1	..	1	1	..	1	4
Burns	1	1	..	..	..	1	3
Hemorrhage	1	..	1	..	2	..	4
Brain tumor	..	..	2	..	..	2	4
Asphyxia	..	1	..	1	..	..	2
Katatonic "Hirntod"	..	..	1	1	..	..	2
Acute mania	1	..	..	1	..	..	2
Collapse after bath	..	1	..	..	..	..	1
Salvarsan	..	..	..	..	..	2	2
Fall	1	..	..	..	..	0	1
Edema brain	1	..	..	..	..	0	1
Arteriosclerosis	1	..	..	..	..	1	2
Ruptured bladder	..	..	1	..	..	0	1
Carcinoma	..	..	1	..	2	1	4
Drowned (accident)	..	..	..	1	..	0	1
Pernicious anemia	..	..	..	..	1	0	1
Acute gastritis	..	..	..	..	1	0	1
Edema glottis	..	..	..	..	1	0	1
Ruptured spleen	..	..	..	..	1	0	1
Ruptured heart	..	..	..	..	1	0	1
Alcohol	..	..	..	..	..	1	1
?	..	..	..	..	..	1	1
Totals	39	45	49	45	51	33	262

[1] The Pathological Service of the Department of Mental Diseases (Massachusetts) has 200–250 autopsies annually in the State Hospitals under its control to which it seeks to supply service where their laboratory activities are suspended from vacation, leave, illness or disabilities of their pathologists.

* Fracture complicated death.

It is striking to note in this list that few deaths are due to edema of the glottis, but unless the deaths are obscure the practice of removing the neck organs is not extensive. There are objections enough to cover in obtaining permission for an autopsy and promises of restoration of cosmetic possibilities in the way of embalming are necessary; to this end the neck organs are left uncut and the data therefore are not always available or not considered regarding edema of the glottis.

The clinical varieties of edema of the glottis are eleven:

1. General anasarca.
2. Infections.
3. Tumors of thyroid or cervical region.
4. Foreign bodies.
5. Trauma.
6. Posture.
7. Neuropathic (Quincke).
8. Toxic.
9. Thermal.
10. Ischemic.
11. Irritant (gas).

If we keep these clinical varieties in mind the obscure sudden deaths may not seem so obscure. 6 to 10 might be considered elaborate, though 6 is a variety seen by medical examiners in autopsies in old alcoholics who sleep on park benches or other peaceful spots with the chin sinking on the chest. In this position they are found dead, and the medical examiner returns a cause of death as due to "edema of the glottis, postural." Variety 7 necessitates infinite care in history and autopsy observations, as do 8, 9 and 10.

The causes of edema are five:

1. Arterial congestion.
2. Stagnation of the blood.
3. Hindrance to outflow of blood.
4. Disturbance of capillary secretion due to changes in capillary walls.
5. *Ex vacuo.*

The mechanisms of edema in general, as recorded in general text-books, involve the condition of lymph channels and lymph, of the bloodvessels and the blood. If the blood is thin (as in anemia and kidney disease) it goes through the vessels more easily, and also whatever is the cause of the thinning of the blood may act unfavorably on the bloodvessel walls. Now whether stagnation of flow, or overdistention because of defective innervation of the capillaries, is present, or obstruction of lymph, the result is a transudation of the liquid elements of the blood. The effect of inflammation on the vessel walls is, of course, a degenerative one, allowing more elements to pass through them. The following

cases are presented to illustrate the deaths directly dependent on edema of the glottis, each case being definite and leaving no borderline of *wrinkling* as evidence. They are compared with a glottis upon which no suggestion of edema could be passed.

1920.42. This glottis presents slow edema due to repeated trauma in an insane white male, aged thirty-three years. The patient died within twelve hours of the first known attack, that of choking him with a towel twisted about his neck. It is probable that not a single choking would have produced this grade of edema, since it takes some hours to produce physiological edema, *e. g.*, in the parturient canal. The evidence presented in court by an eye-

Fig. 1.—Traumatic edema. Death within twelve hours.

witness was that there were applications of the towel at twenty- to thirty-minute intervals. There was no lesion in the body tending otherwise to transudation of serum. The cardiorenal-vascular system was in no wise affected. There was no infectious process in the body, no tumors in the cervical region and no foreign body in the larynx.

The picture shows the water sac edema on the surfaces of the arytenoid cartilages. In the recent state the coaptation of these swelled cartilages closed the passage for air.

The patient, 1915.66, an insane criminal, aged sixty-one years, complained of a pain in his head for seven weeks. No medication

FIG. 2.—Found dead in bed. Toxic edema from pus in pituitary.

FIG. 3.—Edema and new growth from irritation of a foreign body.

relieved it and an intense central headache that interfered with sleep and kept him drowsily awake was almost constant. No increase of temperature was recorded in these seven weeks. He was found dead in bed with edema of the glottis and pus in the pituitary and postpharyngeal tissues. Further dissection shows the pituitary to contain pus, the clinoid and sella turcica to be eroded and the sphenoidal sinuses to contain purulent material. It is thought that a posterior nasal infection was followed by a sphenoid

Fig. 4.—Moderate terminal edema in a tuberculous Chinaman. Note tubercles on inner surface of epiglottis.

involvement which later was transferred to the pituitary and sella turcica; an abscess in the gland followed and erosion of its bony envelope. Infiltration through the soft tissues of the foramen magnum and anterior cervical region to the pharynx and glottis continued where toxic edema extended to the glottis and vocal cords—and death came through increased difficulty of breathing.

This patient, 1920.78, presents a terminal edema of the glottis due to the presence of a foreign body in the larynx. The patient

was an imbecile and after the ingestion of meat had a violent
choking and coughing spell which was followed two days later by
diphtheria. The physicians who saw him in his period of choking
could find no cause for it; examination and manipulation were
unavailing and the subsequent diphtheria put them off the track,
though the patient always maintained he had a bone in his throat.
Periodic neck distress was relieved by gentle massage of his throat
and warm applications, but one night two years after the bone
was lodged he died during one of these attacks.

Fig. 5.—Glottis with no edema.

The autopsy showed a slender, irregular meat bone, not unlike
a portion of a vertebra, its end embedded in the mucosa of the
larynx 3 cm. below the vocal cords. There were wasp-nest-like
growths at the ends of the embedded bone. The tissues over the
glottis were wrinkled heavily and gray. It is thought that the
growth at this stage prevented the flow of air through the rima
glottis in a periodic transient edema due to the irritation of the
foreign body.

This patient, 1920.108, a Chinaman, aged forty-one years, died of pulmonary tuberculosis—a process thought to be of about one year's duration. This lesion was also present in the intestines. Grossly, except for anomalies, there was little otherwise to call pathological. The kidneys, arteries and heart were free from marked changes, and the Wassermann reaction on fluid and serum were negative post mortem. There was no edema elsewhere.

Summary. Edema of the glottis is for the most part clinically a local lesion, but can be a fatal termination in general anasarca and in infections. In obscure deaths careful removal of the neck organs should not be omitted.

REVIEWS.

Rational Treatment of Pulmonary Tuberculosis. By Charles Sabourin, M.D., Medical Director of the Durtol Sanatorium, Puy-de-Dome, France. From the sixth, revised and enlarged French Edition. Pp. 440. F. A. Davis Company, Philadelphia, 1921.

This is a rather unique book in that it appears without a preface or introduction. The work is an English translation of the sixth French edition, but the translator's name is not mentioned. Sabourin is a well-known French phthisiotherapeutist, and gives evidence of having a large experience in this field

No especially new thoughts are presented, and many older ideas and theories are still included in this edition. The subject matter is well covered and all features of treatment are touched upon in sufficient detail. The French are supertherapeutists, and apparently the author is no exception to the rest of his countrymen. He has directed the treatment of consumptives for thirty years, and as such his discussion on creosote, lime salts, tincture of iodine, sulphurous and arsenical waters as remedial agents in pulmonary tuberculosis is exceedingly interesting. The use of guaicol rubbed into the skin as an antipyretic measure is an unusual suggestion.

The translation must be a rather close one and as such the English is at times labored. The work is comprehensive; its viewpoint is sane; two qualifications which should commend the book to all phthisiologists and others interested in pulmonary tuberculosis and its treatment. T. G. S.

Notes on the Medical Treatment of Disease for Students and Young Practitioners of Medicine. By Robert Dawson Rudolf, C.B.E., M.D. (Edin.), F.R.C.P., Professor of Therapeutics in the University of Toronto; Clinician, Toronto General Hospital; Consulting Physician, Victoria Hospital for Sick Children, Toronto; etc. Pp. 457; 3 diagrams. University of Toronto Press; 1921.

This is an eminently practical text-book on therapeutics and only such facts as have a direct bearing upon the treatment of dis-

eased individuals are included. Throughout the work it is apparent that the author is constantly thinking of patients and not merely of disease in an abstract sense. He divides the consideration of the treatment of a diseased person into five parts: diagnosis, environment, diet, removal of the cause of the ailment, and symptomatic therapy. This arrangement is strictly adhered to, and, on account of its simplicity, if for no other reason, it is believed to be valuable.

Under diagnosis he has emphasized particularly the value of a complete understanding of the patient, his habits, surrounding circumstances, resisting power, etc., not being satisfied with a mere name for a diagnosis; and yet he has avoided the temptation of including a presentation of all the possible symptoms of the various diseases. He has not forgotten that many patients have to be treated before the diagnosis is established or when it is only a probability, and warns against undue attention being given to clinical laboratory results.

Under treatment proper he takes up first the environment, discussing under this heading matters of isolation, nursing, exercise, climate, etc., and making the interesting observation that in chronic conditions, when a climate must be decided upon, it is often found that the best is that one in which the patient has spent his early life. Under the heading of diet are given concisely his personal views, and it may be noted that he believes distinctly in rather free feeding in typhoid fever. By specific treatment he refers to the removal of the cause, as when the stomach is rid of a poison, and to specific therapy. Finally symptomatic treatment is taken up, and very sane views are expressed as to the value of drugs. As a guide to the student and young practitioner this work will be found most valuable.   T. G. M.

Feebleness of Growth and Congenital Dwarfism. By Murk Jansen, Lecturer on Orthopedic Surgery, University of Leyden, Holland. Pp. 82; 40 illustrations. London: Oxford Medical Publication, 1921.

It is stated in the introductory note that this monograph is an attempt to work out two principles, viz.; (1) Injurious agents affecting growing cell-groups enfeeble their power of growth. (2) The measure in which growth is enfeebled is proportional to the rapidity of growth.

By comparing the children of the same parents in large families the effects of injurious influences on feebleness of growth are studied. Rather convincing evidence is brought forward to support the author's claims of the causation of congenital dwarfism. It is shown how smallness of the amnion may cause local dwarfism or local death of the rapidly growing parts of the embryo by direct pressure

or by indirect hydrostatic pressure. The result on the fetus depends on the relative time the pressure is exerted. Thus pressure in the third or fourth week of intra-uterine life causes anencephaly; in the fifth or sixth week, achondroplasia; in the seventh week, Mongolian idiocy, and so on.

The book is well written, the illustrations are good and one's interest is held throughout.   A. G. M.

TRANSACTIONS OF THE ASSOCIATION OF AMERICAN PHYSICIANS; Thirty-fifth Session, Atlantic City, N. J., May 4 and 5, 1920. Pp. 322; vol. xxxv. Philadelphia, 1920.

THIS volume contains the papers read at the 1920 session of the Association of American Physicians. Most of them have appeared in some medical journal or other and must be stamped as an unusually good group of presentations. "Intrathoracic Teratomata," by Lambert and Knox, is a splendidly prepared article covering its subject very completely. "Epinephrin Hypersensitiveness and its Relation to Hyperthyroidism" by Peabody *et al.*, is convincingly written on this matter concerning an endocrinopathy. Fussell and Wolferth report a rare case of slow auriculoventricular rhythm and paroxysmal tachycardia with interruptions of the fast rate. Stengel, Wolferth and Jonas show the futility of using lowered oxygen tension breathing as a test of circulatory function. Many other articles are included, too numerous to mention. This volume of the transactions appears in its usually good style and reflects further credit upon the secretary of this splendid association.

                                                        T. G. S.

A TEXT-BOOK OF PHARMACOLOGY AND MEDICAL TREATMENT FOR NURSES. By J. M. FORTESCUE-BRICKDALE, M.A., M.D. (OXON.) M.R.C.P. (LOND.), Capt. R.A.M.C. (T.F.), Physician to the Bristol Royal Infirmary and Clinical Lecturer to the University of Bristol, etc. Pp. 392; 72 illustrations and 5 colored plates. London: Henry Frowde, Hodder and Stoughton, 1920.

WHILE this text-book, with its kymographic tracings, charts showing urine, chloride, and nitrogen elimination curves, and diagrams of various nerve fiber connections, immediately strikes one as being quite pretentious for nurses, who ordinarily have little or no grounding in laboratory work, yet a careful perusal of it reveals a presentation of the subject that is simple and sufficiently elementary. The first section is devoted to the known facts in regard to the action of various drugs on the animal body, the drugs not being

arranged in a wholly scientific manner but in such a way as to be easily understood and remembered. The illustrations are in every instance apt and add much to the clarity of the presentation.

The second section deals with the treatment of the common and more important diseases. Stress is placed on the principles of treatment, and at the same time the practical methods of applying these principles is not neglected. Treatment by methods other than by the giving of drugs is accorded proper consideration.

In the three appendices are considered the various poisonings and their treatment, the methods of disinfection, and radiotherapeutics, a very satisfactory exposition of the underlying principles involved in the use of the roentgen-rays and radium being included.

This book will be of distinct value not only as a text-book for student nurses, but as a reference work for graduate nurses and physicians.   T. G. M.

DERMATOLOGY. By WALTER JAMES HIGHMAN, M.D., Chairman, Section on Dermatology and Syphilology, American Medical Association, Member of the American Dermatological Association, and New York Dermatological Society; Associate Professor of Dermatology, New York Post Graduate Medical School and Hospital; formerly Instructor in Dermatology, Cornell University Medical School; Acting Associate Dermatologist, Mt. Sinai Hospital, New York; Adjunct Dermatologist, Lenox Hill Hospital, New York; Pathologist, Department of Dermatology, Vanderbilt Clinic, New York, etc. Pp. 482; 95 illustrations. New York City: The Macmillan Company, 1921.

HIGHMAN has written his book on dermatology on the basis of a correlation between internal and external conditions; in other words, that in many instances a skin eruption is an external manifestation of an internal cause, thus forming the connecting link between the old Viennese school, headed by Hebra, which viewed dermatology as virtually limited to the skin, on the one hand, and the French School which considered cutaneous outbreaks from the internist's point of view. As Highman has succinctly put it "thus, while the Germans, were cataloguing dermatoses without reasoning backwards from them, the French were studying etiology without reasoning forward."

The ideal classification of cutaneous affections is naturally from the etiologic point of view but this offers many difficulties as a careful study of this excellent work will show. According to the writer, "dermatology is not a science sui generis, but a branch of internal medicine with all that this concept implies."

As one views Highman's excellent tabulation on "skin diseases which are not autochthonous," in other words not of external causa-

tion, it seems like a dream of the future rather than a realization of the present.

We can all agree with the writer that internal conditions modify the skin's reaction to external irritants and that many of the cutaneous outbreaks have their origin from within. Unfortunately, however, in how many instances can we state positively the exact internal reason for an outbreak?

Although all of the skin affections are mentioned, the finer type used for the less important diseases is of help for the beginner in this subject or the busy practitioner in culling out those affections more frequently observed. Photographs have been selected for their help in diagnosis and their grouping together is of use in showing the differences and resemblances between diseases having the same type of cutaneous outbreak.

Highman has lived up to his convictions that the term "Eczema" is meaningless and although it is used parenthetically this class of cases is placed under dermatitis.

The preparations recommended for the treatment of the eruptions are those which have proved successful in the hands of the writer.

There are very few writers on medical subjects who are as concise, lucid and with such powers of description and it is a pleasure to peruse Highman's work.   F. C. K.

INSECTS AND HUMAN WELFARE. AN ACCOUNT OF THE MORE IMPORTANT RELATIONS OF INSECTS TO THE HEALTH OF MAN, TO AGRICULTURE, AND TO FORESTRY. By CHARLES THOMAS BRUES, Assistant Professor of Economic Entomology, Bussey Institution, Harvard University. Pp. 104; 42 illustrations. Cambridge: Harvard University Press. London: Humphrey Milford, Oxford University Press, 1920.

THIS book, as stated in the preface, "is an attempt to present some of the principles and practices of economic entomology in a form that will illustrate the biological relationships of insects to their environment." One not familiar with recent progress in this field of science will be surprised at its great practical importance, not only in the relation of insects to public health, but also to the food supply and to forestry. A special chapter is devoted to household insects; houseflies, stable-flies, roaches, crickets, clothes moths, etc., receiving attention. Of all the insects it is interesting that only two are of outstanding usefulness to man, the honey-bee and the silkworm. While many are directly harmful, of others it can only be said they are nuisances.

The accomplishments of the medical profession in the reduction of malaria, yellow fever, plague, and typhus fever are due to an appreciation of the relation of insects to these diseases, and for

these discoveries medical investigators must share honors with the entomologists. One interested in these important problems will thoroughly appreciate this concise yet illuminating book.

<div align="right">T. G. M.</div>

TUBERCULOSIS OF THE CHILDREN. By PROFESSOR HANS MUCH, Director of the Department for the Science of Immunity and for Research of Tuberculosis at the University of Hamburg, Germany. Pp. 156; not illustrated. New York: The Macmillan Company, 1921. Translated by Max Rothschild, M.D.

THERE are two parts to this small volume. The first section is a treatise on Much's theories of immunity and the treatment of tuberculosis by partial antigens, or, as Much calls them, "partigens." The author believes that tuberculosis always starts in the first years of childhood, and that tuberculosis in the adult develops from this childhood infection. Persons once infected are protected against subsequent infection. The principle enunciated by Much, in the treatment of tuberculosis by tuberculin, hinges on the fact that there are two kinds of oversensitiveness, a harmful one (toxin) and a useful one (antibody). In the tuberculins on the market substances are present which can produce oversensitiveness to toxin as well as to antibodies. It is the separation of these substances and the administration of the proper partial antigen which gives the good results.

In Part II the necessity for the fight against tuberculosis in children is stressed. Tuberculosis of the bronchial glands is discussed at length, as in the majority of cases these glands represent the first site of invasion and localization for the bacilli.

Besides specific treatment, other methods are mentioned and their use noted. Such, for example, are roentgen-rays, salt baths, calcium, nutrition, rest, climate and artificial sunlight.

There is much of interest between the covers of this book. The theory of the "partigens" is unique as far as the reviewer is able to ascertain, and if substantiated the method of specific treatment will be revolutionary.

<div align="right">A. G. M.</div>

VOLUMES II AND III OXFORD SYSTEM OF MEDICINE, Oxford University Press; 35 West 32d Street, New York.

IT would indeed be difficult to justly review the contents of these two volumes in lines many times the number allotted for this purpose. Volume II contains twenty chapters with 817 pages, while Volume III has fifteen chapters with 828 pages devoted to a wide variety of topics included in the field of internal medicine. These

chapters have a distinguished authorship and present their subject-matter with a certain degree of present-day finality. Usually a lone reviewer is liable to regard some system contributions as stronger than others, some as weaker, dependent somewhat upon his own interests. Such a reviewer will, however, find that the chapters in these two Oxford System Volumes are quite uniformly well done and highly satisfactory. Of necessity, they cannot all possess equal merit.

In Volume II, one of the most interesting chapters is devoted to the "Respiratory Excursion of the Thorax." This gives Hoover an opportunity to epitomize his ideas concerning the clinical observation of costal margin movements and the normal antagonism of the diaphragm and intercostal muscles. "Bronchial Asthma and Hay Fever" are well taken care of by Walker. These allied conditions are entertainingly discussed and much space is devoted to protein sensitivity in relation to these diseases. The details of specific protein therapy are reviewed in clear, hopeful detail. What must be considered the masterpiece chapter of this volume is Cecil Drinker's contribution on "The Pathological Physiology of Blood Cell Formation and Blood Cell Destruction." It is difficult to conceive of anything more comprehensive and thorough in execution. The bibliography of this chapter is most complete as are the bibliographies at the end of most of the chapters. Minot devotes splendid pages to the "Clinical Discussion of the Anemias." In addition to these especially interesting chapters, one finds others devoted to all diseases of the lungs, bronchi, mediastinum, heart, bloodvessels and blood.

Volume III presents an equally good lot of chapters. Each one makes its especial appeal. They are devoted to diseases of the gastro-intestinal tract, nephritis, and disturbances of the ductless glands. Perhaps the best chapters of this volume are those given to nephritis. Henry Christian, the American editor of the System, presents this subject in masterful style. The case method is utilized to good advantage, and valuable diet lists are included. Sippey covers gastroduodenal ulcer from his well known angle, while Rehfuss takes up the remaining conditions of the stomach, placing emphasis upon certain points resulting from the fractional method of investigating gastric function. Sir John Rose Bradford discusses war nephritis with no new ideas on the subject. The other English contributor to the volume, Sir Humphrey Rolleston, gives one an excellent analysis of conditions pertaining to the liver, gall-bladder and bile ducts. Pratt handles the diseases of the pancreas in his usually excellent style, while Stockton takes up the intestinal derangements. Pincoffs and Boggs deal with the peritoneum. Riesman and Horax write of adrenal and pituitary dysfunction respectively. Plummer's chapter on the thyroid and parathyroid, although planned for this volume, will be included in a later issue.

These volumes maintain the high standard set by the first one. Their chapters present the best medicine we know today, and much is omitted that has been erroneously included in text-books for years. It is interesting to note generally the concise statement of therapeutic suggestions. The supertherapeutist will look in vain for long lists of superlatively useless remedies to be tried on his patients. A very excellent feature, incorporated in these volumes, is the table of contents at the head of each chapter. This enables the reader to see at a glance what he may expect and where he may find it. These volumes have not been read in their entirety, still enough has been covered to enable one to highly commend the authors and heartily recommend their lines to those interested in internal medicine and its practice.   T. G. S.

PROGRESS

OF

MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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Dislocation of the Navel in Gastric Ulcer and Other Abdominal Affections.—H. Schlesinger (*Wiener klin. Wschr.*, 1921, xxxiv, 1) describes a new sign in connection with gastric ulcer and other acute lesions in the abdomen. If one has the patient sit and strain as if at stool, one frequently notices a characteristic dislocation of the navel. With healthy persons the navel is usually elevated. With an acute abdominal lesion, causing unilateral rigidity of the rectus abdominis, a lateral dislocation of the navel occurs during straining, which lasts several seconds. This transitory dislocation of the navel is toward the diseased side, because of the more marked muscular contraction. The phenomenon is best appreciated if the observer stands at the foot of the bed. The dislocation varies much in different cases (up to 4 cm.). The author finds the navel phenomenon of value at times as evidence that an ulcer persists when other signs, such as tenderness on pressure, have disappeared. Oppenheim has described dislocation of the navel as a sign of unilateral paralysis of the abdominal muscles. Here, the navel is dislocated toward the normal side. Schlesinger has observed his navel phenomenon especially in cases of gastric and duodenal ulcer and in cholelithiasis during or immediately after an attack.

Koranyi's Phenomenon.—H. Faschingbauer and H. Nothnagel (*Wiener klin. Wschr.*, 1921, xxxiv, 46) report their observations on Koranyi's phenomenon. In 1918, Koranyi recommended percussion of the apices of the lungs in the erect posture and with the patient leaning forward. "If the apices are sound, the percussion findings remain

the same in both postures, whereas the upper borders of diseased apices move forward if one marks their position in relation to the spinal column. Thus, asymmetries are recognizable which are missed in the erect posture. Dull areas move, their extent increases. Occasionally small areas of dulness become evident, which are missed in the usual method of carrying out percussion of the apices." The authors confirm Koranyi's findings and are convinced of the practical importance in the diagnosis of beginning apical tuberculosis. In addition to infiltrative lesions of the apices, they have found analogous phenomena in pulmonary emphysema.

Are there Reliable Criteria of Operability in Exophthalmic Goiter.— CHEEVER, D. (*Arch. Surg.*, 1921, ii, 21). From a review of the literature on the subject and an analysis of 4 fatal operative cases at the Peter Bent Brigham Hospital and 6 other cases in which a fatal issue was narrowly averted, the author concludes: (1) During an acute exacerbation of the disease or in periods of great mental depression, operation is contraindicated. (2) Muscular weakness so great that the patient cannot walk, and marked loss of weight with continued loss under absolute rest, are serious contraindications. (3) Organic visceral disease, so serious as to jeopardize patients having an operation of similar technical type, is a contraindication. (4) Operation should not be undertaken in the presence of an enlarged thymus, until its probable activity has been reduced by irradiation. (5) The Jewish race offers a distinctly higher operative mortality. (6) A metabolism of + 30 introduces a serious risk, which undoubtedly increases with high rates, but not necessarily in proportion, and there is no rate of metabolism which alone contraindicates minor surgical procedures. (7) The "vagotonic" type is possibly more vulnerable to the operative ordeal than is the "sympatheticotonic," but evidence on this point is as yet inconclusive. (8) The minor procedures, whether consisting of injections into the gland, cauterizing, or ligating operations, are often most valuable indices of a patient's resistance to trauma.

Advantages of Prophylactic Administration of Quinine Demonstrated Experimentally.—ETIENNE and EDMOND SERGENT (*Ann. de l'Institut Pasteur*, 1921, xxxv, 125). Remarking that a better way of judging the value of quinine prophylaxis against malaria is that of properly controlled experimentation, rather than simple observation, and pointing out the impossibility of this procedure when man is used as the subject, the authors worked with malaria of birds (Plasmodium relictum). The research included (1) a study of the acute infection, (2) the passage from acute to chronic states (3) the curative action of quinine and (4) the preventive action of quinine. Their general conclusions are as follows: (1) If a healthy subject (canary) absorbs quinine as a prophylactic measure, and receives a heavy inoculation of the virus, it will not become sick. On the other hand, the control birds always become ill, 30 per cent. of them dying in the acute stage. (2) This immunity following quinine persists as long as the virus is administered. Where this treatment is stopped the birds are susceptible to infection. (3) The advantages of prophylactic administration of quinine are: (*a*) avoidance of the serious accidents of the acute disease; (*b*) if the

infection is not completely avoided it is rendered much less severe, and confers on the subject a relative immunity to reinoculations; (c) subjects when given quinine as a prophylactic measure are less dangerous as a source of virus for inoculation of others.

Studies in the Treatment of Malaria.—STEPHENS, YORK ET AL. (*Ann. Trop. Med. and Parasit.*, 1921, xiv, 365). In a study of the time of onset of the paroxysms in simple tertian malaria it was found that 90 per cent. of the paroxysms, in cases observed occurred during the hours of activity (7 A.M. to 6.59 P.M.). The maximum number of these paroxysms occurred at 2 P.M. Alteration of the period of activity by one hour produced a corresponding alteration in the time of incidence of the paroxysms.

Variations in the Bacterial Flora of the Upper Air Passages during the Course of Common Colds.—BLOOMFIELD, A. (*Johns Hopkins Hosp. Bull.*, 1921, xxxii, 121). From facts obtained from careful review of the literature on the subject of colds, and from a consideration of the clinical features of the condition, Bloomfield summarizes our present knowledge of the subject as follows: " (1) The common cold is a definite disease generically related to grippe and influenza. The primary disease is often followed by local complications which tend to overshadow the picture. (2) Cold may produce disturbances in the upper air passages which are not to be distinguished from true infectious colds. (3) None of the common bacteria found in the nose or throat have been proved to be the primary cause of colds. (4) The most convincing evidence in the literature favors a filtrable virus as the cause of the common cold."

To investigate the subject further the author made an intensive study of the aërobic flora of the upper air passages of ten individuals suffering from acute coryza, previous studies on normal flora serving as a background. It was found that in uncomplicated colds the flora differed in no fundamental way from the normal. Where an organism normally not present was found, it almost invariably was found in cases presenting complications (bronchitis, tonsillitis, sinusitis, etc.). While it is certain that commonly encountered pathogenic bacteria, such as Staphylococci, Streptococci, Pneumococci, B. influenzæ, etc., are not etiological factors in colds, it seems that the latter may so alter the mucous membrane as to encourage its bacterial invasion by one of these organisms, resulting in the complications commonly met with following coryza.

Variations of Acid Concentrations in Different Portions of the Gastric Chyme, and its Relation to Clinical Methods of Gastric Analysis.—GORHAM, F. (*Arch. Int. Med.*, 1921, xxvii, 434). Feeling that the gastric chyme is not, in the majority of instances, a homogeneous mixture after a test meal, and that the acidity of different portions of it may vary widely, the author introduces the following method of examination: The fasting stomach is emptied and the patient given 30 gm. of dry shredded wheat biscuit and 400 c.c. of water. After forty-five minutes the entire stomach contents are aspirated in 10 c.c. portions in rapid succession. The acidity of these different portions is

determined separately and, by examining a mixture of all samples, the "average acidity" is ascertained. This method is advocated as being superior to the so-called "fractional method," where only a small sample is withdrawn, which may not be representative of the contents remaining in the stomach. The author feels that the "secretory variations" revealed by the "fractional" method of gastric analysis may be explained in part by the fact that the acidity of the fractions removed represents only the acidity of the chyme at the moment of removal in those parts of the stomach from which they were obtained as above.

Paroxysmal Tachycardia of Ventricular Origin, and its Relation to Coronary Occlusion.—ROBINSON, G. C., and HERRMAN, G. R. (*Heart*, 1921, viii, 59). On reviewing 16 reported cases of paroxysmal tachycardia of ventricular origin in which electrocardiograms are published these authors find only 6 undoubted cases. Six others are classified as probable cases of ventricular paroxysmal tachycardia. To this first group (undoubted cases) they add 4 of their own cases. Attention is called to the proved relationship between ventricular paroxysmal tachycardia and coronary occlusion in experimental animals. In one of the 4 human cases herein reported direct evidence of the association of ventricular paroxysmal tachycardia with coronary occlusion was obtained at autopsy. It is felt (for reasons cited) that this relationship was probably present in the remaining 3 cases. The prognosis of paroxysmal tachycardia of ventricular origin is more unfavorable (3 of the 4 cases dying) than that of auricular origin.

Jaundice after Salvarsan.—BROCQ, L. (*Bull. médical, Paris*, 1921, xxxv, 235). The author notes that jaundice following intravenous neoarsphenamine treatment indicates injury to liver cells, which, if not subjected to further damage, soon recover. However, these damaged cells offer a *locus minoris resistentiæ* for spirochetes, so that a complete suspension of treatment seems contraindicated. He suggests, in such a dilemma, the use of mercury or of neoarsphenamine subcutaneously, and insists that in either case the procedure must be carried out with the greatest caution.

SURGERY

UNDER THE CHARGE OF

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Pericardiotomy for Suppurative Pericarditis.—POOL (*Ann. of Surg.*, 1921, lxxiii, 393) says that two features have become generally accepted, first approach and drainage should be to the left of the sternum, secondly

no procedure should be employed which does not drain the lowest part of the pericardium. He offers an improved method—resection of portions of seventh, sixth and fifth cartilages, wherein the pericardium is opened at its lowest point; little risk to the pleura is involved, while ample drainage is provided. Moreover, whatever exploration is necessary either at the time of operation or postoperatively is provided for the added fourth interspace is exceedingly wide. Resection of the sixth and the seventh cartilages seems best in cases where less extensive exposure is imperative. Indeed, this procedure was used in the author's case, giving satisfactory exposure and efficient drainage. The drain was removed in thirty-six hours in the reported case with the substitution of two Carrel tubes and Dakin's solution was introduced regularly. In another case Carrel-Dakin method would be instituted immediately. From former experience and study of case reports, it was felt that thick pus with fibrin would likely wall off the cavity into chambers with resulting retained excretions and subsequent imperfect drainage, especially of the left recess. In theory, it was believed that the solvent effect of Dakin's solution would obviate this risk by rendering the excretions thin. Improvement was striking and sustained, while there was no noxious influence exerted upon the pericardium apparently. Early treatment with Dakin's solution may possibly diminish pericardial adhesions. Resection of sixth cartilage alone may be done readily under local anesthesia and is indeed tempting, by reason of its simplicity, but drainage is not sufficient.

Gastro-enterostomy in Acute Perforated Ulcer of Stomach and Duodenum.—DEAVER and PFEIFFER (*Ann. of Surg.*, 1921, lxxiii, 441) say that all success in perforated ulcer is based on early treatment— early operation and efficient suture of the opening are essential. In subsidiary measures excision of the ulcer offers nothing of immediate life-saving value, while primary gastro-enterostomy is still a debated issue. The senior author has performed primary gastrojejunostomy for fifteen years with very satisfactory end results in a large series of 67 cases. The chief contraindication is the presence of shock or evident systemic toxemia—not frequent within twelve hours after perforation.

Congenital Torticollis.—MEYERDING (*Jour. Orthopedic Surgery*, 1921, iii, 91) says that torticollis of congenital origin is a deformity rarely met with in the general practice of medicine and surgery. The etiologic factor appears to be trauma to the sternocleidomastoid muscle at or preceding birth, producing an ischemia with resulting chronic interstitial myositis. Heredity, infection and syphilis do not seem to be factors. The treatment is surgical as early as possible with subsequent retentive apparatus. Operative technic is outlined.

Hallux Valgus Rigidus and Malleus.—JANSEN (*Jour. Orthopedic Surgery*, 1921, iii, 87) says that two principles make themselves felt in these deformities: (1) disturbance of muscle balance—most prominent in hallux valgus and (2) joint wear, the arthritis deformans of textbooks—most prominent in hallux rigidus. This latter condition is characterized by flattening of the metatarsal head with gradual shorten-

ing of this bone and lipping of the joint cartilage with subsequent pain through the plantar area. By cramp of the flexor brevis, hallux malleus is developed. This condition strips the abductor hallucis of its power. When the adductors prevail hallux-malleo-valgus frequently evolves, noted by the callosity on the plantar side of the interjoint of the big toe. Luxation of the extensor proprius and flexor longus hallucis is needed for hallux valgus in most cases the acknowledged effect of too narrow or too pointed shoes, especially when high heels are worn with them. From the above it follows that well fitting shoes and raising of the inner border may largely contribute toward preventing the development of these conditions. Treatment should be directed both to muscle balance and joint wear. Transplantation of abductor hallucis has proved useful to the author. In quite severe cases it may be combined with shortening of the first metatarsal according to Ludloff's method or by removal of part of the metatarsal neck.

An Integral Traction-providing Splint for Vicious Fractures of the Femur.—MASLAND (*Ann. of Surg.*, 1921, lxxiii, 495) says that all the various modifications of the Thomas and Hodgen splints are equipped with pelvic rings which give a one point support to the ischium. This permits of but limited amount of pressure without pain. The author's splint utilizes all opportunities offered by the body to distribute the strain and so allow greater traction with less discomfort. The joints above and below the fracture are immobile; the individual fit of the splints insures their better retention in position. The body and the fractured part are open for inspection and the needful attention. The strain of traction is distributed in wider degree over salient parts of the body while traction can be applied in the direction and to the degree required for traction is wholly integral to the splint. The patient can move or be moved on the bed without disturbing the direction of traction or the relation of the parts. Comfort and well-being are conserved in the highest degree.

Drainage of Common Duct through Cystic Duct: Cystico-choledochostomy.—REID (*Ann. of Surg.*, 1921, lxxiii, 458) says that Halstead advocated careful and complete closure of incision into the choledochus and drainage of this duct by a tube passed well into it by way of the ductus cysticus as early as 1897. Halstead and the author have done much work upon dogs in this problem and are now doing the operation routinely in the Johns Hopkins Hospital. Their technic is described and cases cited. The procedure offers several advantages, for the incision into the common bile duct may be closed completely and with union by first intention, while emaciation and weakness due to loss of bile for protracted periods is avoided. Healing of the abdominal wound and drainage tract is less likely to be delayed, because leakage of bile is avoided. The patency of the duct may be tested routinely by clamping the tube. Finally on removal of the tube there has been no leakage in more than one-half the cases.

A Perineal Operation for Removal of Stone in Lower End of the Male Ureter.—LOWSLEY (*Surg., Gynec. and Obst.*, 1921, xxxii, 300) says that a careful review of the anatomy of the male pelvis with careful dissection on the cadaver impressed upon him the accessibility of the lower

end of the ureter by means of the perineal route. He describes the developed technic for removal of stone by this route. The perineal route should only be attempted when the stone is less than 4 cm. from the bladder and fixed in position. The patient may be allowed out of bed after the second day and the downhill drainage would seem to be a decided advantage in that the chances of thick scar formation around the ureter are less. Moreover, this downhill drainage prevents absorption of urine and deleterious results from concomitant infection which frequently accompanies urinary lithiasis. Finally chances of wide infection of tissues around incision in ureter and subsequent stricture of ureter are much less.

Resection of Intestine for Acute Intussusception: Two Cases of Recovery.—SOUTHAM and CRAWSHAW (*British Med. Jour.*, February 19, 1921, p. 266) say that the published results show that the mortality of enterectomy in cases of acute intussusception is extremely high. In an earlier collection of 239 cases by Gibson, there was no recovery from irreducible intussusception in a patient under seven years. Barker says that he had never seen a recovery after resection in a gangrenous state and never expected to see it. The 2 reported cases were three years and six months old respectively. In both cases the intestine was gangrenous. Extensive resection was necessary but complete and uneventful recoveries followed. The successful issue was due to measures taken to safeguard the patient from the effects of shock. *Speed* in operating is essential. Everything should be ready to hand while closure of the laparotomy should be carried out by through-and-through sutures. *Body heat* should be preserved by bandaging the child in a suit of gamgee and the theater maintained as warm as possible. The anesthetic appears closely related to the amount of shock present. This was minimized by using gas and oxygen in 1 case while no anesthetic was used in the other. Shock further depends upon water starvation, resulting from the previous vomiting and loss of fluid. In both the reported cases, postanesthetic vomiting was entirely absent. Fluids were given and retained immediately after the completion of the operations.

On the End-results of Colectomies for Intestinal Stasis.—SHEEN (*British Med. Jour.*, December 22, 1921, p. 116) reports the end results of 4 complete colectomies performed in 1913–14. One of them died soon after operation. In the other three there was great improvement; in two, what might be termed complete success. The qualifying details are: in the first case a ventral hernia with dyspeptic symptoms; in the second, adhesions fortunately not interfering with pregnancy; in the third diarrhea occasionally. There is an operative parietal infection in these and similar cases which it is justifiable to regard as coming from within. Possibly the poorly vitalized parietes cannot deal with organisms which the peritoneal cavity can put up with, in these toxic subjects. The usual germ is B. coli. In spite of the good results in these 3 cases, the author confesses that he is not enamoured of this operation. He accepts the toxemia, its signs and symptoms—that it is due to a blocking of the ileal effluent owing to displacements, kinks and adhesions of cecum and colon, these again resulting from upright posture, habitual constipation and tight clothing in women. The surgical "purists" say that there are only two lines of treatment, paraffin

and truss belts for slighter cases and colectomy for the rest. Complete colectomy is a serious operation. Very few are done, for it is not a popular operation among surgeons. The mortality is not easily ascertained. Many cases recover and are greatly benefited while some cases die. There is a third class in which there is neither death nor recovery but an almost hopeless discomfort. Clark records "final results" in 12 cases: in 6 of these it was not satisfactory. The author searches for alternatives for abdominal operations, for various kinds are done and toxemia previously present disappears. It has been said of these types of operations that their good results have been produced by freeing the ileal effluent. Waugh attributes the impairment of mechanical efficiency of the bowel to the elongated retained mesentery of the ascending colon, a developmental survival present in 20 per cent. of individuals born. An easy, safe operation—fixation of anterior colon, cures and symptoms of stasis disappear. The author has carried this operation out in several cases with immediate improvement. Surgery is not the only remedy advocated. Diets, paraffin, massage, exercises, posture, spa treatment, removal of toxic foci, all have their place in treatment of intestinal stasis. Prevention should be our final goal. It should be instituted in babyhood and continue for the earlier the treatment the better, because then the less severe and more effective it is.

Acidosis in Operative Surgery.—FARRAR (Surg., Gynec. and Obstet., 1921, xxxii, 328) says that there is great need for collaboration between the surgeon and the physiologist, as the time may be all too short for the study of a condition suddenly confronting the surgeon at or immediately following an operation. Acidosis is a term used to signify an impoverishment of the body in bases. The alkali reserve (bicarbonates of the blood) is the criterion of the acid-base balance of the body. The determination of the alkali reserve is readily made by Van Slyke's method. (The number of cubic centimeters of carbon dioxide gas which 100 c.c. of blood plasma will take up.) A high carbon dioxide combining power of the blood is of the greatest importance for the maintenance of lung ventilation during operation. The range of the carbon dioxide combining power of the blood in women (150 cases) is 55.2 c.c. to 69.9 c.c. per 100 c. c. of the blood plasma or about 8 points lower than Van Slyke found for men. It follows, therefore, that acidosis is more frequent following operations in women than in men. The fall in alkali reserve during operation depends not only upon the anesthetic and the duration of the operation but upon the nature of the operation and the occurrence of hemorrhage and shock. Moreover, the fall in alkali reserve bears a close relation to the fall in blood-pressure and pulse pressure. If a fall in blood-pressure is prevented, there is a saving in alkali reserve. A solution of glucose given intravenously during an operation at the rate of 0.8 gram of glucose for every kilogram of body weight each hour of the operation will lessen the acidosis incident to operation by promoting metabolism. Vomiting is diminished and diuresis promoted by this measure. Glucose will appear in the urine in one-half hour if this rate has been exceeded. A solution of gum acacia (6 per cent.) in a glucose solution (20 per cent.), if given a subtolerant rate the entire time of operation, is an aid to the maintenance of blood-pressure.

PEDIATRICS

UNDER THE CHARGE OF

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A Mild Chronic Nephritis in Children.—HILL (*Jour. Am. Med. Assn.*, August 28, 1920) gives the test that he uses to determine the presence of acute nephritis. In mild cases a fixation is shown where the phenol-sulphonephthalein test is normal. A fixation does not necessarily mean a severely damaged kidney, but it is an indication at least that the kidney function is abnormal. The child is put on a full normal diet containing a considerable amount of protein, especially at the noon meal. A capsule containing 1 gm. of salt and a 2 grain pill of caffein sodium benzoate is given with each meal, to take the place of the tea or coffee used in the adult test diet. This gives a diet containing a considerable amount of salt, protein and diuretic material, all of which will stimulate the kidney to its maximum effort. Exactly 10 ounces of fluid is given with each meal and no fluid or food whatever is given between meals. The urine is collected in two-hour periods from 7 A.M. to 7 P.M. and the night urine from 7 P.M. to 7 A.M. Then all that is required is to record the specific gravity of each sample of urine. The normal response shows a wide variation in gravity between the different specimens; in fifteen normal children there was always a variation of at least eight points between the highest and the lowest. The night urine in normal children is small in amount, and almost always has a specific gravity of 1020 or over. The child with damaged kidneys on the other hand, is unable to vary the concentration of the urine in this way, and the gravity of the individual specimens may vary only one or two points. The fixation may be at a high or at a low level, and may be high or low in the same patient at different times. It is apparently the fixation of the gravity that is important and not the level at which it is fixed. This is the most practical test for everyday use. There is nothing complicated about it. The food does not have to be weighed, nor is it necessary for the patient to eat all of it. It is merely essential that he consume a good full diet. The rules for fluid intake must, however, be strictly adhered to. As regards blood urea, the writer thinks that the fixation is shown even in cases where there is not sufficient damage to give marked urea retention.

Weight and Height in Relation to Malnutrition.—EMERSON and MANNY (*Arch. Ped.*, August, 1920) point out that malnutrition is a definite clinical entity with characteristic history, definite symptoms and pathological physical signs. Clinical evidence shows that the physical signs that may best serve to identify this group of malnourished children is the relationship between weight and height. The age factor is of secondary importance, and is mainly serviceable in selecting cases stunted by constitutional disabilities such as syphilis, tuberculosis, deficient thyroids, the effect of certain drugs, convalescence from long

illness and the like. The tables derived from the studies of Boas and Burk represent the most extensive records of weights and heights made. Recent studies show that they are essentially true averages for unse- lected groups of American children. The Boas-Burk and other tables in general use are vitiated by the measurements of large numbers of malnourished children, whose measurements lower the averages of weight and height, and make them of only relative value as standards. By setting the Boas-Burk figures the depression of averages is to a great part offset. Individual variations in the relationship of weight to height is of enough importance to make it necessary to use a zone system rather than any single line as a basis of reference. After various experi- ments at determining zone boundaries, clinical evidence is best satisfied by lines lying between 7 per cent. below and 20 per cent. above the "set-forward Boas-Burk figures." Outside of the central zone are found, on the one hand, the obese, and on the other, the malnourished. Within the zone are still a considerable number of malnourished children requiring individual diagnosis. The malnourished child selected by this rule of habitual 7 per cent. underweight for height form almost without variation 20 to 40 per cent. of any group of children in school and pre- school periods. When tables have been constituted from sufficient numbers of children proved to be normal, the line of average weights and heights will lie somewhere between the set-forward Boas-Burke figures and those represented by a line drawn midway between the 7 per cent. underweight and the 20 per cent. overweight boundaries. This has already been confirmed by the special studies of Baldwin and Robertson.

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The Circulatory Reaction to Graduated Exercise in Normal Children. —WILSON (*Am. Jour. Dis. Children*, September, 1920) gives the technic for making this study, which consisted of more than five hundred test exercises comprising one hundred and fifty complete experiments. The test exercises consisted of swinging one or two iron dumb-bells (3, 4, 5, 7 and 10 pounds each) from the floor to the full stretch of the arms overhead and back again between the legs, at a constant rate of two seconds for each swing. This was repeated from ten to sixty times to increase the amount of work. Each child performed at one visit three or four of these exercises graded from moderate to severe, until the maximum effort was approached as evidenced by marked breathless- ness, flushed face, perspiration and fatigue. This was corroborated by an additional exercise of slightly increased intensity. The possible influence of one exercise upon another was eliminated by allowing a full rest between each exercise, and by varying the order of exercises on subsequent visits. The pulse rate at the wrist was taken by an assistant before each exercise until it remained constant. It was taken imme- diately after exercise for fifteen seconds and again at the end of one hundred and ten seconds after exercise for twenty seconds. From these counts the rate per minute immediately after exercise and at the end of two minutes were calculated. A pulse rate within six beats of pre- exercise rate was considered normal. If the pulse was not normal at the end of two minutes, it was taken at one-half minute intervals for from three to five minutes. The systolic blood-pressure after exercise was taken at five- and ten second intervals. Before exercise the systolic

blood-pressure was read until a constant level was reached and at frequent intervals for two minutes. From these experiments upon the circulatory reactions after exercise, it was found that the circulatory reactions to graduated exercise on normal children are similar to those in the adult. The circulatory reactions immediately following similar graduated exercises of two day intervals over a period of weeks were as a rule constant. The time required for the pulse rate to return to normal does not give much information as to the exercise tolerance of the child. A type of systolic blood-pressure after exercise showing an increased rise, delayed rise and summit, and a prolonged fall, and associated with symptoms of marked dyspnea and fatigue would seem to indicate that the exercise tolerance of the particular child has been reached or exceeded.

A Dental Clinic for Children in a Settlement.—Guthrie (*Jour. Am. Med. Assn.*, November 6, 1920) offers a report based on the case records of more than 8000 children, ranging in age from infancy to the sixteenth year. The records showed the age, sex, race, nutrition and history of previous infections. The school history was also noted. Record was made in every case of the number of deciduous and permanent teeth, together with the presence of cavities, abscesses or sinuses, and their location. Special dyscrasias, if present, were noted, as well as abnormal frenum, fifth cusp, and geographic tongue. Roentgen findings and Wassermann reports were recorded when made. It was found that there was a marked reduction in the number of cases of infectious diseases in the children who belonged to this clinic. There was not an epidemic in this neighborhood since the work was instituted. Two special groups of children were studied. One consisted of those who were known to be tuberculous, and the other of those who were proved cases of syphilitic infection. These were observed in order to determine the value of thorough dental care in these types of cases. In the tuberculosis group 95 per cent. of the deciduous teeth had to be removed before the eighth year on account of abscesses. In the syphilitic group only 40 per cent. had to be removed. More cases of retarded absorption of the deciduous roots were noted in the syphilitic group than in the tuberculous. In 9 cases of 60 at the thirteenth year roentgenograms were made to determine the condition of the deciduous roots. These disclosed a beginning absorption. In these 9 cases the 10 deciduous teeth were extracted first on the right side and after about six weeks the ten deciduous teeth on the left side were removed. In a few months the permanent teeth were erupted in correct position. Ulcerative stomatitis occurred with greater frequency among the children from the parochial schools. These patients were all isolated in the hospital and treated with bactericidal measures against anaërobic organisms. There were no deaths but several cases of marked deformity ensued as a result of the extensive operative procedure necessary to overcome the infection.

Meningitis Caused by Lead Poisoning in a Child of Nineteen Months.—Strong (*Arch. Ped.*, September, 1920) reports this case which was admitted to the hospital for a persistent vomiting and a mild diarrhea and a temperature of 99°. The history was that about ten days pre-

viously he had been seen to bite paint from the side of his bed. After a short while he began to vomit his food. He was given castor oil by his parents and after a few days was very much better. The day before admission the vomiting and diarrhea began again. Previous to admission the child had been healthy and teething, and growth and development had been normal. The mother said that he had had a fall from bed a week before admission, and there was a small contusion over the left eye, which had disappeared for the most part and there was nothing else present to indicate that the fall had caused any serious injury. On physical examination it was found that the tonsils were hypertrophied. The vomiting was persistent. The stools of which there were four or five a day, were green in color, and contained much curds and mucus. The temperature for the first ten days after admission did not exceed at any time 100°. During the first forty-eight hours all food was withheld. The stomach was washed and the colon was irrigated. A cathartic was given. The vomiting was persistent for about a week, and at the time was considered as more than the vomiting which ordinarily accompanies an intestinal disturbance of this kind. The paint was considered as an etiological factor, but at this time no other symptoms but the vomiting could be discovered that warranted a diagnosis of lead poisoning. At the end of ten days the child had improved greatly. Because the mother was in the hospital the patient was kept in the hospital, although under ordinary circumstances he would have been discharged. During the following week the improvement was marked. One morning the nurse discovered him biting on the painted rail of his bed, and it was seen that he had bitten off some of the paint, his stomach was washed and he was given a cathartic. The bed was draped with sheets so that he could not get to the painted part. For twenty-four hours he did not give any evidence of any ill-effect from taking the paint this second time. At the end of this time he vomited his food, and the persistent vomiting and diarrhea returned. These symptoms continued for a week and it seemed to be the logical belief that the lead was the cause of the trouble. On or about the eighth day stippled red cells, Grawitz's granules, were shown. About the same time a blue line was observed on his gums near the upper incisors. On the tenth day after the recrudescence of the vomiting, distinct meningeal symptoms appeared. The head was retracted, and the extremities were extended and rigid. Kernig's sign was negative. Brudzinski's neck sign was positive. Brudzinski's collateral reflex was negative. The child seemed distinctly toxic. A ptosis of the left upper lid was occasionally present. The child was comatose most of the time. There was variable pupillary reflex, and occasional strabismus of the left eye inward. There was no nystagmus. The respiration was markedly irregular as to time and depth and later became of the Cheyne-Stokes type. The temperature did not rise to above 100° until just before death, when it rose rapidly to 103°. Laboratory examinations were for the most part negative except for the Grawitz's granules in the blood and the findings of a serous meningitis in three spinal fluids. Convulsions were few and milder than were expected. The child died on the twelfth day after the appearance of the meningeal symptoms. The etiological diagnosis was based on the presence of Grawitz's granules,

the lead line and the history of twice having ingested paint from his bed. The recognized fact that lead is capable of affecting the central nervous system, and the absence of any infection seem to justify the conclusion that the meningitis was due to lead poisoning.

The Treatment of Pyelitis in Infancy and Childhood.—KRETSCHMER and HELMHOLTZ (*Jour. Am. Med. Assn.*, November 13, 1920) treated a series of 11 cases by pelvic lavage with silver nitrate. They claim nothing new for the treatment by pelvic lavage, and they do not think that silver nitrate is a specific. The excellent results obtained in the treatment of B. coli infections in adults by means of silver nitrate injections of the renal pelvis seem to justify an attempt to treat a series of cases by this method in order to determine whether or not this could be applied to the treatment of pyelitis in infants and children, and whether this method was a better one than the treatment by medicines and vaccines. There are two factors that have prevented this method from being employed more frequently and these are because it is not generally known that it is possible and because general anesthesia is necessary. With the rapid advance in developing and perfecting small cystoscopes, this field has been materially enlarged so that cystoscopy can be performed in infants as easily as in adults. In boys, because of anatomic considerations, cystoscopy cannot be carried out as early as in girls, but one of the authors has done this repeatedly in boy babies of fourteen months. It has been suggested that external urethrotomy be done in boys to facilitate the procedure, but this has not been done. The youngest patient was seven months of age. In this case both ureters were catherized simultaneously, and both renal pelves were treated with silver nitrate. The oldest child was ten and a half years. The other patients were one child one and a half years; one two years old; two two and a half years old; one five years; one seven years; two eight and a half years. All these cases were girls. No untoward symptoms followed instrumentation and treatment. The object sought was to render the urine free from pus and sterile. No case was considered cured until these were accomplished. In 9 of the 11 cases complete cures were obtained. The cultures were reported sterile if no growths were found at the end of forty-eight hours. In order not to overlook the possibility of the development of slow growing organisms, the plates were kept in the incubator for five days before a final report of a sterile culture was given, so that in all of the cases it can be said that the culture was negative after five days. One patient left after one treatment, and the cultures showed the presence of infection. This is not included under the cured cases, although the urine was free from pus. Silver nitrate solution was used in each case. The strength of the solution was 0.5 per cent. The amount injected varied from 1 c.c. in the infants to 5 c.c. in the older children. The number of injections required to render the urine sterile varied. Three patients required but one injection. Five required two injections and one required three injections. In 2 cases the kidney urines were sterile before the bladder urines, in 1 case after two injections and in 1 case after one injection. This patient had a B. paratyphosus infection. A subsequent examination after one week showed that the kidneys were again infected. In 10 of the 11

cases the colon bacillus was found in pure culture. The eleventh case was the one just mentioned. In all the cases the pyelitis was bilateral. In none of them was a colon cystitis found; that is, in which the bladder infection alone was present. Routine leukocyte counts were made on all urines. This method gives a more accurate estimation of the amount of pus present in the urine. Further in comparing the counts it can be readily seen how the improvement is progressing.

OBSTETRICS

UNDER THE CHARGE OF

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The Prevention and Treatment of Puerperal Sepsis. — BONNEY (*British Med. Jour.*, August 21, 1920) contributes the first paper in a discussion upon the subject, before the British Medical Society. In considering the original source of the organisms which infect a puerperal patient, he differs from the view commonly held that infection is introduced from without. He holds that infection in some cases originates from intrinsic sources, although he recognizes that this is not the view which up to now has been generally held. He believes that infection from extrinsic sources caused the epidemics of puerperal sepsis which formerly decimated obstetric hospitals. These have been largely abolished by the introduction of antisepsis and where a series of cases occur in the practice of a midwife or doctor, such must be ascribed to an extrinsic source. At the present time, however, he believes that puerperal septic infection is sporadic and not epidemic. At present the average practice of obstetrics is sufficiently clean to prevent, under ordinary circumstances, infection and when patients are not brought together in institutions such infection rarely arises. The streptococcus of high virulence is a delicate organism which dies rapidly in the open air and which is easily overgrown in an incubator by other organisms even at the temperature of the body and still more readily at the temperature of a room. If the effort is made to transplant it by experiment, it is difficult to do so, and this is probably also true regarding accidental inoculation of puerperal fever. In institutions the sterilization of instruments and appliances and the use of gloves render its occurrence unlikely and infection is less apt to occur in cases conducted in the homes of patients. In spite of these facts there is no essential diminution in the occurrence of puerperal sepsis. He estimates for every one woman who dies of sepsis, four are more or less seriously ill and besides this there are a much larger number of cases of slight fever due to minor degrees of sepsis. These facts would seem to point to the conclusion that the conveyance of septic organisms from one patient to another is comparatively rare but that there is some other medium far more common

by which infection arises. He finds that from the lower bowel and
the skin about the anus, organisms capable of producing puerperal
sepsis, can constantly be isolated. The extensive study of infected
gunshot wounds during the recent war, shows that the more virulent
bacteria in these wounds came from excrement either from the feces
of the wounded person or from the feces of some other, or of some
animal in the form of manure. Among these the Bacillus coli com-
munis is that most often found. There is a streptococcus constantly
present in the bowel which may cause appendicitis, pelvic inflammation,
suppuration after operation in the abdomen, and puerperal or post-
abortional sepsis. When the uterus is examined in puerperal sepsis
the streptococcus found is not, as a rule, of this variety, but on the
other hand another variety of streptococcus can be isolated from the
bowel. In the large intestines the character of the organisms is con-
stantly changing; streptococci may constantly be discharged into the
cecum. A catarrhal patch on the mucous membrane of the colon, or
a chronically inflamed hemorrhoid may cause a most violent puerperal
sepsis. It may readily be shown that the skin about the anus and
perineum contains more bacteria than any other region of the body;
against this, however, it is sometimes stated that the anatomy of the
human body has been the same since the human race began and yet
puerperal septic infection has not always existed, and further that
when the perineum was torn these lacerations frequently became con-
taminated with feces and yet healing by first intention may take place.
While bacteria may be frequent in this region, the tissues have increased
power of resistance at this point to these germs. In the removal of
the appendix the very best results are obtained where every precau-
tion is taken to prevent infection from the stump. When the rectum
is resected in abdominal operations every care is taken to exclude
organisms in the bowel from the operation area, and penetrating
wounds of the rectum are usually followed by severe infection. When
infection occurs after Cesarean section upon an infected uterus, the
phenomena are the same which are observed when infection from
intestinal organisms has taken place. It is very difficult in conduct-
ing labor to prevent contamination of the genital tract from the rectum.
The introduction of antiseptics belonging to the aniline and chlorine
group places at our disposal means for rendering tissues about the
vagina practically sterile: a 1 per cent. solution of equal parts of
crystal violet and brilliant green in half and half alcohol and water,
may be applied to the vagina and the tissues about it may be used as
a lubricant for vaginal examinations. A few use a 2 per cent. solu-
tion of iodine but ordinarily a weak solution of lysol or bichloride of
mercury is employed. The latter he does not believe of any practical
value. When labor is conducted with the patient upon the side the
danger of infection he considers greater than when patient lies upon
the back. Regarding the method by which the organisms enter the
uterus he calls attention to experiments that show that there is a
current from below upward in the pelvic tissues and in the uterus.
It does seem possible that organisms passing through the wall of the
bowel into the abdominal cavity cause puerperal sepsis. Contrary
to the commonly held opinion, the writer contends that puerperal
sepsis is not associated with retention of gross fragments of placental

tissue in the uterus. In a great majority of cases he believes that the uterus is completely empty after labor or abortion, hence it is of little value to explore the recently emptied uterus for the organisms are in the uterine wall almost from the beginning of the infection and have now passed more deeply in or beyond it. Infection usually spreads along the ovarian veins accompanied by lymphangitis producing thickening of the broad and other pelvic ligaments which can often be detected by palpation. When chills occur large veins are usually involved, although pyosalpinx is not common after labor at term; ovarian abscess is more frequently found, active peritonitis is unusual and is generally seen around a suppurating ovary or tube, but in fatal cases passive peritoneal infection is usually present. A blood-stained fluid rich in streptococci is present in the peritoneum in these patients. Pneumonia, pleurisy and pericarditis may also develop. In the treatment of these cases flavaine or one of the antiseptics of the chlorine group, thoroughly applied in the uterine cavity may be useful. By the time symptoms have developed in most cases the organisms are in the uterine wall beyond the reach of antiseptics, hence the practice of giving an intra-uterine douche when there is considerable fever, to wash out or destroy organisms in the uterus, is useless. If tubes be introduced by the Carrel method with the hope of destroying bacteria the process is a difficult one. The writer believes that if the uterus can be thoroughly curetted so soon as the first symptoms arise, and this be followed by insertion of irrigating tubes in the Carrel-Dakin method, this treatment may prove efficient. To be successful this should be done within twelve hours of the first considerable rise of temperature. If a considerable mass of placenta be retained, this should be removed. In treating war wounds the excision of infected tissue in the wound before infection had time to develop was often successful but in the treatment of puerperal septic infection such a method would require the performance of hysterectomy. The writer has little confidence in vaccines or the intravenous injections of antitoxic serums or antiseptic injections of colloidal metals. Ligature of the ovarian veins and lymphatics accompanied by excision frequently gives good results. The writer is accustomed in dealing with sepsis after abortion when definite thickening can be felt, to remove the whole of the thickened pelvic ligament from the side of the uterus up to the highest accessible point in the line of the ovarian vessels. He has seen marked improvement follow this procedure. Prevention, however, is far more successful than the attempt at radical cure.

The Surgical Treatment of Puerperal Sepsis.—WHITEHOUSE (*British Med. Jour.*, August 21, 1920) continues the discussion of this subject before the British Medical Association. He has applied the Carrel method to 15 cases of very severe septic infection with one death. Under anesthesia the uterus is very carefully curetted with a sharp curette; should hemorrhage follow this must be controlled before the Carrel tubes are introduced and often a gauze pack is required. The application of absolute alcohol is efficient in some cases when bleeding is severe. From four to six tubes are introduced at varying heights within the uterine cavity, these should be suffi-

ciently long so that the connecting transverse glass tube may be rested upon the pubis to permit further manipulation; the tubes can be kept in position by packing the vagina lightly with strips of bismuth or plain gauze. An antiseptic ointment is thoroughly applied to the vulva or perineum to prevent excoriation. A pad of gauze and absorbent wool is placed over the vulva and the transverse glass tube attached to the bandage over the abdomen. Fresh solution is injected every two hours. As a rule the patient's temperature falls within twelve hours and the tubes are often expelled by uterine contraction. Should the tubes be expelled while the temperature is still high, they must be replaced and for this anesthesia is usually not necessary. A well-known argument against curetting was that it broke down the zone of resistance, but it has been shown that this zone or tissue acts as a nidus for the production of bacteria. A constant application of the antiseptic solution to the interior of the uterus is essential for the success of this method. The writer's experience shows that the risk of pyemia, thrombosis or parametritis is not increased by the use of a sharp curette. When these conditions developed after treatment strep-tococci had already been found in the blood. The only case of parametric abscess observed by the writer developed in a patient in whom curetting was not done. This treatment cannot be carried out by any but experienced and trained obstetricians and in such cases the risk of perforation is not great. The writer has not had success by using colargol and bichloride of mercury intravenously. A solution of flavaine 1 to 1000, in normal salt, he has employed intravenously in doses of 10 to 15 c.c. given in the median basilic vein, the same technic is employed which is used in the treatment of syphilis by salvarsan. One injection is given daily, sometimes two, night and morning. The results have been good, but sufficient experience has not accumulated to justify a positive conclusion.

Intravenous Protein Therapy in Puerperal Septicemia. — Gow (*British Med. Jour.*, August 21, 1920) contributed a paper before the British Medical Association describing his experience by this method. He uses a solution of peptone injecting intravenously from 8 to 10 c.c., this is increased 2 c.c. every other day or so until from 16 to 20 c.c. are given at one time. The injection must be administered slowly and carefully. A marked and rapid fall in blood-pressure follows, the pulse becomes more frequent and if leukocytosis has been present there develops a high degree of peripheral leukopenia, this condition lasts but a short time. The quality of the pulse is of special value and the radial pulse should be counted during the injection, if more than thirty-four beats to a quarter of a minute are noted the injection is temporarily stopped. A hypodermic of adrenalin 1 to 1000 may become necessary. With the latter injections there is slight fulness in the head, slight cough, a stabbing pain in the bottom of the back or a little nausea, sometimes a chill, after the chill improvement is the rule. This treatment the writer considers a valuable adjunct to the use of sensitized vaccines. A vaccine made from the Streptococcus pyogenes may be used subcutaneously in doses of from 1 to 5,000,000, on three successive days; intravenously, larger doses may be employed. If intravenous injections are used they should not be given after eating, but when the stomach is empty if possible.

Serums and Vaccines in the Treatment of Puerperal Sepsis. — MURRAY (*British Med. Jour.*) continues the discussion of puerperal sepsis in this paper. He believes that puerperal pyelitis is not an uncommon condition but one which is frequently overlooked. If this received adequate attention many cases of sepsis readily subside. Peritoneal infection may also accompany puerperal sepsis. In these cases serums and vaccines are of very little use and if anything can be done, surgical help is required. In making a diagnosis it must be remembered that a blood culture from which no growth is obtained does not necessarily signify a sterile blood stream. If anti-strepto-coccus serum is given, 50 c.c. diluted with an equal amount of normal salt solution may be given intravenously. This should be repeated in from twelve to twenty-four hours unless marked improvement occurs. Fresh normal horse serum may often be added to advantage. Autogenous vaccines are also of considerable value in this condition, small doses with serum give the best results. When symptoms develop during the second week with chills, autogenous vaccines obtained by puncturing the vein during a chill, are exceedingly useful. A prepara-tion of immunized serum from the blood of a relative or person having suitable blood and its injection into the patient, seem to be worthy of trial. The writer has had no experience in the inoculation in vacci-nation form of organisms devitalized but not absolutely killed. In the discussion which followed, in the Women's Hospital of Birming-ham, 889 cases of puerperal sepsis, 164 died. Various methods includ-ing the Carrel, were employed without marked success. Rectal examination in place of vaginal were recommended by some. Routh, in suspicious cases is accustomed to douche the uterine cavity imme-diately after labor with strong iodine solution. If the temperature rises on the next day under anesthesia, the uterus should be explored by the finger, pieces of placenta or membrane removed and the interior thoroughly swabbed with gauze. From 1 to 4 per cent. solution of iodine should then be applied especially over the placental site. Fixa-tion of the uterus or parametritic thickening was considered a favorable symptom. Chloride of iron in large doses is useful.

The Diastase-content of the Urine in the Toxemias of Pregnancy.— WALLAS (*British Med. Jour.*, August 21, 1920) has examined the blood of women in normal pregnancy finding the diastase content 10 to 33.3 units. The blood urea is normal and so is blood sugar. The urea concentration tests show 2 per cent. or more. The test indi-cates that normal pregnant women are in a state of unstable equilibrium as regards carbohydrate metabolism and that acetone bodies are readily produced and make their appearance in the urine. In the toxemia of pregnancy there is a large quantity of diastase in the urine. The blood analysis shows urea and sugar content normal. When vomiting of pregnancy is neurotic, the diastase in the urine is normal. In neurotic vomiting ammonia coefficient is often higher than in cases of true toxemia. When the pregnant woman has nephritis, the urine shows albumin with very low globulin. Sugar and diastase are usually below normal 10 units. The blood analysis shows the urea-content higher than normal, and marked rises occur in severe cases in which the urea content of over 0.1 gm. per cent. should be regarded as unfavorable, and uremia with fatal termination may result.

Pendulous Abdomen Complicating Rachitic Pelvis.—MICHOLOTI (*Zentralbl. f. Gynäkol.*, May 15, 1920) describes the case of a primipara, aged forty-two years, at term, who had rupture of the membranes and forty-eight hours ineffectual labor. The abdomen was very pendulous and the uterus was sharply anteflexed, the fundus over the thigh. There were deformities in the spine, both legs, and signs of rachitis in various parts of the body. The fetus was alive. The os permitted examination by two fingers only and the lower segment was found tightly drawn over the fetal head. Under anesthesia the uterus could not be raised nor could the patient assume various postures, accordingly she was delivered by section, a large vigorous child being born. Under deep anesthesia the uterus could be raised because the muscles, previously in state of marked contraction, became relaxed.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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Studies on Measles. II. Symptomatology and Pathology in Monkeys Experimentally Infected.—In a second communication, BLAKE and TRASK (*Jour. Exper. Med.*, 1921, xxxiii, 413) detailed the symptoms, course of the reaction and the histology of the lesions of the skin, labial mucous membrane and tongue which were found in the monkeys after intratracheal inoculations with nasopharyngeal secretions of human patients in the preëruptive and early eruptive stages of measles. The incubation period of the sixteen monkeys inoculated on the respiratory mucous membrane was seven days in the majority of animals but varied from six to ten days. After intravenous inoculation of whole blood, the incubation period was four days. The onset was characterized by listlessness, loss of appetite, drowsiness and diminution in the total leukocyte count. At times a sharp rise in temperature was encountered. The conjunctivæ became injected, photophobia and increased lacrimation ensued and small, discrete, hyperemic macules appeared on the labial mucous membrane, which latter tended, in two or three days, to increase in number and coalesce to form a diffuse, hyperemic enanthem on the labial and buccal mucous membranes. From one to five days after onset a red, maculopapular rash appeared on the skin, as a rule coming out first on the face and eventually spreading to the neck, arm and chest, abdomen and thighs and reaching its height in two or three days, at a time where the enanthem was fading. The exanthem in turn progressively faded and by six to ten days after onset all symptoms had disappeared. Some of the enanthematous

macules showed the minute bluish, white center as seen in Koplik spots. Occasionally a moderate diarrhea was noted in the earlier stages of the reaction. No symptoms of rhinitis and bronchitis were encountered. The skin and lesions, as shown by microscopic examination after fixation in Zenker's fluid and staining with alum hematoxylin and eosin, corresponded very closely to those described in cases of human measles by Ewing and by Mallory and Medlar. The lesions of the skin occurred both in the corium and epidermis, those in the latter being less numerous and conspicuous than in the former, where they were definite and typical. In the corium, they consisted of swelling and proliferation of the endothelial cells lining the capillaries and smaller veins, accumulation of endothelial leukocytes about the capillaries and active multiplication of these emigrated leukocytes. In addition there is a moderate exudation of serum into the pericapillary tissues, where in the earlier lesions, a very few eosinophils, polymorphonuclear leukocytes and lymphocytes might be present. No diapedesis of erythrocytes could be made out. The endothelial cells of the capillary walls appeared swollen and their cytoplasm was finely granular. Occasionally one was seen in mitosis. The emigrated endothelial leukocytes were young and active. Their nuclei were frequently lobulated and in the early cases these leukocytes were in active mitosis. In the epidermis in early cases, there were minute foci of serous exudate leading to swelling and vacuolation of the epithelial cells of the Malpighian layer. The serum sometimes accumulated under the cornified layer, producing tiny vesicles. There was a slight infiltration of these foci with endothelial leukocytes. The lesions in the labial mucous membrane were essentially the same as those occurring in the skin. Invasion of the epithelium was more marked than in the case of the epidermis. The lesions in the mucous membrane of the tongue were identical with those in the labial mucosa.

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

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Acute Respiratory Infection in Man Following Inoculations with Virulent Bacillus Influenzæ.—Cecil and Steffen (*Jour. Infect. Dis.*, 1921, xxviii, 201) state that virulent influenza bacilli, when injected into the nose and throat of healthy volunteers, may excite in them an acute respiratory disease similar in many respects to influenza but falling short of the typical clinical picture. In such cases influenza bacilli, biologically identical with those inoculated, may be recovered

from the discharges as long as symptoms persist and often for some time thereafter. Filtrates of Bacillus influenzæ cultures when similarly injected into two healthy volunteers produced neither local nor constitutional reaction. The inoculation of healthy volunteers with virulent hemolytic streptococci may in some cases induce an acute follicular tonsillitis with fever and leukocytosis. A virulent pneumococcus Type IV, on the other hand, was injected into the nose and throat of two healthy volunteers with impunity.

Botulism in Cattle.—GRAHAM and SCHWARZE (*Jour. Bacteriol.*, 1921, vi, 69) isolated an anaërobic bacillus biologically resembling Bacillus botulinus (Type B) from a corn silage. Several cattle of the herd consuming the silage developed symptoms of forage poisoning on two different occasions and four animals died. It is possible that botulinus toxin in the ensilage was primarily related to the disease in question. The silage was regarded as unsafe for cattle, and after discontinuing its use in the daily rations the animals remained healthy. Botulinus antitoxin (Type B) proved efficacious in protecting guinea-pigs against lethal doses of toxin in unfiltered broth cultures produced by the anaërobic bacillus isolated from the corn silage. Forty-three cattle were injected with botulinus antitoxin and subsequently fed on silage. The animals remained apparently healthy. One control or untreated animal did not show visible illness and the value of the antitoxin in the feeding operations is therefore not conclusive. It is worthy of record that the treatment did not injure the animals and encouragement is offered for more extensive field trials in determining the value of the antitoxin in cattle against the ill-effects of otherwise nourishing rations containing Bacillus botulinus toxin which heretofore has advisedly been discarded. The latter item is of importance considering the increased cost of producing grain and forage.

Concerning the Antiseptic Action of Some Aromatic Fumes.—MACHT and KUNKEL (*Proc. Soc. for Exp. Biol. and Med.*, 1920, xviii, 68) state that while their experiments were of a crude character the results obtained were of so uniform a nature that they are inclined to conclude that the fumes produced by the burning or destructive dry distillation of various gums, spices and other aromatic substances of a similar nature certainly tend to exert an antiseptic action on the bacteria studied. This is, of course, of interest not only from the scientific point of view, but also to the historian as offering a possible explanation for the extensive employment of incense in connection with sacrificial rites, etc.

The Distribution of the Spores of Bacillus Botulinus in Nature.—MEYER and GEIGER (*Public Health Reports*, 1921, xxxvi, 4) regard the soil as the common source of the spores of the botulinus organism and cite examples to support this view. They consider it likely that the soil may be contaminated by manure. They regard the soil infection as prevailing in certain localities. The practical point is that food should be so sterilized in canning as to obviate danger. Cooking the canned food just before using is an added safeguard, and any canned fruits or vegetables showing the least sign of spoilage should be discarded.

Studies of the Nasopharyngeal Secretions from Influenza Patients.—
OLITSKY and GATES in recent studies (*Jour. Am. Med. Assn.*, 1921,
lxxvi, 640; *Jour. Exp. Med.*, 1921, xxxiii, 373) report the cultiva-
tion, from the filtered nasopharyngeal washings from early cases of
uncomplicated epidemic influenza and from the lung tissues of experi-
mental animals, minute bodies of characteristic morphology which
are strictly anaërobic, are filtrable and withstand glycerolation for a
period of months. The effects on the blood and in the lungs of
rabbits and guinea-pigs injected with these bodies are similar to
those produced by the filtered and unfiltered nasopharyngeal secre-
tions from early cases of epidemic influenza. The authors found that
the intratracheal injection of the influenzal agent in rabbits exerts an
influence on the pulmonary structures of these animals of a nature to
encourage the invasion of the lung and the subsequent multiplication
there, with lethal outcome, of such bacteria as the pneumococcus,
streptococcus and Bacillus pfeifferi, which otherwise in the doses
employed are without marked effect. The control experiments show
that the injection of normal rabbit lung exerts no such predisposing
influence. While the experiments are perhaps not an exact reproduc-
tion of the conditions occurring in man in secondary pneumonia follow-
ing influenza they bear directly on these conditions. Concurrent infec-
tions may be regarded as of accidental nature and are not casually
related to the typical effects induced in rabbits by a material wholly
free from ordinary bacteria. The influenzal agent exerts an effect on
the pulmonary tissue which encourages the invasion of the lung and
subsequent multiplication there of ordinary bacteria, such as the pneu-
mococcus, streptococcus and Bacillus pfeifferi. A similarity is believed
to exist between the conditions under which concurrent infections arose
in the inoculated rabbits and those which seem to favor the occurrence
of concurrent infections during epidemic influenza in man. In no
instance did death occur in the rabbits as a result of the uncomplicated
effects of the influenzal agent alone. When death occurred in any of the
inoculated animals concurrent infection of the lungs by ordinary bac-
teria was present. The microörganisms most commonly met with under
these conditions were Pneumococcus Type IV and atypical Type II
streptococci and hemoglobinophilic bacilli. Other kinds were encoun-
tered less often.

**An Outbreak of Botulism at St. Anthony's Hospital, Oakland,
Calif., in October, 1920.**— GEIGER (*Public Health Reports*, 1920, xxxv,
2858) reports a series of six cases of botulism due to spoiled com-
mercial canned spinach. There were three deaths among the four
severe cases. One of the cases appears to have been saved by the
botulinus antitoxin. The epidemiological evidence was complete in
incriminating the spinach.

**Concerning Anaphylaxis Following the Administration of Diphtheria
Antitoxin.**— BRONFENBRENNER and SCHLESINGER (*Proc. Soc. for Exp.
Biol. and Med.*, 1921, xviii, 147) studied experimentally the ques-
tion of the apparent tolerance of human beings to anaphylaxis dur-
ing diphtheria intoxication. They state that sensitized guinea-pigs
receiving subcutaneously large excess of diphtheria toxin withstand the
intravenous injection of at least five lethal doses of the antigen to which

they were previously sensitized. This apparent resistance appears about twelve to fourteen hours after the administration of toxin and just about the time when the outward symptoms of intoxication begin to manifest themselves. With a view to eliciting the mechanism of this phenomenon they have made the following observations: The anti-tryptic titer of the blood of guinea-pigs injected with the toxin does not appreciably deviate from normal up to the time of death. The mechanism regulating the antitryptic titer of the blood remains unimpaired in these animals, however, since an injection of antigen to which they are sensitized is followed by a typical rise of antitrypsin. This rise of antitrypsin incidentally can be interpreted as an indication that the humoral phase of the anaphylactic response of the animals is not abolished by the previous injection of toxin. If the same dose of toxin is overneutralized with antitoxin *in vitro* before injection it does not protect the sensitized guinea-pigs from immediate death when even a single minimal lethal dose of antigen is introduced intravenously. On the contrary the same dose of toxin heated for thirty minutes at 80° C. protected guinea-pigs from anaphylactic shock just as unheated toxin did. Heating of the toxin for thirty minutes at 100° C., however, destroys this property of toxin even if a much larger amount of such toxin is injected. Since the culture medium containing toxin contains also 1 per cent. peptone, a control sensitized guinea-pig, instead of toxin, received peptone in the amount ten times that present in culture medium carrying the toxin. This guinea-pig died immediately after the intravenous injection of antigen, thus showing no protection. It seems thus that the clinical observation concerning apparent diminution of anaphylactic reactivity during diphtheria intoxication is borne out by this preliminary experiment.

Studies in the Physiology of Vitamines: Is Water-Soluble Vitamine Identical with Secretin?—COWGILL (*Proc. Soc. Exp. for Biol. and Med.*, 1921, xviii, 148) states that a similarity in the physiological effects of vitamine B and substances which promote secretion has been alleged by VOEGTLIN and MYERS (*Jour. Pharm. Exper. Therap.*, 1919, xiii, 301). The author has examined a number of solutions such as extracts of rice polish, wheat embryo, navy bean and yeast and neutralized tomato-juice, demonstrated to contain vitamine B, for their possible action on the secretory function of the pancreas and liver. The products used were tested for vitamine B content on polyneuritic pigeons and on dogs which had lost their appetite for several days after having been fed on a diet lacking this dietary essential. Vitamine B has been shown to restore appetite in such animals. The effect of the products on the flow of pancreatic juice and bile was noted in anesthetized dogs in which the pylorus was ligated to prevent secretion due to discharge of acid chyme from the stomach, and the gall-bladder bile was prevented from discharging by ligation of the cystic duct. Normal dogs and dogs fed a diet lacking vitamine B were used. It is planned to experiment upon polyneuritic dogs as well. Fresh secretin solutions prepared by the usual method were injected as a control. Except in the case of tomato-juice all of these products gave negative results. The secretin solutions, however, in comparatively small amounts always produced a characteristic and vigorous flow.

The Effect of Heat and Age Upon the Antiscorbutic Vitamine in Tomatoes.—GIVENS and McCLUGAGE (*Proc. Soc. for Exp. Biol. and Med.*, 1921, xviii, 148) conducted feeding experiments upon guinea-pigs in order to determine the effect of heat and age upon the antiscorbutic accessory in tomatoes. They found guinea-pigs protected against scurvy by daily doses of 2.5 grams of fresh raw tomatoes; by 10 grams of fresh raw tomatoes heated one hour at 100° C.; by 2 grams of dried tomatoes heated fifteen minutes at 100° C.; by 10 grams of tomatoes canned at fifteen pounds' pressure for thirty minutes; by 3 c.c. of commercial canned tomatoes three years old, and by 10 grams commercial canned tomatoes, three years old, cooked fifteen minutes at 100° C.

Immunological Distinctions of Encephalitis and Poliomyelitis.—AMOSS (*Jour. Exp. Med.*, 1921, xxxiii, 187) states that lethargic encephalitis is an epidemic disease, the main manifestations of which relate to injury inflicted upon the central nervous system and in particular the basal ganglia of the brain. Poliomyelitis is an epidemic disease, the main manifestations of which relate to injury inflicted upon the central nervous system and in particular the gray matter of the spinal cord and medulla oblongata. At the outset of the epidemic of lethargic encephalitis the two diseases tend to prevail at distinct and different seasons of the year, although recently cases of epidemic encephalitis have arisen in the midsummer months. The two maladies therefore are perhaps less distinguished by seasonal prevalence than has been supposed. They are, however, distinguished by great differences in communicability to monkeys. Epidemic poliomyelitis is readily transmitted through inoculation of the affected central nervous tissues of man to monkeys, while it may still be regarded as doubtful whether lethargic encephalitis has been communicated to monkeys in this manner. The two diseases can be distinguished through the power of the blood serum under certain circumstances to neutralize the virus of poliomyelitis. The blood serum of convalescent cases of poliomyelitis, whether in man or monkey, possesses this neutralizing power, while the blood serum of recently convalescent cases of epidemic encephalitis is devoid of it. On the basis of the distinguishing characters described it is regarded as desirable at the present time to hold epidemic poliomyelitis and epidemic encephalitis as integrally distinct affections. The latter also may be infectious, yet the main lesions of poliomyelitis are present in the spinal cord and of epidemic encephalitis in the midbrain.

ORIGINAL ARTICLES.

DIAGNOSIS AND CLINICAL MANIFESTATIONS OF CARDIO-SPASM ASSOCIATED WITH DIFFUSE DILATATION OF THE ESOPHAGUS.[1]

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I. **General Consideration.** Definition. A condition in which there occur diffuse dilatation of the esophagus with maintenance of the normal contour of the gullet and a varying degree of unusually strong and prolonged contraction or hypertrophy of the cardiac sphincter.

There may coexist hypertrophy of the muscle layers of the lower esophageal wall. The hypertrophy of the cardiac sphincter may be of but moderate extent, but when it is associated with powerful spasmodic or long-continued contraction there results transient or long-maintained, frequently complete obstruction to the passage of esophageal contents from the gullet into the stomach. Again, the hypertrophy of the cardiac sphincter may be advanced and then such hypertrophy may of itself result in functional stenosis of the cardia, whether or not there is the complication of associated spasm. In marked instances of the affection, the hypertrophy of the cardiac sphincter may resemble in degree such hypertrophy as is found at the pyloric sphincter in patients affected with the hyper-

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[1] Read at the Twenty-third Annual Session of the American Gastro-enterological Association, Atlantic City, N. J., May 3 and 4, 1920.

trophic stenosis of infancy. Cases of "cardiospasm" described in
which muscular hypertrophy of the cardiac sphincter could not be
demonstrated at autopsy or operation would seem to be errors in
diagnosis or faults in the observation of what actually constitutes
muscular hypertrophy in a dilated, enlarged, static esophagus.
There have been too few studies of the normal cardiac sphincter
to permit comparison. During the past few years many papers
have appeared purporting to describe "cardiospasm," but, in truth,
such have dealt with instances of spasm at the cardia or of transient
esophageal spasm, local or general.

NOMENCLATURE. It should be understood definitely that the
terms "spasm at the cardia" and "cardiospasm" are not synony-
mous. Only the latter form of affection includes hypertrophy of
the cardiac sphincter or the wall of the lower portion of the esophagus,
combined with general, diffuse dilatation of the esophagus. "Spasm
at the cardia" is a transient lesion of itself. It is not associated with
uniform, diffuse dilatation of the esophagus until it has been so long
existent or is of such constant maintenance as to produce esophageal
changes not of a transient nature, particularly an associated, per-
manent dilatation of the gullet.

ETIOLOGY. In cardiospasm the dilatation of the esophagus
would appear to be due to rather indefinitely understood causes.
Rosenheim has suggested, as an explanation, primary atony of the
muscular coats of the gullet. Kraus considers the condition due to
the development of persistent, long-maintained spasm of the cardia,
associated with paralysis of the circular muscles of the esophagus,
the latter occurring as a consequence of degenerative changes in
the vagi. Numerous authors, as, for example, Fleiner, Zenker and
Sievers, maintain that dilatation results from a congenital predis-
position on the part of the esophagus. Martin considers a primary
esophagitis as an important factor. In addition there have been
advanced other explanations, viz.: kinking of the esophagus at
the cardiac opening; anatomical defects associated with the esophagus
or the stomach, such as ulcer or carcinoma, and congenital or
acquired asthenia. Plummer, following Mikulicz and Meltzer, is
inclined to the opinion that, in addition to the changes occurring
at the cardiac sphincter, there exists some disturbance of the nerve-
muscle mechanism of the esophagus which may permit diffuse
dilatation of the gullet irrespective of actual stenosis due to hyper-
trophy of the cardiac sphincter. Plummer emphasizes that in
some patients there may be noted the occurrence of a habit of spasm
at the cardia, and this, without anatomical, diffuse dilatation of the
esophagus. Numerous such instances have found their way into
the literature, misnamed "cardiospasm."

In our opinion it is likely that such extra-esophageal lesions as
give rise to repeated, powerful, long-maintained contractions of the
cardia are capable of producing the muscular hypertrophy of over-

work; coincidently, this alteration in sphincter reflex-time second-
arily disturbs the normal neuromuscular coördination in the
esophagus above it. As a result, the overworked sphincter seems
to develop its own independent contraction rate, and this of a
duration beyond the normal time limits and out of the normal
rhythm of the swallowing act. In such circumstances, the stimuli
from above (formerly passing down to a cardiac sphincter, nor-
mally contracting and relaxing in appropriate time and with limited
degree) are delivered in an uncoördinated fashion and at irregular
time intervals, with little or no effect upon the systole and diastole
of the cardiac sphincter. The initial overstimulation to the cardia
would seem to be exerted by numerous anomalies. Such may be
extra-esophageal or intrinsically esophageal. These stimuli may
arise from the central nervous system, from the esophagus itself,
from the diaphragm, the intrathoracic organs, from the stomach,
duodenum, gall-bladder, appendix or other abdominal viscera. In
some patients it would seem that more than usually powerful
cardiac contractions are initiated by psychic upsets. However, it
should be emphasized that cardiospasm is by no means an affection
only of psychasthenics or of neurologically unstable individuals.
While the initial cause of spasm at the cardia may produce a more
active response in individuals who are psychically or nervously
abnormally responsive to all stimuli, it should be recognized that
in well-developed instances of cardiospasm the lesion which has
to be dealt with is an anatomical one and not a mere functional
disturbance. In these patients, in spite of the opinion to the con-
trary held by some clinicians, I believe there always exists a definite
hypertrophy of the muscular cardiac ring (such as can be shown
when skilled fluoroscopic study is made during the taking of food).
With this is always readily demonstrable (although of varying
degree) generalized dilatation of the esophagus. It is important
that these facts be recognized because upon their realization depends
the exhibition of proper methods of treatment. Patients affected
with this lesion require more accurate therapeutic procedures than
rest-cures, cessation from mental, psychic or physical overactivity,
quieting medicines, Christian Science, osteopathic hocus-pocus and
the like.

STRUCTURAL CHANGES IN THE ESOPHAGUS. The anatomical
anomalies present in cardiospasm should be emphasized, viz.:
hypertrophy of the cardiac sphincter, atypic cardiac contractures
(powerfully spasmodic or abnormally persistent) and diffuse enlarge-
ment of the esophagus without local or general gross alterations
of its contour. The effect of these anatomical changes is to cause
dysphagia, imperfect passage of foods into the stomach and, generally,
some degree of permanent esophageal retention. The quantity of
retained food varies widely in different patients and in a given
patient at various times during the study of his affection. The

esophagus may retain from less than an ounce to as much as several liters of fluid or mixed food. Upon the patient, the systemic effects are those consequent upon slow or rapid starvation. The degree of malnutrition may be so pronounced and of such acute development as to suggest malignant disease or advanced cicatricial stenosis caused by peptic, luetic, tuberculous or traumatic ulcer of the gullet.

II. **Material Studied.** During the past seven years 76 instances of cardiospasm associated with diffuse dilatation of the esophagus have come under my observation. Tabulated records of 47 of these cases are available for study.

Sex. Of the 47 cases there were 25 females and 22 males. This approximate equality of the sex ratio is rather striking in view of the prevalent opinion among practitioners that females are much more likely to be affected than are males.

Age. The average age for the series was 39.2 years; the youngest case was aged nineteen and the oldest seventy years. It is thus seen that true cardiospasm is a disease common to midadult life, the majority of instances occurring between twenty-five and thirty-five years.

Occupation. Occupation appears to play a very small part as an etiological factor, but the ailment seems to be relatively common in those individuals who are very active, physically and mentally. Temperament has been rather unduly emphasized in its relation to the initiation of cardiospasm. While it is true that some of these patients are delicately balanced psychically, yet a goodly number are of what one would call stable temperament.

Ailments previous to the onset of cardiospasm, with a few exceptions, appear to have little bearing with regard to causing the affection. It was noticed in our series that in 8 instances frequently recurring attacks of bronchitis or asthma were associated with dyspepsia and ultimately with dysphagia. These severe coughing spells might be a not unimportant factor in causing cardiac irritation and neuro-muscular fatigue of the diaphragm. There were 3 instances of gastric ulcer proved by laparotomy, but the cardiospasm was in no way influenced by the operative procedure upon the stomach. In but 7 instances did shock, fright or acute fatigue precipitate the symptoms (2 were neuroses). Excessive smoking, particularly of cigarettes, was observed in 5 cases. This might offer an interesting etiological suggestion to those who attribute cardiospasm to vagus malfunction.

Mode of Onset. In but 17 instances the affection with the associated dysphagia was acute in its inception (36 per cent.). In 30 cases (74 per cent.) the affection appeared gradually and was not infrequently punctuated by attacks of exaggerated distress.

Duration of All Symptoms. This averaged for the series 5.6 years and ranged in the individual cases from three months to twenty years. The degree of dysphagia or esophageal retention not infre-

quently bore no relation whatever to the time that symptoms had been present. Not rarely, esophageal retention of as great as 1000 c.c. arose in individuals who had been ill for less than a year (9 cases).

The duration of the presenting trouble averaged for the series 4.2 years, with a range in the individual cases of from two months to twenty years.

DYSPHAGIA is not commonly painful. Usually there is a sensation of fulness or tension beneath the sternum, a feeling of tightness or a discomfort often described as "crowding of the heart." There may be dyspnea or cough. The first swallows of food may produce the uncomfortable sensation. It is of diagnostic significance to know that liquid foods are more prone immediately to bring about distress than are solids. In this way the type of dysphagia differs strikingly from that common to various forms of anatomical stenosis (ulcer, cancer, trauma, etc.) along the course of the esophagus. There are instances, however, in which the swallowing-act at once excites sharp cramp-like pains, usually located beneath the xiphoid or along the spine, from the ninth to the twelfth dorsal vertebræ. The pain may be at first sufficiently acute to cause incapacitation and then may be followed by intermittent or continuous gripping, binding or a "sticking" type of discomfort.

In our series of patients there was *constant* dysphagia in 45 cases. There was dysphagia to *fluids only* in 21, to *solids only* in 14 and to *all foods* in 12 cases.

Dysphagia is nearly always accompanied by *vomiting* or spasmodic food regurgitation so long as esophageal muscle tone remains good. A fairly characteristic and differential feature of the vomiting is that it is usually sudden, frequently explosive and very often occurs shortly after the ingestion of food. Liquids are more liable to produce sudden, copious emesis than are solids; in fact, the ingestion of soup or fluid at the early part of a meal may bring about spasmodic emesis of such sudden and forceful nature that the individual is compelled to rush hastily from the table to avoid accidents. This prompt vomiting of liquids is frequently aggravated by the fact that, but rarely, in general practice is the lesion of cardiospasm recognized. To the average physician a dysphagia presumably indicates a liquid diet, and he accordingly orders such. Solids or partly solid foods are generally well borne, particularly in the early stages of cardiospasm. The constant attempt to take liquids is followed promptly by vomiting, lack of nourishment and malnutrition, and doubtless added damage to the weakened esophageal wall. The patient frequently finds this out himself and refuses to follow his physician's instructions when liquid diet has been urged. In advanced cardiospasm practically all the food taken may be vomited within an hour or two following its ingestion, or if dilatation of the esophagus is pronounced, morning retention-vomiting is common and constant.

The vomitus consists commonly of material whose appearance resembles that of food as eaten. It is alkaline in reaction, usually contains much mucus, rarely lactic acid or blood and may have a high, bacterial content. At times vomiting is "delayed" and only when a large meal is taken at night is emesis produced. At that time, food eaten at breakfast or even the night before may be vomited unchanged. Sometimes the vomitus is copious at night and prevents proper rest and sleep. A few cases of even marked cardiospasm do not manifest actual vomiting, but there is constant belching, bad taste in the mouth, eructations of food and, frequently, copious regurgitation of ill-tasting fluid, food or mucus. Sometimes nausea is pronounced and there occurs remarkable increase in the secretion of saliva. This may indicate central irritation of the salivary glands. Even when some food passes the cardia the regurgitation of frothy, thick, tenacious mucoid material is apt to be annoying, particularly when such occurs toward evening. Consequent upon the vomiting appear evidences of lack of fluid in the tissues, constipation, diminution of urine output, headaches, dizziness and anemia.

In this series of cardiospasm patients, 31 vomited daily (frequently many times during the day). In 22 cases retention-vomiting was observed. Frequently, food (fruit skins, pieces of tomato, meat, lettuce, milk-clots, etc.) was retained in the lower part of the dilated esophagus for as long as a week. In 17 of our patients the vomiting was projectile. In such cases it was a common experience that patients began vomiting as soon as food was swallowed. There was vomiting of blood in 14 cases. This hematemesis, seemingly, bore relationship to dilated or varicose veins in the lower esophagus, although one could not always be certain that ulceration had not taken place in some portion of the esophageal wall where varicosities were not present. In one case the hematemesis appeared to be definitely "vicarious," inasmuch as it occurred on two occasions just before menstruation.

Regurgitation, without actual vomiting, was especially annoying in fifteen patients. This regurgitation was generally uncontrollable and the regurgitant food-mass was frequently very copious in quantity and of a foul, sickening odor. There were patients in which periods of intermittent regurgitation preceded cycles of exhausting vomiting.

Miscellaneous Clinical Symptoms. Weight loss was experienced by all our patients. It averaged, for the series, 28.2 pounds. In individual cases it ranged from ten to as much as eighty-two pounds. The appetite was stated as being lessened or as being poor in 44; 9.5 per cent. patients experienced pronounced anorexia. Normal bowel movements occurred in 47 per cent. In the remaining cases there was obstinate constipation. This constipation seemed to be due largely to insufficient quantities of food or fluid passing the cardia into the stomach and bowel.

III. Special Diagnostic Maneuvers.—In true cardiospasm, an unguided *stomach tube* passed into the esophagus usually excites free food regurgitation about the tube and the spasmodic emesis of much food and liquid through the tube. The tube may be generally passed freely as far as the normal cardia, but there it meets an elastic resistance. This resistance is occasioned either by the tube's impinging on the distended esophageal wall and depressing its lower sixth into a sac-like pouch, or by pronounced and persistent contracture of the cardiac sphincter. In only but a few not well-established instances of the affection does the cardia lie in a line direct from the pharynx and thus allow an unguided stomach tube to be passed to it, and then, upon exertion of pressure, admit of the cardia's being forced, the tube being carried into the stomach. If the tube is guided upon a silk cord to the cardia (as suggested by Mixter, of Boston, seventeen years ago and emphasized by Henry Plummer clinically), it can be carried direct to the cardia, and, provided the tube is a stiff one, can, with the exertion of a moderate degree of force, be passed into the stomach. The "giving way" of the tight, elastic cardia can be felt as the stomach tube passes the hypertrophied or permanently contracted sphincter.

If not guided to the cardiac orifice by a cord, a *bougie* passed into the esophagus traverses the lumen farther than the average distance of the cardia from the incisor teeth. Usually the olive may be passed considerably farther than normally and the unsuspecting manipulator may fancy that he is well beyond the cardia and that the olive lies in the stomach, it having passed the cardiac sphincter without the operator's knowledge. This mistake occurs as a result of the bougie's passing downward and to the right in the folds of the sac-like, pendulous lower esophagus. In such circumstances forcible pressure is dangerous: in our own experience one case of esophageal rupture occurred after the patient had been elsewhere "dilated by olives" for six months and the cardia was later divulsively dilated. At the autopsy it was found that at the lowest point of the dilated esophageal sac, and about two inches from the cardia, there were denudation of the mucous membrane, marked thinning of the wall of the esophagus and peri-esophageal inflammatory thickening. The area of the esophageal attenuation was about the size of a large olive, somewhat depressed, and lay in a straight line from the pharynx to the lowest part of the esophageal sac, but was out of the straight line from pharynx to cardia. In this patient, a divulsing dilator, guided upon a silk cord, passed freely into the cardiac orifice, but the increase in intra-esophageal pressure during dilatation was sufficient to cause rupture of the esophagus at the spot where repeated bouginage had weakened the walls.

Even in long-established, obstinate cardiospasm it is generally possible for a silk cord guide to pass from the esophagus into the stomach, but at times the cord may be held in the esophagus several

days and may pass freely only when spasmodic contracture of the
cardia has been minimized by the free use of atropin or of belladonna.
However, unless the dilated esophagus be washed clean of retention
contents silk cords may lie for weeks without passing from the
gullet to the stomach.

An olive bougie of large size passes readily to the cardia upon a
taut string; moderate pressure "forces" the sphincter and permits
the bougie's passing into the stomach. Withdrawal of the bougie
may be accompanied by a readily recognizable, elastic resistance.
It is usually the experience that the bougie exerts little influence
with respect to permanent enlargement of the cardiac opening or
permanent relief of the dysphagia. It is quite as sensible to expect
permanent dilatation of a cardia in cardiospasm by bouginage as it is
to expect that a spasm of the anal sphincter will be relieved by fre-
quent digital examinations. If the patient be examined at different
times of the day or upon different days a variation in the amount
of resistance at the cardia may be determined, but it is characteristic
of the affection that at every examination there is resistance present.

The roentgen examination is of great aid in diagnosis but the
evidence which it supplies is not infallible. Fluoroscopic observa-
tion and plate studies must be carefully interpreted in the light of
clinical history, physical examination and examination of the
esophagus by guided instruments.

Fluoroscopically when the patient swallows the opaque meal it will
be seen that usually a small amount of the mixture immediately passes
through the cardia into the stomach. In moderately well-established
instances of the affection the cardia then closes quickly, with or with-
out several, easily recognized, squirty contractions and continued in-
gestion of the opaque mixture results only in filling out the esophagus;
practically nothing passes into the stomach. It can then be shown
that the esophagus is uniformly dilated, that its wall is regular, that
dilatation occurs along anatomical lines and that the cardiac end of
the esophagus down to the hypertrophied sphincter presents no gross
irregularities of contour. In shape such a dilated esophagus re-
sembles, characteristically, a large lily-of-the-valley leaf, or is
roughly pear-shaped. The dilatation may be enormous and extend
so markedly throughout the entire length of the esophagus as to
produce pressure upon the heart, the aorta or the trachea. The
obstruction at the cardia may be absolute and may be maintained
for hours or days until emesis or lavage results in an apparently
reflex partial relaxation of the hypertrophied cardiac sphincter.
Again, in moderately advanced cases esophageal retention may persist
from a half to two hours and then the opaque meal passes in a jerky,
spasmodic fashion, slowly through to the stomach. Even in these
cases, however, one rarely finds that the esophagus completely
empties itself within from two to six hours. In the early, incom-
pletely established cases esophageal retention may be but a tran-

sient one.   Fluoroscopically it is possible to observe alternate, spasmodic contractions and relaxations of the cardiac sphincter,
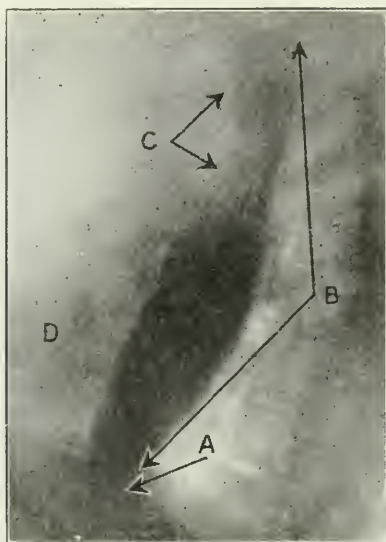
Fig. 1.—Lateral roentgenogram, showing bismuth meal retention in case of "cardiospasm." *A*, closed cardia, without malformation; *B*, diffusely dilated esophagus, normal contour maintained; *C*, anterior depression caused by aortic arch; *D*, shadow of heart.   (Roentgenogram by Joseph Johnson.)
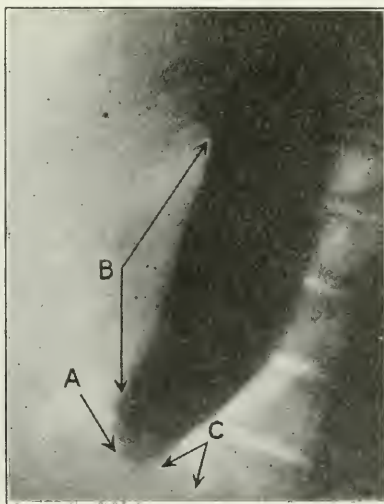
Fig. 2.—Lateral roentgenogram of bismuth meal retention in case of "cardiospasm." *A*, cardia, in contraction, without malformation, but with stenosis complete; *B*, diffusely dilated esophagus of rather marked degree, but contour normal; *C*, diaphragm line.   (Roentgenogram by Joseph Johnson.)

associated with the intermittent passage of small amounts of the opaque meal from the lower esophagus into the stomach. The esophagus will thus empty in from a few minutes to an hour. Mild
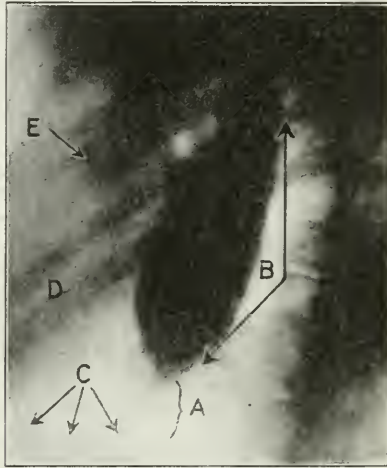
Fig. 3.—Lateral roentgenogram, showing retention of bismuth meal in a case of ring cancer involving the lower one-sixth of the esophagus, with complete stenosis. *A*, zone of cancerous involvement; *B*, dilated esophagus, proximal to cancer; *C*, diaphragm line; *D*, heart shadow; *E*, aortic arch. The lower portion of the esophagus has a contour resembling normal, and plate might readily be mistaken for one of "cardiospasm" if care is not exercised in locating the cardiac end of the esophagus in relation to the position of the diaphragm line and the gas shadow in the stomach. (Roentgenogram by Joseph Johnson.)
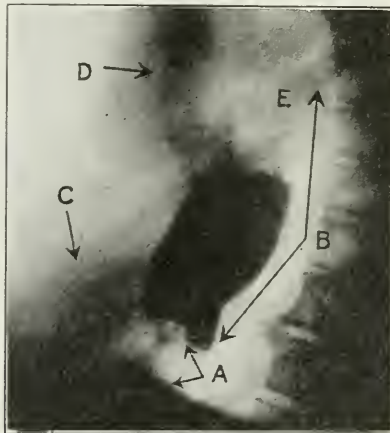
Fig. 4.—Lateral roentgenogram of retained bismuth meal in the esophagus, the cardiac end of which is stenosed by cancer of the nodular, cauliflower type. *A*, zone of cancer, irregularly canalized; *B*, dilated and partly filled esophagus; *C*, heart shadow; *D*, shadow of aortic arch; *E*, dilated, but not filled, esophagus, the dilatation extending above the tracheal bifurcation. (Roentgenogram by Joseph Johnson.)

SMITHIES: MANIFESTATIONS OF CARDIOSPASM instances of the affection are not generally associated with great sac-like esophageal dilatation.

In rare instances, fluoroscopy and roentgen plates fail to make the diagnosis, the roentgen findings seem characteristic for cardiospasm, but in the dilatation of the esophageal sac, ulceration, diffuse scirrhus carcinoma or lues may remain masked even until they have advanced sufficiently to produce extensive stricture or to cause death from metastasis. Not rarely, fluoroscopy clearly demonstrates torsion of the terminal esophagus with or without rather sharp angulation or displacement, usually to the left of the midline of the thorax.

In several instances of well-developed cardiospasm with diffuse dilatation of the esophagus I have noted unusual "doming" of the diaphragm. In these patients the diaphragm movements were atypic: degree of depression was unequal on the two sides, rates of downward movements were not equal on the two sides, *i. e.*, the diaphragm depressions were not synchronous and, locally, in the region of the hiatus there seemed to be a sort of "piling up" of diaphragm (local hypertrophy). Observation of the above phenomena has suggested to me that at times the fault primary in initiating cardiospasm lies in the muscle or serous layers of the diaphragm (inflammatory processes in the serous coverings of the esophagus, lungs, heart, diaphragm or a local myositis of the diaphragm itself), with resultant disturbance in the neuromuscular mechanism of the diaphragm, and, subsequently, of adjacent viscera with their correlated nerve supply.

It should be scarcely necessary to mention that fluoroscopy, conducted with the patient only in the anteroposterior position, can at its best give but incomplete information. Unless the patient is examined also laterally so that the course of and the anomalies in the esophagus are susceptible of complete exposure much of interest and of clinical usefulness will be lost. It is advisable to examine fluoroscopically during the swallowing act with the diaphragm depressed by deep inspiration, the breath being held and the diaphragm fixed during swallowing. The patient may be turned rapidly from the anteroposterior to the lateral ("quartering") position, and by this maneuver one may secure views of the lowest portion of the esophagus, of the sphincter, the contour, peristaltic activity and the position and shape of the diaphragm. For careful scrutiny of the terminal esophagus and the cardiac sphincter the fluoroscope's diaphragm should be closed to such point as will permit minute study of the esophageal contour inch by inch. Such procedure is necessary to detect or rule out ulcers, scirrhus carcinoma, etc., and to properly study the sphincter and its action. The successive employment of thin fluid and thick mush-like, opaque suspensions gives useful information relative to sphincter action, esophageal peristalsis, stasis, contour and degree of dilatation.

The patient should be examined at least on two successive days. The second study should be carried on after the exhibition of antispasmodic medicines to physiological tolerance. Only in this way can one determine the true condition existing at the cardia and the actual size of the esophagus. If this procedure were routinely followed, many "literature" cardiospasms would disappear—for many such are only "spasm at the cardia."

Roentgenograms should be made with the patient in the semilateral or "quartering" position as well as the anteroposterior. When plates are made with the patient in the semilateral position the entire esophageal contour may be delimited. In order to bring out the cardia and the lower portion of the esophagus it is advisable to have the patient drink as much of the opaque meal as he is able to, then clasp his hands high above his head and take a deep breath. The inspiration depresses the diaphragm and generally enables accurate visualization of the lower esophagus. The best roentgenograms are made with the patient standing with his left side next to the plate. When extensive esophageal dilatation is present, anteroposterior roentgenograms also should be made in order to determine the lateral limit of the esophageal sac and to demonstrate the degree of encroachment of the enlarged esophagus upon the heart, aorta and lungs. Such plates frequently demonstrate that the lowest limit of the dilated esophagus lies several inches below the level of the cardiac sphincter. This shows, vividly, how futile is the effort to pass bougies or tubes into the stomach without their being guided from pharynx to cardia by a swallowed silk thread. In patients in whom the cardiospasm is not far advanced, anteroposterior roentgenograms even may fail to indicate that the condition is present. In such circumstances the esophageal shadow is overlapped and hidden by the shadows of the heart, the aorta and the spine. Series of plates should be made before and after the administration of antispasmodic medicines (belladonna, benzylbenzoate, etc.). Such permit of interesting comparative studies and furnish valuable records of anatomical changes as the functions of the esophagus are restored by treatment.

Esophagoscopy. Inasmuch as in certain cases of cardiospasm the initiating fault lies in an esophageal lesion it would appear a proper procedure to explore by sight the entire esophageal mucosa from pharynx to cardia, that is, provided that one who is familiar with esophagoscopes and who knows the significance of what he sees is able to do the work. Much esophagoscopic work as done is worthless because the operator knows little of the appearance of the normal esophagus. In well-established instances of cardiospasm an actual view of the interior of an enormously dilated gullet and an anomalously acting sphincter is truly worth while if for no other reason than to satisfy one's curiosity. When some doubt exists respecting whether or no a cardiospasm is complicated by

scirrhus cancer, peptic ulcer, foreign body, gumma or extra-esophageal ailment, certainly, esophagoscopy is a justifiable procedure to clear up doubtful points in diagnosis even though it is annoying to the subject. A thoroughly cleansed esophagus, carefully administered intratracheal anesthesia and a good esophagoscope, such as the particularly ingenious Sussmann, greatly facilitate the procedure. When powerful contractures of the cardiac sphincter persistently recur, following most expert divulsive treatment, it would seem necessary always to perform esophagoscopy with the object of searching for and treating locally irritative mucosal lesions.

Prognosis. If the affection is properly managed, there is clinical and functional recovery in about 70 per cent. of even well-established instances of cardiospasm. Improvement occurs in 20 per cent. About 10 per cent. of the patients are not permanently benefited by any form of treatment at the most expert hands. The lesion seemingly resists all forms of therapy. In this class are patients extremely emaciated, instances of irritable esophagus where proper treatment cannot be carried out and very likely cases in which there is a congenital defect, or, as Plummer has emphasized, the persistence of a "habit of spasm." For these unfortunates, gastrostomy may be required to save or prolong life. If with cardiospasm there are such associated lesions as gastric ulcer or malignancy, gall-stones, appendix infection or ulceration or inflammation of the cardia or esophagus itself prognosis is seriously limited unless these lesions are amenable to appropriate medical or surgical treatment. Even after the restoration of the cardiac sphincter action, the esophagus may remain much dilated and permit food retention. However, it is surprising how dilatation of the esophagus may persist, and yet such is unaccompanied by troublesome dysphagia, provided the cardiac orifice is patent and the sphincter acts normally.

THE SPLEEN AND DIGESTION:

Study I.—The Spleen and Gastric Secretion.[1]

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The exact rôle of the spleen in digestion is not known. Numerous hypotheses have been advanced and much experimental work has

been done with contradictory results. Various conclusions arrived at have been:

1. The spleen is an endocrine organ with the function of influencing, in an obscure manner, some portion of the digestive apparatus by way of the blood stream or of activating one or more of the digestive enzymes by an internal secretion.

2. The spleen is a storehouse for the temporary reception of the products of protein digestion, much as the liver is for glycogen.

3. The spleen is merely a diverticulum of the portal system to receive the excess blood rushed to the splanchnic area during the digestive period and to act as an abdominal heart for supplying this blood to the stomach and other abdominal organs as needed.

The idea that the spleen must be of some significance in this regard has been prompted by the gland's intimate anatomic connections with the portal system, marked congestion and swelling observed during the digestive period, proportionately excessive atrophy during starvation and inanition, and by references by many experimental investigators, as well as many clinicians, to a state of hunger and voracious appetite after splenectomy.

The present study approaches the rôle of the spleen in digestion from the viewpoint of its relationship to the stomach, especially the effect of splenectomy on gastric secretion. All previous work on this aspect of the problem is foreign, and most of it given in publications not readily accessible; for this reason I am reviewing the literature in some detail.

Review of the Literature.

The spleen and stomach from the earliest times have been supposed to possess some close interrelationship. Stukeley in his most excellent dissertation on the spleen, published in 1723, definitely assigned to this organ as its second major function the duty of being an adjunct to gastric digestion, and admirably reviewed the tenets of previous authors. He approached the subject thus:

"But let us proceed to what I imagine one of Nature's primary purposes in the formation of this curious organ (spleen): That is, for an assistant of the great business of digestion or concoction of the aliment in the stomach; the first and highest importance of all others, for preservation and support of the individuum, the mainspring of the wonderful machine, rightly by Plato from Hippocrates called the primum mobile, alluding to the imagined first agent of the rotation of the huge celestial orbs. This is no new opinion but rather an old one, well started by the Ancients, but neglected by their successors, especially the Moderns. The divine Hippocrates, to whom scarce any truth was unknown, thought the office of the spleen was to help concoction, by drawing off the superfluous humidity from the stomach, whom Aristotle copies after. Others

supposed this assistance was performed by furnishing the stomach with its acid ferment, whence it excited hunger, stirring up the vis appetitrix. Aristotle made it, being a sanguineous organ, the concocter of the crudities that otherwise would offend the stomach. Some have thought the spleen's fancied melancholy useful to the stomach, by its acid, austere, styptic and astringent quality which contracted and strengthened the fibers thereof and enabled it the better to concoct and retain the aliment whilst digested and expel it afterward, as Galen says in the lion, leopard, bear, wolf, pard, etc.; and the Arabians fell pretty much into this notion, for they always thought it strengthened the stomach."

Stukeley was of the opinion that any common observer in anatomy naturally would be tempted to conclude that the spleen has some relation to the stomach when he found the one placed directly under the other, and with the intimate intercommunications by means of their common veins, arteries, nerves and connections that exist invariably in all creatures.

He was led to answer the questions why the principal bloodvessels of the stomach arise from the splenic artery in its direct route to the spleen and why vessels go immediately from the spleen to the stomach, as ordinarily do the vasa brevia, by formulating the theory that the spleen acts as a "heart to the stomach," that it is a magazine, diverticulum or necessary receptacle of the blood for the use of the stomach, ready, as occasions and emergencies require, to send plentifully of its supply into the gastric vessels, later when the blood is not needed there to receive it back again. This is of great service in a part that must so suddenly alter its dimensions, extend its bulk and contract itself in its great business of digestion as does the stomach.

However, this was not the only office wherein the spleen was subservient to the stomach, for (in common with Aristotle, Anonymous Graecus and Galen, who affirmed that the spleen assists in warming the stomach, and with the great Vesalius, who said *Lienem suo calore innato ac frequentibus quae illum intertexunt arteriis ventriculi concoctionem favere*) he advanced the opinion that the spleen by its proximity, great vascularity and timely congestion furnishes heat to the stomach. He asked " — does not nature proclaim its (spleen's) great eminence by its situation, being placed on the left side of the stomach where digestion is chiefly performed, and closing it up, as it were, like the door of a furnace, that it may have an equable warmth quite around so that the spleen alone in this single requisite of heat is apposed to all the rest of the bowels put together that encompass the stomach." He further adduced as proof of this assumption the "notorious" and "terrible" effects produced by eating ice and snow liquors in hot countries! Is this not in accord with the fancy entertained by the ancients "that creatures which drink much have larger spleens, whose business it is to warm the stomach against such a quantity of cold fluid"?

Stukeley's position can then be summarized happily in his conclusion "that if the stomach in the opinion of Q. Serenus deserves to be called *Rex totius corporis*, the spleen deserves to be called its viceroy."

The "immortal" Haller in reviewing hypotheses concerning a *secretio lienalis* mentioned the idea that had been advanced that the spleen elaborated an acid juice which, sent to the stomach through the vasa brevia, aided in digestion. He himself denied such a function. (*Lien non est acidus. Vasa brevia nihil a liene in ventriculum sani hominis vehere; et lange minus aliquid in arteriam remittunt.*)

Oken maintained that the gastric juice and chyme undergo a process of oxidation, and that the spleen in this respect holds a somewhat similar relation to the stomach to that which exists between the air and the lungs or the placenta and the fetus.

Finally, Burdach denied any relationship between the two organs because *aucune des hypothéses dans lesquelles on fait concourer ce viscere a la digestion, ne repose sur la moindre preuve.*

However, Baccelli has been credited generally with being father to the hypothesis of a distinct functional relationship between the spleen and the stomach, for he was the first scientifically to base his deductions on original clinical observations and anatomic studies. In 1868, at Rome, he gave his theory to the world in a discussion on malaria. In his extensive experience he had noted that during the prodromal and defervescent periods of paludism the patient frequently showed a voracious appetite; conversely, during a period of malarial cachexia a special dyspepsia intervened, resistant to all therapy. In the first instance only a soft evanescent splenic tumor was present, in the latter a lasting hyperplasia of more or less of the organ modified only by the amount of hyperemia. This dyspepsia was most marked toward albuminoid food material, and he found in the vomitus of the patients unchanged meat fibers, even after two or three days, indicative of impaired peptic activity.

Baccelli then carried on anatomic studies in which he demonstrated a definite gastrosplenic circulation. He found that the veins of the vasa brevia form five or six rectilinear canals, with intercommunicating smaller vessels, from the spleen to the cul-de-sac of the stomach, which are devoid of valves, so that the blood can pass in either direction; it may go at one moment to the stomach, at another to the spleen or remain in the interposed vascular system. These vascular connections he designated as *una piccola circolazione addominale*. The largest number of gastric glands are situated in the cul-de-sac at the area supplied or drained by these veins. The manner in which the blood streams of the vena coronaria sinistra and vena splenica are confluent he summed up as follows: *Difatti, dalla milza a capillari dello stomaco pe'vasi brevi- da'capillari dello stomaco alla vena coronaria sinistra- dallo stomaco pe'vasi brevi alla*

milza- dai capillari della milza alla vena splenica- dalla vena splenica e dalla coronaria sinistra al confluente. On the basis of this anatomic relationship Baccelli formulated the following hypothesis: Considering the large amount of carbon entering into the molecular composition of pepsin it seems likely that the spleen is deputized to furnish this material, in the form of carbonic acid, to the peptic glands for their proper function. The stomach dilated by the blood given it compresses the splenic vein against the vertebral column, obstructing thus the venous splenic outflow and causing still greater splenic engorgement, with the forcing of blood through the veins of the vasa brevia to the cul-de-sac of the stomach. Thus the *ragione d'essere* of the little venous abdominal circulation was explained, in which the carbonic acid was used in perfect antagonism to its rôle in the little thoracic circulation where it is eliminated.

Baccelli's anatomic research was repeated by Roseo in 1870 and confirmed in all particulars. Nothing further was done on the subject until 1901. In this year Tarulli and Pascucci, working in Luciani's laboratory, carried out a set of experiments on dogs in which they determined the digestive activity of the gastric juice before and after splenectomy. Gastric fistulas were made according to Claude Bernard's method. A preparatory meal, consisting of 500 gm. each of cooked meat and broth and 200 gm. of bread, was fed with the idea of exhausting the pepsin accumulated in the gastric glands. Sixteen hours later the mucous membrane of the stomach was washed out with isotonic salt solution and a secretory meal consisting of 100 gm. of cartilage and tendons given. The resulting secretion of gastric juice was collected and tested for peptic activity by placing 1 gm. cubes of coagulated egg white in 10 c.c. samples of pure juice for twenty-four hours at 39° C., the amount of digestion being determined by the loss in weight of the cubes after this period. The results obtained led Tarulli and Pascucci to the conclusion that the digestive power of the gastric juice is constantly decreased to a greater or less extent after splenectomy. Furthermore, they found that by feeding an infusion of congested spleen, that is, spleen excised five or six hours after a meal, the digestive power was increased again for from one to three days. From these results they assumed that during gastric digestion the spleen elaborates a pepsinogenic substance which is carried to the gastric glands through the blood stream and induces an increased amount of pepsin secretion.

Gallenga, in 1902, performed some digestive experiments on a patient splenectomized for a large blood cyst of the spleen. The spleen was large and hard and showed hyperplasia of the connective trabeculæ, with reduction of the tissue propria. The patient recovered from the operation, maintained a good appetite and had no subjective digestive disturbance. A month later Gallenga started his experiments with three test-meals: the Ewald (vegetable), Leube (vegetable and meat) and Ferrannini (meat). No determina-

tions were made preceding splenectomy. His results he summed up as follows:

1. Insufficient and delayed digestion of albuminoids *in vitro* by the filtrate of the gastric contents.

2. Protracted and augmented chloride secretion, especially of combined hydrochloric acid.

3. Abnormal amount of fermentation.

4. Retarded motility of the stomach.

5. Increase in activity of the pepsin of the gastric filtrate in artificial digestion by the addition of an extract of lamb's spleen.

6. Subjective phenomena on the part of the individual showing a certain gastric hyperexcitability with the paste of Ferrannini and a discrete diminution in the body weight.

From these data Gallenga concluded that:

1. The spleen most probably has an active part in the gastric digestion of albuminoids, as is proved to occur in pancreatic digestion.

2. This action of the spleen must depend on an internal secretion, pepsinogenic, which exerts an influence on the quantity of the juice poured out and the activity of the pepsin.

3. In persons splenectomized the peptonization of albuminoids in the stomach and *in vitro* with extracted gastric juice is markedly delayed and diminished, although in a certain degree compensated for by an augmented chloride secretion.

In 1903 Silvestri performed some animal experiments which led him to the conclusion that the digestive power and the quantity of the gastric juice are constantly augmented after splenectomy. He found that in the dog and cat immediately after removal of the spleen gastro-intestinal phenomena intervene, and that though appetite is conserved, weight is lost. When the animals were sacrificed after four days an enormous dilatation of the stomach was observed which Silvestri thought could not be blamed to operative trauma. To three dogs before and after splenectomy he administered a secretory meal of soup and meal and injected apomorphin after four, six and eight hours respectively in order to secure vomiting. He observed that the material vomited was in less quantity and in a more advanced state of digestion in the splenectomized dog. Later he fed animals a mixture of bread with 200 gm. of meat divided into small cubes, and after five hours opened the stomachs; they contained brownish liquid with pieces of meat more abundant and larger in the control animals than in the splenectomized animals. In artificial digestion with the non-filtrated gastric contents he found less peptic activity in splenectomized dogs, but on the contrary more activity after filtration of their chyme. This, he considered, proved that digestion was more advanced in those splenectomized. Again, using *in vitro* experiments with filtrated gastric contents, he found a hyperpepsia following removal of the spleen. Splenec-

tomized dogs had the capacity of transforming enormous quantities of albuminoids in their stomachs.

In a later communication he stated that:

1. An internal secretion of the spleen with trypsinogenic or pepsinogenic function cannot be demonstrated.

2. The spleen plays a mechanical part in digestion and can be considered as a regulator of the circulation of the abdominal digestive organs.

3. The infusions of spleen in the height of digestion most probably exert influence on pancreatic extracts and the gastric mucosa by virtue of their leukocyte content, since these cells, as has been shown by other workers, contain a ferment, kinase, with digestive powers.

Silvestri reported the case of a woman of thirty with syphilis who had a large spleen and was splenectomized. Four months later she aborted a two months' fetus, after which Silvestri took up the study of the patient's gastric motility and chemistry. He found the gastric motility intact while the digestive power was superior to normal.

Likewise Tini, in 1909, found an augmentation in the gastric secretion and peptic activity, concluding that there is an antagonism between the pancreas and the stomach in the mode of action exercised on them by the spleen, splenectomy decreasing the trypsin function of the pancreas and augmenting the pepsin activity of the stomach.

Betti, in 1909, reported observations on a dog with a gastric fistula. He used Mett's method of determining peptic activity and also introduced 10 gm. meat cubes into the stomach. These cubes lost from 2.8 gm. to 3 gm. in weight before splenectomy and only 0.6 gm. to 0.4 gm. after splenectomy. The dog became markedly voracious. The author explained the objection that splenectomized animals live and digest well by citing the fact that animals can also live without a stomach. His deductions were therefore (1) in splenectomized animals the digestive power is notably diminished and (2) the spleen intervenes in gastric digestion by sending a substance that can be considered, as much from its genesis as its action, analogous to the enterokinase of Pawlow, and with all probability it serves to activate the zymogen into active ferment. This would easily explain the observations of Baccelli that the spleen in malaria, sclerotic and inelastic from the process of chronic splenitis, receives much less blood than a spleen normal and elastic; as a result there is a notable diminution in kinase.

Gross, in 1910, reported the case of a young man who was splenectomized ten hours after rupture of the spleen due to a hoof-kick in the abdomen. After recovery he attended a reception at which he overate and was seized with abdominal cramps. This suggested to Gross the advisability of investigating the patient's digestive juices. The amount of trypsin in the duodenal contents and stools was normal. The peptic activity of the gastric juice was determined

after an Ewald meal by the method of pepsin determination introduced by Gross and now known by his name (precipitation of faintly alkaline solutions of casein by means of acetic acid; no precipitation on complete digestion). He found, four weeks after splenectomy, a marked decrease in the pepsin strength, which gradually rose almost to normal within three months and was completely normal at the end of seven months. At the same time he carried on studies of the blood and noted a relative lymphocytosis which disappeared gradually in ratio as the strength of the pepsin rose. From this he suggested an interrelation between the lymphocytosis and the decrease of peptic activity.

Trampedach, in 1911, carried on a careful and exhaustive series of researches:

In the first investigation he sought to simulate the method of Gross as nearly as possible; a dog was given a test breakfast, which was removed by the stomach-tube. Chyme was obtained which was not acid, a finding which the experimenters, in view of the newer observations on the distribution of the acidity of the stomach in layers, did not consider wonderful. Later a Pawlow cannula was inserted into the dog, the chyme obtained after a test breakfast and an analysis for its pepsin content made. The determinations were carried out with Mett's tubes filled with wether serum instead of egg albumen.

In the second investigation Trampedach attempted to avoid the incomplete emptying of the stomach, which might have happened in the first investigation. To this end a special cannula, 2 cm. in diameter, was inserted into the duodenum. By the introduction of rubber balloons, barriers were put up and removed at will in order to have all the experiments exactly alike. As test-meals, 100 gm. portions of sterilized flesh and 25 gm. portions of dried ground white bread were used. The chyme obtained was tested (1) for its content of dissolved nitrogen in the filtrate, and by this means the degree of digestion in the stomach determined; (2) it was put with equal parts of tenth normal hydrochloric acid and let stand to digest for twenty-four hours, the amount of peptic activity then being ascertained by the determination of the dissolved nitrogen in the filtrate; and (3) it was investigated for proteolytic power by means of Mett's tubes.

In the third investigation pieces of mucous membrane were cut from different places of a dog's stomach and the spleen extirpated at the same time. The infusions from the pieces of mucous membrane obtained were tested for pepsin activity after the method of Mett. When the animal had completely recovered from the interference it was killed and similar pieces of mucous membrane from corresponding parts of the stomach were tested for their pepsin content.

In the fourth investigation the spleens were extirpated in a number

of rats. After the animals had recovered from the operations a splenectomized rat and a control rat were killed, and the infusion of each stomach tested for its peptic power.

From these experiments Trampedach arrived at the conclusion that extirpation of the spleen has no diminishing influence on the digestive power of the stomach. He found no relation between the post-splenectomy lymphocytosis and the secretion of pepsin.

Rusca, in 1912, reported a case of splenomegalia malarica with torsion of the splenic pedicle and anemia. Splenectomy was performed; the anemia improved and ten days later gastric researches on the patient were made. By percussion and roentgenologically the stomach was found to be ptotic and the emptying time four hours. Ewald, Boas and Leube test-meals were used. An increase of free hydrochloric acid was found but not invariably, and a constant and marked diminution in the content of pepsin, more striking with the method of Gross than with that of Mett. After Leube's meal a diminution in the power of fragmentation and disintegration of meat fiber was quite in evidence microscopically. Gastric motor function was good.

Rusca produced cirrhosis of the spleen in a dog by injecting the pneumobacillus of Friedländer and found diminished peptic activity thereafter. He surmised that the sclerosis thus caused interfered with the gastrosplenic circulation described by Baccelli and so hindered the afflux of the hypothetical activating ferment to the stomach.

In two cases of leukemia and two of malaria Rusca determined the size of the spleen, the leukocyte count, the relative lymphocytosis, the gastric acidity, the gastric activity of digestion of meat fibers and the trypsin content of the feces, but he could reach no conclusions from his results as to the rôle of the spleen in digestion. One patient with leukemia showed a marked reduction of pepsin, whereas in the others the gastric digestion was normal. All, however, had hyperchlorhydria.

Rusca also studied in 1912 the gastric function in six dogs before and after splenectomy, using an Ewald test-meal of 50 gm. bread and 250 c.c. water, and extracting it with the stomach-tube three-quarters of an hour after ingestion. He found a slight diminution in pepsin after splenectomy and slight unimportant variations in the amount of total acids. He obtained evidence neither of digestion of starch nor of lipolytic activity. There was no free hydrochloric acid. The dogs had voracious appetites and gained weight. The diminution in peptic power he thought to be compensated for by the augmentation of appetite and the greater amount of aliment taken.

Rusca likewise observed that in a dog with a gastric fistula following splenectomy peptic activity decreased somewhat after meals of milk, meat and oil. In experiments on a bitch which had been

splenectomized about three months previously he found a marked
persisting voracity and could not corroborate Gross's findings that
the pepsin power returned to normal after several months.

He considered the question of the influence of the spleen on diges-
tion not yet settled. In just what manner the spleen acts he thought
it not possible to say; probably it has a purely vascular influence,
forming a sort of receptacle for the blood which accumulates there
in its ample lacunæ coincidently with the congestion of all the
abdominal organs during digestion. The spleen then contracts and
sends the blood through the peculiar gastrosplenic system to the
peptic cells, offering there in greater quantity the necessary pabulum
for the elaboration of pepsin.

Soler and Madero made an experimental communication in 1912
with regard to this subject. They used dogs with Pawlow stomach
pouches. At first they had great difficulty in keeping the dogs
alive; the animals lost 40 per cent. of their initial weight and died
within from one to one and one-half months. After diets of milk
and of meat an immediate and marked drop was found in the peptic
power of the gastric secretion following removal of the spleen, while
coincident and parallel with this the erythrocyte count diminished.
Pepsin was measured by Mett's tubes, amylolytic ferment (?) by
titration with Fehling's solution (after clearing with lead subacetate
the sugar solution acted on), lipase by allowing 2 c.c. of juice to
stand ten hours at 38° C. with 1 c.c. of olive oil, dissolving this then
with 50 c.c. of alcohol and titrating with sodium hydroxide the
amount of fatty acids developed. They noted a diminution of lipase
after splenectomy, and concluded that there is a like diminution
of gastric amylase if such exists. More lipase was secreted after a
meal of milk than after one of meat. By computing the peptic
activity in digestive units (obtained by multiplying the amount
of secretion by the quantity of pepsin) they found a greater drop in
the amount of pepsin after splenectomy than when this was meas-
ured directly by the number of millimeters of Mett's tubes digested.
With both milk and meat secretory meals the digestive curve before
splenectomy rose to the highest points the first and second hour
and dropped fairly acutely to end in seven hours. After splenectomy
the fall in the digestive curve was more gradual and did not reach
normal for from nine to twelve hours. This they considered was
because the digestive units were fewer and thus the juice would
have to act longer to accomplish a given amount of digestion.
Soler and Madero concluded: "We think, therefore, in view of
the proof as we have offered it, that the spleen is an organ which
evidently assists physiologically in the elaboration of the gastric
ferments."

|In 1915 Soler and Madero published a paper reviewing their
former work and discussing it and their methods in detail. Further-
more, they gave the results of a series of injections with splenic

products, "hormonal," and decoctions and macerations of dog's
spleen. Invariably they obtained an increase in peptic activity
after such injections. Some of these experiments were performed
on a dog splenectomized three years previously. This influence of
splenic extract they determined was not due to the solution used for
decocting and macerating spleens, for injected alone in greater
amounts it had no effects. Next they studied the influence of the
serum of the splenic vein as compared with that of the splenic
artery and found it much superior in stimulating effect. They
considered this distinctive action due to elements in the spleen,
most probably to the leukocytes which exist in this organ in such
enormous quantity. Later they used extracts of lymph glands, of
the spleen, leukocytes and washed erythrocytes (which probably
contained a large amount of leukocytic material) both of the dog
and of the horse, with similar results. The mesenteric lymph
glands alone gave negative findings in contrast to those mentioned,
their excitosecretory function on the stomach being nil. They
found after the injection of splenic products that the erythrocytes
increased as much as the leukocytes.

In *resume*, Soler and Madero concluded that (1) splenectomy
diminishes the digestive power of the stomach; (2) the injection of
macerations and decoctions of the spleen whether obtained from
the same or different species increases the digestive power of the
stomach; (3) the splenectomized animals diminish in weight to reach
a stationary level, but require double the amount of nutriment for
sustenance; (4) the injection of splenic products provokes a frank
augmentation of weight in the dogs splenectomized, but has little
or no influence on those not splenectomized; and (5) the blood for-
mula shows that in splenectomy the erythrocytes follow a curve
parallel with that of the fermentative power, being inverse to that
of the leukocytes, while following the injection of macerated mate-
rial (splenic infusion) the augmentation of both occurs conjointly.

Experimental Methods.

In the present experimental study healthy female dogs weighing
on the average about 10 kg. were used. Accessory stomachs or
fundic sacs with blood and nerve supply intact and communicating
with the outside were made according to a slightly modified Pawlow
technic. Fifteen animals were prepared, on three of which only were
complete data obtained before and after splenectomy. Most of the
others succumbed to distemper, then epidemic in the laboratory, a
few to the primary operation.

The dogs were placed in pillories and the juice collected by insert-
ing into the pouches large fenestrated rubber tubes with wide funnel-
shaped cuffs which were held snugly against the abdominal wall by
an appropriate harness. The loss of juice in collection was negligible.

However, digestion of the skin about the openings of the miniature stomachs could not be prevented entirely although it was obviated as much as possible by the use of divers ointments, beds of sand or shavings, continuous drainage by leaving the tube in place at all times and so forth.

The animals were deprived of food on the evening previous to the experiment and of water one hour before the giving of the secretory meal, which consisted of raw meat cut into small cubes. The diet at other times was bread and milk. In some instances the amount of continuous gastric secretion was determined by collecting the juice for one hour previous to feeding. In all cases the dogs lost some weight after each operative procedure, but, on the whole, their state of nutrition remained good with the exception of those which developed distemper and of Dog. E.

The gastric juice was collected for six hours after feeding, the amount measured, the free and total acidity ascertained by titrating 1 c.c. of clear juice diluted with 25 c.c. of distilled water, with dimethylamidoazobenzol and phenolphthalein as indicators, and the pepsin activity determined by Mett's method. Fortieth normal sodium hydroxide was used for the titration, the acidity found being expressed in percentages of hydrochloric acid; and 1 c.c. of juice diluted with 5 c.c. of tenth normal hydrochloric acid placed with Mett's tubes (egg albumen coagulated just below boiling) at 39° C. for twenty-four hours for the digestive strength, the result being expressed directly in the number of millimeters of albumen digested (average of four readings). When a norm was established for the gastric secretion in each instance the spleen was removed under ether anesthesia preceded by an injection of one-fourth grain morphin and one one-hundred and fiftieth grain atropin. Determinations were again made on the gastric secretion as before, and at the conclusion of each experiment a necropsy was performed to rule out the presence of unremoved or accessory splenic tissue.

Experimental Data.

The protocols of experimental data are as follows:

PROTOCOL 1.—DOG D: NORMAL WITHOUT SPLENECTOMY. PAWLOW POUCH MADE APRIL 11, 1917. SECRETORY MEAL, 100 GM. MEAT.

Date, 1917.	Amount of juice for six hours. c.c.	Free acid.	Combined acid.	Total acidity.	Pepsin (Mett's tubes), mm.
April 16	18.2	0.09	0.11	0.20	3.70
17	24.6	0.24	0.09	0.33	3.05
18	9.7	0.08	0.08	0.16	3.05
19	15.8	0.09	0.09	0.18	3.05
20	14.3	0.04	0.08	0.12	4.30
Averages	16.5	0.11	0.09	0.20	3.43

Dog D remained in good condition until April 21 when symptoms of distemper appeared. The dog died from distemper April 28.

PROTOCOL 2.—DOG F: NORMAL WITHOUT SPLENECTOMY. PAWLOW POUCH MADE APRIL 19, 1917. SECRETORY MEAL, 150 GM. MEAT.

Date, 1917.	Amount of juice for six hours. c.c.	Free acid.	Combined acid.	Total acidity.	Pepsin (Mett's tubes), mm.
April 23	14.0	0.09	0.16	0.25	2.75
24	49.0	0.00	0.20	0.20	2.70
25	56.0	0.09	0.17	0.26	1.50
26	43.3	0.07	0.20	0.27	2.90
27	43.9	0.00	0.20	0.20	3.85
28	42.6	0.00	0.16	0.16	2.30
29	34.3	0.00	0.20	0.20	5.00
30	32.2	0.00	0.14	0.14	3.05
May 14	19.6	0.00	0.07	0.07	2.00
16	28.0	0.00	0.18	0.18	4.60
Average	37.3	0.25	0.168	0.193	3.065

Dog F remained in good condition until May 1 when it developed a mild distemper and lost weight markedly; it recovered May 13, and two more determinations were made. A marked inanition developed, however, and because of this and the extreme variability of the normal determinations the experiment was abandoned.

PROTOCOL 3.—DOG L: PAWLOW POUCH MADE JUNE 10 AND SPLENECTOMY PERFORMED AUGUST 1, 1917. SECRETORY MEAL, 150 GM. MEAT.

BEFORE SPLENECTOMY.

Date, 1917.	Amount of juice for six hours. c.c.	Free acid.	Combined acid.	Total acidity.	Pepsin (Mett's tubes), mm.
June 30	12.0	0.17	0.09	0.26	3.25
July 2	14.0	0.17	0.10	0.27	4.00
3	21.0	0.16	0.10	0.26	3.875
4	17.0	0.18	0.09	0.27	3.25
7	14.0	0.16	0.10	0.26	3.5
8	16.0	0.21	0.07	0.28	3.375
10	14.6	0.12	0.10	0.22	3.68
11	10.0	0.05	0.14	0.19	3.375
12	27.0	0.19	0.15	0.34	1.50
24	24.0	0.21	0.11	0.32	2.625
26	30.0	0.15	0.26	0.41	2.625
28	39.0	0.18	0.07	0.25	1.80

AFTER SPLENECTOMY.

Aug. 4	26.7	0.32	0.07	0.39	2.20
5	12.0	0.20	0.07	0.27	3.50
6	12.0	0.23	0.09	0.32	3.50
7	18.0	0.16	0.10	0.26	3.80
8	40.0	0.21	0.11	0.32	3.70
9	15.0	0.08	0.16	0.24	3.25
10	20.0	0.36	0.10	0.46	3.00
11	18.4	0.15	0.08	0.23	3.85
12	16.0	0.10	0.07	0.17	2.68

AVERAGE BEFORE SPLENECTOMY.

19.9	0.16	0.12	0.28	3.05

AVERAGE AFTER SPLENECTOMY.

14.9	0.20	0.095	0.295	3.25

Dog L remained in good condition throughout the experiment and at its conclusion was killed by etherization. No accessory splenic tissue was found at necropsy.

PROTOCOL 4. — DOG M: PAWLOW POUCH MADE JUNE 17. SPLE-
NECTOMY PERFORMED JULY 31, 1917. SECRETORY MEAL,
150 GM. MEAT.

BEFORE SPLENECTOMY.

Date, 1917.	Amount of juice for six hours. c.c.	Free acid.	Combined acid.	Total acidity.	Pepsin (Mett's tubes), mm.
July 4	15.0	0.34	0.09	0.43	4.0
6	18.0	0.29	0.10	0.39	4.1
7	19.0	0.15	0.16	0.31	4.5
8	20.0	0.21	0.13	0.34	2.6
9	19.7	0.14	0.17	0.31	2.04
10	24.0	0.17	0.21	0.38	3.16
11	34.0	0.35	0.10	0.45	3.75
12	25.0	0.10	0.13	0.33	3.00
24	15.0	0.15	0.29	0.44	3.50
26	18.0	0.13	0.26	0.39	3.00
28	30.4	0.23	0.16	0.39	3.85
29	20.0	0.36	0.11	0.47	2.875
30	25.0	0.27	0.11	0.38	2.69

AFTER SPLENECTOMY.

Aug. 4	14.4	0.16	0.15	0.31	2.40
5	13.0	0.20	0.15	0.35	3.50
6	16.0	0.21	0.11	0.32	3.60
7	23.0	0.25	0.16	0.41	3.60
8	19.0	0.23	0.15	0.38	3.44
9	30.0	0.29	0.12	0.41	3.50
10	17.0	0.15	0.22	0.37	4.00
11	19.2	0.13	0.11	0.24	2.90
12	17.0	0.14	0.15	0.29	3.30

AVERAGE BEFORE SPLENECTOMY.

	21.8	0.22	0.16	0.38	3.31

AVERAGE AFTER SPLENECTOMY.

	18.7	0.20	0.15	0.35	3.31

Dog M remained in good condition throughout the experiment and at its con-
clusion was killed by etherization. No accessory splenic tissue was found at necropsy.

TABLE 1. — DOG L: HOURLY DETERMINATIONS BEFORE AND AFTER
SPLENECTOMY.

BEFORE SPLENECTOMY.

Date. July 9, 1917.	Pepsin (Mett's tubes), mm.	Amount of juice, c.c.	Free acid.	Combined acid.	Total acidity.
First hour	5.00	4.20	0.11	0.09	0.20
Second hour	4.75	3.80	0.20	0.06	0.26
Third hour	3.75	3.20	0.18	0.07	0.25
Fourth hour	3.00	3.00	0.18	0.05	0.23
Fifth hour	2.90	2.00	0.12	0.04	0.16
Sixth hour	2.50	2.20	0.07	0.21	0.26

AFTER SPLENECTOMY.

August 2, 1917.

First hour	3.25	3.20	0.14	0.06	0.20
Second hour	2.50	3.60	0.13	0.07	0.20
Third hour	2.25	2.00	0.10	0.07	0.17
Fourth hour	2.25	2.60	0.06	0.08	0.14
Fifth hour	2.31	2.40	0.09	0.06	0.15
Sixth hour	3.44	2.20	0.06	0.07	0.13

PROTOCOL 5.—DOG E: HEIDENHAIN POUCH MADE APRIL 13. SPLENECTOMY PERFORMED APRIL 26, 1917, AT 9 P.M. SECRETORY MEAL, 100 GM. MEAT.

Date	Hour preceding feeding	Amount collected each hour.						Amount of mucus.	Pure juice.	Total amount collected	Free acid.	Combined acid.	Total acidity.	Pepsin (Mett's tubes).
		First.	Second.	Third.	Fourth.	Fifth.	Sixth.							
1917.					Before Splenectomy.				C.c.	C.c.				
		C.c.	C.c.	C.c.	C.c.	C.c.	C.c.	C.c.						
April 18	2.8	11.4	11.0	12.0	14.8	9.4	7.2	3.8	62.0	65.8	0.32	0.10	0.42	2.00
19	.6	6.2	5.0	7.6	8.4	11.0	9.2	1.8	45.6	47.4	0.36	0.07	0.43	2.10
20	.6	6.8	7.2	10.6	9.2	6.5	3.7	...	...	45.4	0.34	0.09	0.43	1.88
21	3.5	9.8	5.2	10.6	12.7	9.6	5.1	2.4	50.6	53.0	0.32	0.10	0.42	2.10
22	1.8	11.2	15.2	13.0	7.0	4.4	3.2	0.8	52.3	54.0	0.41	0.06	0.47	1.92
23	1.2	9.0	17.8	20.8	11.3	13.7	12.0	1.6	83.1	84.7	0.41	0.06	0.47	1.95
24	2.4	11.2	7.0	5.4	8.0	7.6	7.0	0.8	45.4	46.2	0.40	0.05	0.45	2.14
25	1.0	5.9	5.6	5.4	7.4	6.8	6.5	0.8	36.2	37.0	0.37	0.08	0.45	1.83
26	1.2	10.2	13.6	17.6	13.6	12.8	9.4	0.6	76.6	77.2	0.46	0.04	0.50	1.81
Average before Splenectomy.	2.08	9.1	9.7	11.6	10.3	9.1	7.0	1.6	56.6	57.0	0.38	0.07	0.45	1.97
					After Splenectomy.									
April 27	.7	7.0	4.0	7.0	3.8	2.8	2.5	1.4	25.7	27.1	0.36	0.09	0.45	1.56
28	0.7	8.0	9.4	8.7	5.2	5.0	5.4	3.0	38.7	41.7	0.40	0.05	0.45	1.50
29	0.8	10.2	6.8	6.4	7.8	5.6	6.6	0.6	42.8	43.4	0.43	0.04	0.47	1.74
30	3.4	15.2	22.0	21.6	14.2	11.2	12.0	0.8	95.4	96.2	0.46	0.04	0.50	1.87
May 1	2.8	6.2	11.6	12.8	6.2	3.8	2.6	2.2	41.6	43.8	0.34	0.08	0.42	2.10
2	1.6	10.0	10.2	8.0	9.2	6.8	4.0	2.4	45.8	48.0	0.33	0.09	0.42	2.00
3	2.4	11.8	9.4	12.8	12.6	6.6	5.6	2.2	56.6	58.8	0.39	0.07	0.46	2.00
4	...	5.6	7.2	7.3	7.6	7.2	6.2	2.4	38.7	41.1	0.33	0.05	0.38	2.00
5	...	5.2	5.2	6.8	6.2	6.0	4.8	1.4	32.8	34.2	0.30	0.60	0.36	1.85
Average after Splenectomy; first two days omitted.	2.5	9.2	10.3	10.8	9.2	7.0	6.0	1.5	50.5	52.2	0.37	0.06	0.43	1.94

Dog E began losing weight immediately after the operation and lost steadily and progressively until its death, May 9. No other abnormal findings, save the development of bloody stools the last forty-eight hours of life, were noted. At necropsy the isthmus connecting the pouch to the main stomach was very small, making it probable that the vagus fibers to the pouch were partially, if not totally, severed at the time of the first operation. There was no accessory splenic tissue. No cause for death could be found.

TABLE 2.—DOG M: HOURLY DETERMINATIONS BEFORE AND AFTER SPLENECTOMY.

BEFORE SPLENECTOMY.

	Pepsin (Mett's tubes).			Amount of juice.			Free acid.			Combined acid.			Total acidity.		
	July 9, 1917.	July 28, 1917.	Average.	July 9, 1917.	July 28, 1917.	Average.	July 9, 1917.	July 28, 1917.	Average.	July 9, 1917.	July 28, 1917.	Average.	July 9, 1917.	July 28, 1917.	Average.
	Mm.	Mm.	Mm.	C.c.	C.c.	C.c.									
First hour	2.80	4.30	3.55	3.0	9.0	6.1	0.17	0.22	0.195	0.17	0.14	0.155	0.34	0.36	0.35
Second hour	1.50	3.60	2.55	3.3	6.8	5.05	0.17	0.30	0.235	0.21	0.16	0.185	0.38	0.46	0.42
Third hour	1.87	3.50	2.685	2.6	4.0	3.3	0.14	0.26	0.20	0.17	0.15	0.16	0.31	0.41	0.36
Fourth hour	1.70	3.50	2.60	3.6	4.0	3.8	0.16	0.25	0.205	0.20	0.16	0.18	0.36	0.41	0.385
Fifth hour	2.56	4.00	3.28	3.2	3.4	3.3	0.15	0.19	0.17	0.18	0.17	0.175	0.33	0.36	0.345
Sixth hour	2.61	3.80	3.205	2.4	3.0	2.7	0.16	0.09	0.125	0.18	0.19	0.185	0.34	0.28	0.31

AFTER SPLENECTOMY.

	Pepsin (Mett's tubes).			Amount of juice.			Free acid.			Combined acid.			Total acidity.		
	Aug. 11, 1917.	Aug. 12, 1917.	Average.	Aug. 11, 1917.	Aug. 12, 1917.	Average.	Aug. 11, 1917.	Aug. 12, 1917.	Average.	Aug. 11, 1917.	Aug. 12, 1917.	Average.	Aug. 11, 1917.	Aug. 12, 1917.	Average.
First hour	4.00	4.75	4.375	2.2	3.6	2.9	0.00	0.08	0.04	0.12	0.17	0.145	0.12	0.25	0.185
Second hour	4.35	3.19	3.77	3.0	3.6	3.3	0.04	0.20	0.12	0.21	0.15	0.18	0.25	0.35	0.30
Third hour	3.55	2.75	3.15	4.2	2.2	3.2	0.11	0.16	0.135	0.16	0.16	0.16	0.27	0.32	0.295
Fourth hour	2.34	2.60	2.47	3.0	2.8	2.9	0.12	0.14	0.13	0.17	0.12	0.145	0.29	0.26	0.275
Fifth hour	2.65	2.44	2.545	3.8	2.6	3.2	0.09	0.15	0.12	0.20	0.11	0.155	0.29	0.26	0.275
Sixth hour	3.27	3.60	3.435	3.0	2.2	2.6	0.07	0.11	0.09	0.21	0.16	0.185	0.28	0.27	0.275

TABLE 3.—DOG E: HOURLY DETERMINATIONS BEFORE AND AFTER SPLENECTOMY.

BEFORE SPLENECTOMY.

	Pepsin (Mett's tubes).			Free acid.			Combined acid.			Total acidity.		
	Mar. 24, 1917.	Mar. 25, 1917.	Average.	Mar. 24, 1917.	Mar. 25, 1917.	Average.	Mar. 24, 1917.	Mar. 25, 1917.	Average.	Mar. 24, 1917.	Mar. 25, 1917.	Average.
	Mm.	Mm.	Mm.									
First hour	1.80	2.70	2.25	0.40	0.32	0.36	0.06	0.04	0.05	0.46	0.36	0.41
Second hour	1.35	2.05	1.70	0.44	0.36	0.40	0.04	0.04	0.04	0.48	0.40	0.44
Third hour	1.65	1.70	1.695	0.39	0.36	0.375	0.05	0.04	0.044	0.44	0.40	0.42
Fourth hour	2.00	1.70	1.85	0.39	0.39	0.39	0.05	0.05	0.05	0.44	0.44	0.44
Fifth hour	1.75	1.40	1.575	0.41	0.38	0.405	0.05	0.06	0.055	0.46	0.44	0.45
Sixth hour	1.65	1.40	1.525	0.39	0.38	0.385	0.06	0.07	0.65	0.45	0.45	0.45

AFTER SPLENECTOMY.

	Pepsin (Mett's tubes).			Free acid.			Combined acid.			Total acidity.		
	Mar. 28, 1917.	Mar. 30, 1917.	Average.	Mar. 28, 1917.	Mar. 30, 1917.	Average.	Mar. 28, 1917.	Mar. 30, 1917.	Average.	Mar. 28, 1917.	Mar. 30, 1917.	Average.
First hour	2.80	2.00	2.40	0.43	0.39	0.41	0.04	0.08	0.06	0.47	0.47	0.47
Second hour	1.90	1.30	1.60	0.48	0.41	0.445	0.04	0.07	0.055	0.52	0.48	0.50
Third hour	1.45	1.50	1.475	0.48	0.40	0.44	0.04	0.07	0.055	0.52	0.47	0.495
Fourth hour	1.95	1.45	1.70	0.46	0.38	0.42	0.05	0.07	3.06	0.51	0.45	0.48
Fifth hour	1.75	1.15	1.45	0.46	0.34	0.40	0.04	0.09	0.065	0.50	0.43	0.465
Sixth hour	1.40	1.60	1.50	0.44	0.34	0.39	0.05	0.06	0.055	0.49	0.40	0.0445

The peptic strengths and acidities in Protocol 5 corresponding to those of the four days in Table 3 were obtained by multiplying; for example, each hourly strength of pepsin by the amount of juice collected the corresponding hour, these added, and the total divided by the total amount of juice collected that day.

REVIEW OF EXPERIMENTAL DATA.

Our experimental data show that splenectomy had apparently little influence on gastric secretion.

Protocols 1 and 2 illustrate the normal findings of gastric secretion under the conditions of this study and serve as controls for the splenectomized animals of Protocols 3 and 4. From the first four protocols it is seen that normally an amount of pepsin is secreted sufficient to digest approximately 3 mm. of egg albumen (Mett's tubes) in twenty-four hours. Ordinarily the peptic activity as illustrated in Protocols 2, 3 and 4 is quite constant and fluctuates little from day to day; the inconstancy shown in Protocol 2 is exceptional and the most marked that we have observed. The daily variation, however, in the proteolytic power of the juice in the cases of Dog L and Dog M was less marked after splenectomy. It is doubtful whether any significance can be attached to this.

In Protocol 4 the total acidity is about that generally cited as normal, whereas Protocols 1, 2 and 3 show a subnormal acidity, approximately 0.2 per cent. The total acidity in each instance is likewise fairly consistent in amount, but not so consistent as the pepsin. On the other hand the amounts of free and combined acid fluctuate widely, in such manner, however, as to be mutually complementary. Hence changes in the relative proportions of these acidities after extirpation of the spleen mean little. It is interesting to note that Dog F showed the presence of free acid on a few occasions only.

In the quantity of secretion obtained in six hours the important determining factors are the size of the Pawlow pouch and the amount of the secretory meal. In the experiments under discussion about 25 c.c. for each 150 gm. of meat given were secreted by the miniature stomach. This is rather a low rate, but the pouch in each instance was small. The daily variation in the quantity of juice was quite marked, depending probably to a large extent on psychic and other extrinsic factors influencing the stomach through its secretory and motor nerves. Because of this variability slight changes following any experimental procedure cannot be given the weight otherwise to be accredited them.

In Protocols 3 and 4 the only noteworthy result following splenectomy was a diminution in the quantity of secretion, 25 per cent. decrease in Dog. L and 14 per cent. in Dog M (Fig. 1). This might possibly have been due to the interference with, and resulting decrease of, the gastric blood supply consequent on the operation, especially the injury to the gastrosplenic circulation through the vasa brevia. The determinations in each case were made too soon after the removal of the spleen for the post-splenectomy anemia to play a causative role.

The data given in Protocol 5 are considered separately, for, as was

found at necropsy, we were dealing with an accessory stomach of the Heidenhain type rather than of that of Pawlow as we thought. This lack of nervous control over the pouch gave noteworthy differences from the normal secretory findings: (1) With a secretory meal of only 100 gm. of meat, the amount of juice obtained in six hours, 50 c.c., was twice that of the other dogs with a meal of 150 gm.; (2) the daily fluctuation in amount of juice was less; (3) the free acidity was persistently and consistently high, approximately 0.4 per cent.; and (4) the strength of pepsin was low (2 mm.) but quite constant. This daily non-variability of the quantity of juice secreted, of the acidities, and of the proteolytic power would be expected from severance of the pouch from extrinsic influences through the nervous system. Since no cause for death could be
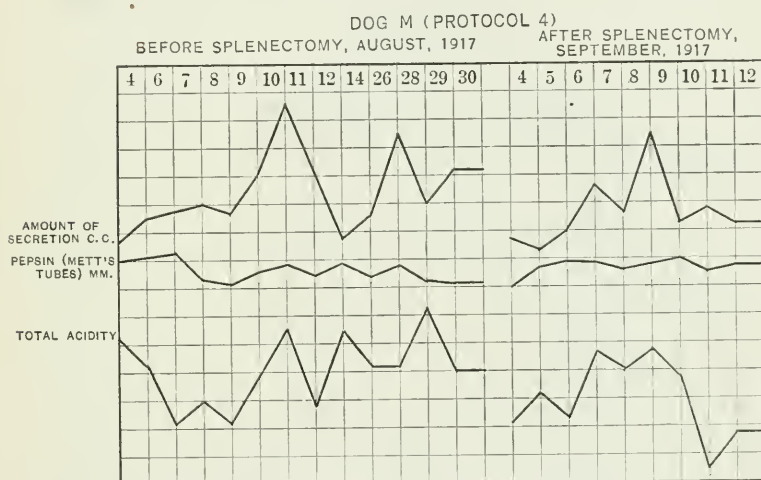
FIG. 1

found in this dog the idea suggests itself that possibly the loss of large quantities of juice from daily secretory meals, especially the loss of such great quantities of acid as occurred in this case, may have set up metabolic and acid-base-equilibrium disturbances sufficient to cause death.

Dog E of this experiment was splenectomized at 9 in the evening after it had had a secretory meal the same day, and was given a similar feeding the next morning, with the express purpose of seeing the immediate effect of splenectomy. After operation the pepsin strength was reduced, gradually rising to regain its normal about the third or fourth day. However, it seems logical to attribute this fall in proteolytic activity to the effect of the operation— anesthetic with following nausea and decrease in appetite, shock resulting from the operative trauma with the reaction on all the

body processes, and the effect of the atropin, given just before the operation, in checking gastric secretion. Hence it seems justifiable to omit from the general averages in this protocol the first two days after splenectomy, allowing this amount of time for recovery from the operation.

This experiment likewise shows no marked change in gastric secretion following splenectomy, though it is again noted that there is a decrease (8.5 per cent.) in the amount of juice obtained.

Tables 1, 2 and 3, and a portion of Protocol 5, give hourly determinations of gastric juice before and after splenectomy (Fig. 2). The average continuous secretion of juice from the pouch with the animal fasting was about 2 c.c. each hour in Dog E and much less than this in the other animals (figures not given). The amount of

DOG M (TABLE 2)
HOURLY DETERMINATIONS
AVERAGES
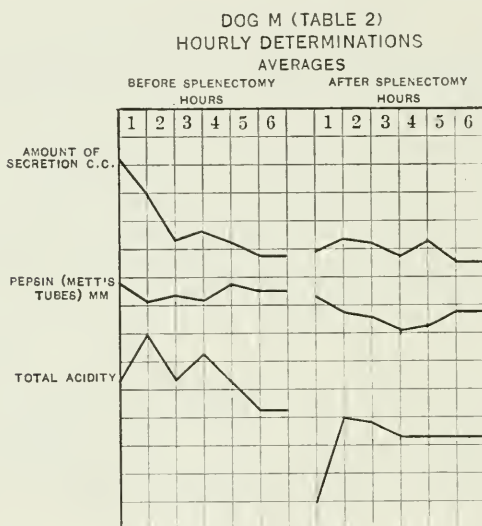
Fig. 2

juice secreted each hour varied through wide limits. With the Heidenhain pouch it rose gradually to reach a maximum the third hour and then diminished; with the Pawlow pouch the maximum occurred at any of the first three hours, most frequently at the first.

The pepsin content in nearly all instances was greatest the first hour, then dropped to show frequently a later secondary slight rise. The free acid and total acidity, it will be noted, reached a maximum from the second to the·third hour only to fall again, whereas the combined acid remained about constant. These results (save·the amount of juice secreted each hour in Dog E, which corresponds more to the normal of an intact pouch on a milk diet) coincide with those given by Pawlow as the normal hourly variation in gastric secretion in dogs on a meat diet.

Our protocols show that after splenectomy there is no noteworthy change in the hourly variations of gastric secretion after a secretory meal.

DISCUSSION.

As is true of almost every field of research on the spleen it is apparent that the experimental results of different investigators with regard to the relation of this gland to gastric secretion are widely different. Just where the reasons lie for this it is difficult to determine.

The methods used in the investigations of some of the workers are possibly open to criticism. It is well recognized that collection of gastric juice for analysis from a gastric fistula is not so satisfactory as from the Pawlow stomach, since the former admits of contamination with saliva and duodenal contents, and the secretory meal is not separated from the juice tested; in fact, almost any results can be obtained with a gastric fistula. Cubes of coagulated albumin for pepsin determination offer less accuracy than the Mett method, though the latter is not ideal; the surface of albumin exposed to the action of the pepsin is more variable and less easily controlled and the handling and weighing of the cubes fraught with possibilities of error. The data obtained clinically on splenectomized persons are of inconclusive value irrespective of results, since there is always present some disease process rendering splenectomy advisable which may enter into consideration, and, further, the unreliability of determinations of gastric secretions obtained through stomach tubes is notorious. Likewise in animals analyses of stomach contents obtained after a test-meal by means of the tube or by vomiting induced by apomorphin are to be questioned. Furthermore, some of the experiments were made without comparative control determinations before splenectomy, for example those of Gallenga and Gross, and the clinical researches of Silvestri and Rusca. In other instances insufficient experimental data were offered on which to base conclusions, for example Betti, who gave a few results obtained from only one dog.

The most recent researches, those of Soler and Madero, were carried on practically under the same experimental conditions as the present study, yet with greatly different results. In their papers they make no reference to preceding work and are alone in their maintenance of the theory that the spleen assists in the physiologic elaboration of several gastric ferments, pepsin, gastric lipase and gastric amylase (?) Their results with injections of splenic products, leukocytes, lymph glands and so forth are interesting and find support, so far as splenic extracts are concerned, in the observations of Tarulli and Pascucci.

The work of Trampedach is the most thorough, painstaking and exhaustive that has been done. His investigation like the present

study, does not demonstrate any change in gastric secretion following splenectomy.

These findings are further corroborated by the general experience of clinicians that splenectomy in man has no obvious effect on gastric digestion. However, since pepsin normally is furnished in excess of the amount absolutely needed a slight diminution following removal of the spleen need not necessarily cause gastric symptoms (for example the absence of complaint in many cases of achylia), and hence clinical observations in themselves mean but little.

It does not follow that although the spleen has no pepsinogenic function it may not have some other relation to the stomach. Only further researches can elucidate this point. It seems likely, however, that at least the gastrosplenic circulation through the vasa brevia is of some significance, whether merely mechanically cannot be said. The hematemeses of the splenomegalies, especially those of splenic anemia, have been explained on the basis of gastric varices and obstruction to the gastrosplenic circulation, and from a clinical standpoint suggest at least a pathologic splenic-gastric interrelationship.

From a critical review of the literature and my experiments I am led to believe that the spleen does not exert any influence on gastric secretion except possibly in a circulatory manner suggested by finding a slight diminution in the amount of secretion following splenectomy.

SUMMARY.

The spleen and the stomach from the earliest times have been supposed to possess some close interrelationship. Baccelli, in 1868, demonstrated a gastrosplenic circulation through the vasa brevia, and first put forward the theory that the spleen plays a role in the elaboration of pepsin. Subsequent studies of this question have been made on dogs by testing gastric secretion before and after splenectomy. This has been done by the use of gastric fistulas and Pawlow pouches and by the removal of secretory meals through the stomach-tube. Similar studies on humans have been made by gastric analyses after splenectomy for various reasons. The results of these experiments have been contradictory. They may be summarized as follows:

1. Removal of the spleen causes a diminution of the proteolytic power of the gastric juice (Tarulli and Pascucci, Gallenga, Betti, Gross, Rusca, Soler and Madero).

2. Injection of splenic extracts (Tarulli and Pascucci, Soler and Madero) and of leukocytes and of extracts of lymph glands (Soler and Madero) increase the proteolytic power of the gastric juice of splenectomized animals.

3. Removal of the spleen causes an augmentation of the proteolytic power of the gastric juice (Silvestri, Tini).

4. Removal of the spleen has no effect whatsoever on gastric secretion (Trampedach).

The chief theory put forward by the first group of investigators has been that the spleen gives to the blood stream during digestion a substance which activates or leads to the further elaboration of the gastric enzymes, especially pepsin.

In this experimental study I have reported data concerning the gastric secretion findings before and after splenectomy on three dogs with accessory stomach pouches (secretory meal of meat) and on two similar dogs serving as controls. Removal of the spleen in these experiments caused no noteworthy changes in gastric secretion except a slight diminution in the quantity of gastric juice obtained.

I am led to conclude from my experimental inquiries and a critical review of the literature that a definite pepsinogenic function of the spleen has not been demonstrated and that the relation of the spleen to gastric secretion is probably merely vascular, the diminution in the amount of juice secreted after splenectomy being attributable to decreased gastric blood supply from injury to the gastrosplenic circulation.

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EVENTRATION OF THE DIAPHRAGM, WITH REPORT OF A CASE.[1]

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AMONG the rare lesions of the diaphragm is the condition originally described by Petit in 1790 and termed by him eventration. This term, though generally used, is a misnomer because no abnormal opening of the diaphragm exists. Such an opening constitutes a hernia diaphragmatica vera when the projecting abdominal viscera are covered with peritoneum or a hernia diaphragmatica spuria when no peritoneal covering exists. In eventration there is simply a thinning or relaxation of the diaphragm, the layers remaining intact and the structure assuming an elevated or higher position than normal. Isolated writers have preferred such terms as these: "high position," "elevation," "dilatation," "relaxation" and "congenital insufficiency." Bayne-Jones, in 1916, collected the reported cases to that time and reported one of his own, making 45 in all. Since that time we have been able to find reports of 2 more. These cases with the one we report make a total of 48 cases on record at the present writing.

With regard to the etiology the weight of evidence would seem to favor a congenital origin. Some of the arguments advanced are (1) its occurrence in the fetus and the newborn, (2) its association with other congenital anomalies, (3) the involvement of the left side in almost all cases, which coincides with the complexity of the development of the left diaphragm, and (4) the absence of compression of the lung and contiguous structures.

[1] Presented in abstract before the Association of American Physicians, Atlantic City, May 4, 1920.

Considered as an acquired lesion it has been supposed to follow disease of the muscle or of the nerves, and as a result of greatly increased abdominal pressure. Among the latter conditions pregnancy, ascites and megalocolon are important in producing increased pressure. However, as Bayne-Jones points out, "If this factor of increased pressure in the abdomen bore an important etiologic relationship to eventration the frequency of pregnancy in general and oftentimes in the same individual should find a counterpart in a large number of women suffering from eventration of the diaphragm." As a matter of fact the lesion is uncommon in women. Among 45 collected cases there were 36 males and 9 females.

The high position of the diaphragm due to the contraction of pulmonary fibrosis and adhesive pleuritis is a different lesion from that under consideration and will be discussed under diagnosis.

The clinical notes of our case are briefly as follows:

E. N., white, female, married, aged thirty-nine years, was admitted to the Jefferson Hospital on December 4, 1919, complaining of pain in the epigastrium and in the back with attacks of vomiting.

Family History. Negative.

Past Personal History. Negative, except for the usual diseases of childhood. She states that she has always been in good health until the present trouble. No pregnancies.

History of Present Illness. In September, 1919, that is about three months prior to coming under observation, she began to have pain in the epigastrium and left lower chest associated with attacks of vomiting. The pain radiated to the back. The pains have continued, with varying intensity, until the present time. At times they seem to bear some relation to the taking of food, but the relationship is not constant. Shortly after the onset the patient noticed that she became easily short of breath on exertion and was losing weight. The physician who saw her at the beginning of her illness made a diagnosis of gastric neurosis and a roentgen ray at that time aided in the elimination of gastric ulcer or cancer.

Physical Examination. This revealed the following: A fairly well-nourished adult female, no jaundice, eyes, mouth, ears and neck normal. Chest: Well formed and symmetric; expansion definitely limited on the left side, especially over the lower portion. Apex-beat not visible or palpable. Percussion revealed tympany below the third rib in the anterior axillary line, merging with the tympany over the stomach below. Posteriorly on the same side the percussion note below the middle of the scapula was high pitched and resembled the so-called flat tympany. The percussion note of the rest of the chest was clear and resonant. Breath sounds were everywhere normal except over the area of the altered percussion note on the left lower chest, where they were practically absent. During the auscultation of this area a sound suggesting

a splash was heard when the patient was moved. No coin sound could be elicited. The physical signs elicited suggested the possibility of a hydropneumothorax, and this was our provisional diagnosis when the patient was admitted to the hospital.

Blood: Examination revealed the following: Hemoglobin, 88 per cent.; red blood cells, 4,700,000; white blood cells, 9600; differential white cell count; large mononuclears, 8 per cent.; small mononuclears, 19 per cent.; polynuclears, 69 per cent.; eosinophils, 4 per cent.

Urine: Examinations were repeatedly negative.

A paracentesis of the left chest in the sixth interspace in the midaxillary line was negative. The fluoroscopic and stereoscopic x-ray examination revealed the following:

The left diaphragm was found considerably higher than the right and does not move on forced inspiration. The dome-shape is retained and no adhesions are evident at the costophrenic angle. The diaphragm has the appearance of an eventration, the cause of which is not apparent. There is just a suggestion of a slight amount of infiltration at the left apex. The barium meal in the stomach shows the cardiac end of the stomach in its proper relation to the left diaphragm, but because of the enormous distention of the colon with gas we are unable to determine whether the stomach is normal or not. We believe that the position of the diaphragm is not due to the gas in the colon.

As we were preparing this paper for presentation before this Association we came across another case of high position of the diaphragm in a baby, a few days old, who was referred for a roentgen-ray examination for a fractured arm. The left diaphragm was at the level of the second interspace. The heart was not displaced. There was no question of any abdominal trouble and there were no symptoms of any kind suggesting trouble either above or below the diaphragm. This case would seem to emphasize the congenital origin.

Discussion. In the past most of the diagnoses were made at postmortem or operation. The symptomatology and physical examination suggested a variety of lesions. In one group the symptoms were referable to the chest and pneumothorax, pneumo-hydrothorax, pulmonary fibrosis, chronic adhesive pleuritis with elevation of the diaphragm, etc., were diagnosed.

In another group gastro-intestinal symptoms predominated and the patient was considered as having a gastric lesion, a diaphragmatic hernia, etc. With the advent of the roentgen ray many of the difficulties in the differential diagnosis of these lesions were cleared up. The case of Sailer and Rhein[2] illustrates well this point. Their patient was considered as having at various times either a

[2] Am. Jour. Med. Sc., 1905, cxxix, 688.

pneumothorax, diaphragmatic hernia, pulmonary cavity or an elevated diaphragm. The roentgen ray was taken immediately after death and not developed until after autopsy, but the study of the plates showed that the diagnosis could have been readily made by this method.

The roentgen ray made the diagnosis in our case. In a number of physical examinations made after the roentgen ray had established the diagnosis we came to the conclusion that we could have been put on the right track if we had paid more attention to the inspection and palpation of the costal margin movements as pointed out in recent years by Hoover. There was a distinct widening of the subcostal angle on inspiration. The widening seemed to be due principally to a divergence of the left costal border. Several physicians who saw the patient with me at different times were able to verify this observation. The high position of the diaphragm placed it at a mechanical disadvantage in its function as an antagonist to the intercostal muscles. Low position of the diaphragm occurs in many of the conditions confused with eventration, such as pneumothorax, hydropneumothorax, etc., and, as a result of which, narrowing of the subcostal angle occurs. In certain forms of obsolete pleurisy with adhesions to the diaphragm and the chest wall and the diaphragm and lung there is likewise narrowing, according to Hoover, because under these conditions it has acquired a mechanical advantage in its traction to the costal border by reason of the adhesions which, acting as points of fixation, give approximately a straight line to the phrenic muscular strands from the central tendon to the left sternocostal region.

Among the reported cases the left half of the diaphragm is noted as being involved in all forty-six instances excepting three. The dome is usually regular in outline in contradistinction to that which is seen in the elevated diaphragm of adhesive pleuritis. As the structure is thinned its outline on the fluoroscope screen is less distinct than the normal diaphragm shadow. The lung on the affected side is often hypoplastic. The heart is oftentimes normally placed, although it may be found displaced in either direction in involvement of the same half of the diaphragm.

One of the arguments adduced in favor of the congenital origin of this lesion as against an acquired elevation due to the traction of adhesions is the external symmetry which the chest presents on inspection. This is in striking agreement with the observations which Ellis[3] noted in his report of a case of congenital absence of the lung. This same writer collected eighteen instances of what appeared to be certain examples of the condition. In all of them the chest was externally symmetrical, the opposite lung, heart,

[3] Am. Jour. Med. Sc., 1917, cliv, 33.

fluid or abdominal organs taking the place of the missing organ. If this is true in pulmonary aplasia it is likewise true in eventration with pulmonary hypoplasia, and is one of the strongest arguments against an acquired origin of the disease. In acquired lesions elevating the diaphragm to the extent seen in congenital eventration there is obvious flattening of the chest wall. The lung is the seat of obvious and demonstrable disease and the roentgen ray shows many and dense shadows. The lung above the diaphragm in eventration is normal unless there be some intercurrent pulmonary disease, such as pneumonia, which, however, has no etiologic relationship to the diaphragmatic condition. The inspection of the chest reveals nothing of note as far as symmetry is concerned. In cases of eventration associated with aplasia of the lung on the affected side the opposite lung may be enlarged sufficiently to extend over and furnish sufficient pulmonary tissue to give physical signs on the side of the absent organ. Even in hypoplasia the opposite lung may extend over to the hypoplastic side. Clinically it is not possible to demonstrate such overlapping. Even with the roentgen ray considerable difficulty may be encountered unless the shadows of the bronchial tree are clear and suggest a different distribution than normal.

THE RELATIVE VALUE OF LABORATORY AND CLINICAL METHODS OF STUDY IN THE DIAGNOSIS OF TUBERCULOSIS.[1]

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DURING the past three or four decades medicine has undergone a greater development than in all preceding centuries. The fact that we have lived during that time and been a part of that development makes it difficult for us to view this progress in its proper perspective, so we must leave the final estimate of this era to future generations. We may, however, not without profit stop and consider some of the general trends of this age and see where we have gone and where we are going.

This era has been marked by several particular characteristics, among which may be mentioned: (1) The development of bacteriology with the light which it has shed upon the causative factors of many diseases; (2) the intensive study of pathologic anatomy, familiarizing the physician with the macroscopic and microscopic

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[1] Read before the Medical Society of the District of Columbia, Washington, D. C., October 20, 1920.

characteristics of the tissues as affected by disease processes, at first in the dead, and later in the living as found at operation; (3) the development of biochemistry with its revelations as to the reactions which take place within the body; (4) the development of the necessary technic to solve the problems in the various fields of laboratory research; (5) a gradual dependence upon laboratory and mechanic measures in study in preference to clinical observation; (6) the gradual development of specialties for the intensive study of subjects, diseases and methods.

We have now arrived at a stage of development where we can be proud of our profession and its achievements. While medicine is still far from being an exact science, we have eliminated much of the inexactness and have located some of that which remains. It is still well for us, however, to pause and see if we are working to the best advantage and developing in that manner which will be most productive of advancement for the future.

Sir James MacKenzie, that great teacher of modern medicine, possessed of a keen imagination and endowed with a broad vision, has pointed out many of the errors to which medicine has committed itself and has endeavored to direct present and future investigation into channels which will make it broader, more practical and more efficient.

The laboratory age will probably always stand out as the golden age in medicine. It is impossible for use to conceive of another like period of time in which so many truths could be revealed as in the period through which we are now passing. To be sure progress will continue and present knowledge will be elaborated and made more accurate and more practical. Such an era of progress through which we are now passing forces many hardships upon those who must keep pace with the advancements. With the truths which have been enunciated there have also been many half-truths and much error, all of which must be segregated and properly evaluated. This is a task which now lies before us.

With the preponderance of laboratory study has naturally come the revelation of a preponderance of laboratory facts, and these have absolutely dominated the medical mind. Things outside of the laboratory have been minimized and considered less worthy of study. Even the application of the ascertained facts in the clinic has been looked upon as being less worthy than their discovery. The result has been not so much an exaggeration of the importance of the laboratory, for its importance can hardly be exaggerated, but a relative minimizing of the value of study and investigation carried on outside of the laboratory. The time has now come, however, when we must devote greater study to this non-laboratory side. We must devote more time to investigating the patient. We must remember that he, too, is a laboratory in which actions are followed

by reactions. It is our duty to observe and investigate the patient with the same zeal and earnestness that our workers have been investigating his disease—its pathology, bacteriology and chemistry.

Then, too, this era through which we are now passing has been characterized by the development of mechanical methods of examination. The general tendency has been toward measuring things by the microscope, test-tube and mechanical devices, and away from study which depends upon man's power of observation. While these methods are extremely important and our modern scientific medicine has been established through them, yet there is something lacking which must be supplied if we will have medicine rounded out so as to meet the requirements of the patient. It seems to me that there are two outstanding needs in medicine today: (1) The correlation and unification of the recent scientific discoveries which have been made, and (2) more accurate clinical observation.

While all should know better, yet the opinion seems to be prevalent that laboratory and mechanical means of arriving at truth are accurate while clinical observation is inaccurate. To emphasize this opinion, laboratory and mechanical measures are termed methods of precision, intimating that clinical methods are naturally inaccurate. Nothing could be further from the truth. The laboratory and mechanical measures have back of them the errors incident to the reaction and the apparatus plus the errors of the observer; while clinical observation has the errors of the observer only. These I shall illustrate later in my discussion.

One cannot practise medicine alone by data obtained by the microscope, in the test-tube and through so-called apparatus of precision. The patient must be considered. There has been entirely too much of a tendency to reduce things to so-called normal standards. There can be no absolute normal as long as individuals differ as they do. Difference makes human beings interesting as individuals and makes their reactions differ in disease. He who tries to reduce all maximum daily temperatures to 98.6°; all pulses of men to 72 and of women to 80; blood-pressures during middle life to 130; and the time of the meal leaving the stomach to six hours is trying to practise medicine mechanically. He is omitting consideration for the most important element in disease, the patient who has it. This is the man who removes tonsils or sacrifices teeth if a patient has an ache, a temperature of 99° and a tired feeling without finding out the cause. He also condemns a nervous woman, with a blood-pressure of 180 to invalidism, simply on the blood-pressure reading alone.

It is now time to make advances. In order to do so we must evaluate these measures and learn what is error and wherein the error lies. One great error has been to think of tests apart from the patient tested; to think of each test as an entity when in reality it is

simply a procedure applied to some portion of the human body in order to determine certain of its characteristics.

Our rapid development has favored or made necessary specialization, and specialization in turn has hastened the discovery of scientific facts. Unfortunately it has also had a disintegrating influence upon medicine as a whole, for illogically it has divided the human body into parts and separated them from the whole.

One of the greatest criticisms that can be made of modern medicine is that all of this study along special lines, of individual diseases, individual organs and systems of the body and individual methods, has emphasized the part and minimized the whole. It has emphasized disease processes and methods of examination and minimized the patient. It is now time to realize the importance of the patient, to emphasize that the blood, urine and sputum examined in the laboratory, and the heart, lungs, eyes, throat and stomach which are now presided over by separate specialists all belong to a patient; and that the patient's organs and tissues are so linked together that every part is influenced by every other part and that every part influences the whole.

The necessity of correlation and unification then is self-evident. In order to do this we must know the patient and his reactions. The reaction of the normal individual belongs to the study of physiology, his reactions when ill, when a patient, belong to pathologic physiology. In the past it has been emphasized that the best clinician was the one who was well grounded in pathologic anatomy. This has probably been true, but I seriously doubt whether it will hold for the future. While diseases produce pathologic-anatomic changes in tissues, they also produce injuries to the organism which are recognized as symptoms. These symptoms are changes in function or pathologic physiology. Therefore the best clinician in the future will be the one who is not only grounded in pathologic anatomy but likewise in pathologic physiology; in other words, the physician who knows the disease and the disease process and at the same time understands the patient's normal and pathologic physiologic reactions.

It would be erroneous to say that clinical observation today is a lost art; it is the truth, however, that it has lagged behind other methods of investigation. It has not kept pace with laboratory investigation. Clinicians have been particularly remiss in not keeping themselves informed of discoveries in physiology. They have not learned to read the actions and reactions of patients in terms of physiology, which they must do if they would be good observers and accurate interpreters of their observations.

They must know and learn to recognize the differences in the patient's physiologic reactions in the presence of disease just as they have learned to know and recognize the pathologic changes as

revealed macroscopically or microscopically, or in the test-tube in the presence of disease. We would not hark back to the good old times in the pre-laboratory days when all there was in medicine was a doctor with common-sense and human feelings who knew only what he read in his patient; but we do look forward to the future when the practice of medicine will be based on an understanding which comes from a combination of facts derived from both laboratory investigation and accurate observation of the patient, interpreted by a mind which knows the patient no less than he knows the disease.

The principles herein discussed may be well illustrated in the development of our knowledge concerning tuberculosis. From the time of Hippocrates it has been the task of medical men to study tuberculosis. For centuries they groped in the dark, yet every now and then a new observation was made which materially increased the sum total of knowledge of the disease. At first knowledge depended almost wholly on observation of the patient, then later this observation was supported by crude pathologic observations; later by more accurate methods; but the greatest aid to progress during the last part of the eighteenth and the first part of the nineteenth centuries came when Auenbrugger, Skoda and Laennec made their contributions to the study of thoracic disease.

Louis in his preface to the second edition of *Researches on Phthisis* (1843) gives a splendid picture of the state of investigation at the time. He praised the researches of Bayle and Laennec as adding greatly to the knowledge of the subject but insisted that progress could be made only by recording and studying symptoms and then comparing them with the condition of the organs found after death, which is a correlation of the pathologic physiology with the pathologic anatomy. He recorded the number of times each symptom occurred in a group of patients and tried to analyze the patients in such a way as to explain why such and such a symptom was present in one patient and not in another.

He says: "I was led to the adoption of this method, designated as that of numerical analysis, not by choice, but naturally, involuntarily and necessarily, solely because I *seriously believed* what it has long been the fashion to repeat concerning medical science—namely, that it is a science of observation and observation purely." He then quoted Trousseau, who expressed his opinion of this method of medical study as follows: "I was one of the most violent and unjust detractors of this method; *I did not understand it.* Now that I have studied it I feel that it alone is capable of ensuring the solid advancement of our science, that it alone can enable the observers of one age to avail themselves to useful purpose of the labors of preceding ones, and slowly raise a structure which the reveries of a Galen or a Paracelsus must fail to overturn."

While these observers were rejoicing in the apparent security of methods based upon clinical observation and the study of the patient, developments were taking place which a little later were to withdraw attention from the patient and center it upon the pathology produced in the lung and the tubercle bacillus which caused the pathology. Then for a time clinical observation and study of the patient lagged and physicians became afraid to give an opinion on a case of suspected tuberculosis unless such an opinion was based on laboratory examination.

During the last few years an ever-increasing number of clinicians have been made to see the futility of depending on the laboratory for progress in the diagnosis of early tuberculosis. They are convinced that laboratory methods should be supplemented by more intense study of the patient; or what represents their opinion still better, they believe that intensive study of the patient should come first and that this should then be supplemented by laboratory study. The diagnosis should not depend on the laboratory findings, but the laboratory findings should be weighed along with those elicited by clinical methods and the diagnosis be based on the analysis and correlation of all data obtained. The diagnosis should be the result of a process of reasoning.

We shall now proceed to analyze the methods of diagnosis, particularly of early tuberculosis; for it is early tuberculosis that we must discover if we wish to make satisfactory progress in treatment.

The most useful and most commonly employed methods of examination for pulmonary tuberculosis are: (1) Clinical history; (2) physical examination; (3) examination of sputum; (4) roentgen rays; (5) tuberculin test; (6) complement fixation.

Of these, through clinical history and physical examination, the physician elicits data directly from the patient. The examination of sputum and complement fixation are wholly impersonal and the tuberculin test and roentgen rays are *quasi* personal. The roentgen rays might be classed as a laboratory method and the tuberculin test as a clinical method.

Sputum Examination. Of the purely laboratory methods we shall first discuss the examination of sputum: Sputum in suspected tuberculosis should be examined (1) for tubercle bacilli; (2) for the presence of albumin; (3) for lymphocytes. When tubercle bacilli are present in the sputum there is no question of the presence of pulmonary tuberculosis. This does not indicate, however, that the disease is active, for cases of old chronic quiescent tuberculosis will often show bacilli in the sputum, although no signs of clinical activity are present. In this they are tubercle bacillus carriers the same as certain patients are typhoid carriers. This is of interest mainly as a scientific fact and should not upset anyone's mind and make him worry, wondering if he has recommended patients for

care and treatment who did not need it.   It is one of those facts in medicine which should be known but which will be employed infrequently.

The presence of tubercle bacilli in the sputum of the patients who present for chest examination, for all practical purposes, may be taken as meaning the presence of active pulmonary tuberculosis. Thus far this method of examination is of great value.   On the other side, however, the absence of bacilli cannot be taken as meaning the absence of tuberculosis.   Tuberculosis is often present, sometimes even in a widely scattered area, and at times may be causing marked clinical symptoms without the tubercles rupturing and bacilli appearing in the sputum.   In fact, most patients show symptoms which to the alert diagnostician would warrant a diagnosis of active tuberculosis, before bacillus-bearing sputum appears.   Secondly, the usual methods of diagnosis are subject to far greater error than is generally believed.   I am surprised to find how generally the results are considered absolute for the specimen examined. Ordinary methods of treatment and staining sputum will detect bacilli if present in 2000 to a cubic millimeter.   The most refined method with which I am conversant, that of homogenization, by treating the sputum with gasoline or xylol and shaking will enable one to find them if present in numbers of 200 to a cubic millimeter. Then, too, if a sample of sputum only is taken a great source of error creeps in, as patients with early tuberculosis may expectorate ten times a day, but expectorate bacilli only once; so, by a sample, the chances of failure would be nine out of ten.

For the examination of sputum in cases suspicious of early tuberculosis, it should be collected for twenty-four hours or for three days and homogenized before examination, otherwise the examination is unreliable.   Even then the data are of no value in those cases in which tubercles have not yet broken down.

Sputum in cases suspected of early tuberculosis should also be examined for the presence of albumin.   The presence of albumin, except in the smallest quantities, is suspicious of tuberculosis in patients who are not suffering from pulmonary abscess, bronchiectasis and the infected bronchi which are now so common since the influenza epidemic.   When these are present they, too, produce the albumin reaction.

The presence of lymphocytes in the sputum beyond 30 per cent. is also suspicious of a tuberculous lesion.

The examination of the sputum is thus surrounded by more errors than are usually recognized.

Complement Fixation.   Complement fixation is an immunity reaction but has many sources of error.   It is theoretically positive in all cases of active tuberculosis.   Practically, however, there are certain patients who have bacilli in the sputum who will not react,

and certain others who have slightly active foci without symptoms who will show a positive reaction. As an isolated test it would be unsafe to follow in diagnosis, but interpreted in conjunction with other data it is of value.

Roentgen Rays. The roentgen ray may be used to great advantage in the diagnosis of pulmonary tuberculosis. In order to be of value in the detection of early clinical tuberculosis, however, it should be operated and interpreted by those who are expert in its use; and, even in the hands of many of these the result is doubtful. I have my doubts whether it should ever, except in the hands of a real genius, be relied upon wholly for a diagnosis. In conjunction with other data it is very valuable. Aside from the purely scientific discussion of the question as to which method is the more reliable in the diagnosis of pulmonary tuberculosis, the roentgen ray or clinical examination, the roentgen ray has a great field of usefulness in the detection of comparatively early tuberculosis, and should be used generally and routinely in cases in which the clinician is in doubt. The diagnosis, however, should be made on data obtained by all methods of examination and not by the roentgen rays alone.

Tuberculin Tests. Personally I have had much more help from the various tuberculin tests than most of those who write on this subject indicate. Here, too, it is the interpretation after careful technic that counts. The tuberculin test like complement fixation is an immunity reaction. Immunity reactions are theoretically strongest when the body cells are busy combating antigen—that is, when the cells are fighting an active tuberculosis. Then they should produce more antibody, and this in turn, in coming in contact with the antigen artifically introduced, should produce a more marked reaction than when an active infection is not present. After comparing the tuberculin reactions in several hundreds of cases of suspected tuberculosis, with my opinion based on other methods, I find that a prompt marked reaction coincides closely with my opinion of clinical activity and a slight reaction or a delayed reaction coincides with my opinion of partial quiescence. I employ either the intradermal test, using $\frac{1}{10}$ to $\frac{2}{10}$ c.c. of a 1 to 5000 dilution of Koch's O. T. injected between the layers of the skin, or the cutaneous test using full strength of Koch's O. T. I prefer the intradermal.

This test must not be relied upon any more than the complement fixation and roentgen rays in making a diagnosis. It is only one source of obtaining information, but one that at times offers considerable aid. It should always be used in conjunction with the purely clinical methods.

It is evident from our discussion so far that these laboratory and *quasi* clinical methods have an important place in furnishing data to be used in the diagnosis of clinical tuberculosis. It is equally

evident that it would be unscientific and unwise to depend alone
for diagnosis on any one of these methods. They should be inter-
preted only in conjunction with the data obtained by other and
especially clinical methods. Unfortunately none of these methods
gives an idea of the patient and the resistance which he is showing
to the infection.

Clinical History. The clinical history elicits the various ways in
which the normal physiologic processes of the body are disturbed.
It is a physiologic inquiry. The facts are revealed either by the
description of the patient—subjective symptoms—or by the percep-
tion of the observer—objective symptoms. No matter how revealed
they express the manner in which the normal physiologic processes
of the body have been disturbed.

This leads us to inquire how the physiologic processes of the body
are controlled? So far as is known every act in the body is controlled
either by the nerves or the endocrine glands; or by these conjointly;
and these are subject to two classes of stimuli, physical and psychical.

Therefore in studying and interpreting symptoms it is necessary
to know what there is in the disease, tuberculosis, which disturbs
the nervous system and also what there is that disturbs the endocrine
glands; and, further, in what way these stimuli act and what symp-
toms are produced by each. It can readily be seen that the symp-
toms of tuberculosis must vary according to the stability of the
nervous and endocrine systems. This will make them differ in
different individuals and in the same individual at different times.
I recently observed a patient who developed an active clinical
tuberculosis at the same time that she was developing a post-
adolescent hypopituitarism. She gained some thirty pounds in
spite of the early active tuberculosis.

In order to make our clinical observations of greatest value we
must start with an adequate conception of the disease pulmonary
tuberculosis and the manner in which it disturbs the normal physio-
logic action of organs. Starting with the conception that pulmonary
tuberculosis is an infectious inflammation, chronic in nature, which
(1) disturbs the nerve and endocrine balance of the patient and
particularly produces sympathetic effects by toxins which are liber-
ated from the disease areas, and in this manner produces general
symptoms, and (2) irritates nerve-endings in the lung and in this
manner produces reflex symptoms, we have a basis for explaining
two groups of common symptoms found in this disease.

On this conception I have classified most of the symptoms of
pulmonary tuberculosis into two groups, the toxic and the reflex.
To these I have added one more in early tuberculosis, in which I
place those symptoms which are incident to the disease itself; and
still another in advanced tuberculosis in which are placed the symp-
toms and syndromes which result from the disease.

This classification is shown in the following groups:

SYMPTOMS OF TUBERCULOSIS IN GROUPS ACCORDING TO ETIOLOGY.

Group I. Symptoms due to toxemia.	Group II. Symptoms due to reflex cause.	Group III. Symptoms due to the tuberculous process per se.
Malaise	Hoarseness	Frequent and protracted colds.
Lack of endurance	Tickling in larynx	Spitting of blood.
Loss of strength	Cough	Pleurisy.
Nerve instability	Digestive disturbances (hypermotility and hypersecretion, which may result in loss of weight)	Sputum.
Digestive disturbances (hypomotility and hyposecretion)		
Metabolic disturbances, resulting in loss of weight	Circulatory disturbances	
Increased pulse-rate	Chest and shoulder pains	
Night-sweats	Flushing of face	
Temperature	Apparent anemia.	
Blood changes		

SYMPTOMS WHICH RESULT FROM PULMONARY TUBERCULOSIS.

Respiratory changes.
Dyspnea.
Circulatory changes.
Changes on part of nervous system.
Changes in blood.
General metabolic changes.
Degenerative changes.
Menstrual irregularities.
Other changes in internal secretions.

When the symptoms are analyzed and grouped in this manner they have a very different meaning from that which is attached to them when treated individually. The presence or absence of certain symptoms and the presence of certain ones in combination give a basis for not only suspecting a tuberculous process but for judging whether or not it is active.

If we discuss the meaning of these groups we see that Group I is made up of some of the very common symptoms of active tuberculosis; but it is necessary to emphasize the fact that these symptoms varying in their combination and in the degree of their severity are not pathognomonic of the toxemia of tuberculosis, but are the same though differing in severity, in all toxemias. Many of this same group may be present in cases of nerve or endocrine unbalance and many of them are due to overwork. So there is nothing in this group when taken alone upon which we may base a diagnosis of active tuberculosis. It is a group due to general nerve and endocrine disturbances and when due to active tuberculosis is indicative of toxemia.

Those symptoms found in Group II are due to reflex action. They are caused by the inflammatory process in the lung acting upon the sensory fibers of the vagus and sympathetics and sending impulses centralward to the medulla and cord and there transferring

them to the nerves which go to other structures to produce action. This group contains those symptoms which are usually designated as "functional." It is characteristic of them that the impulse arises in one structure and the disturbed function occurs in another. It will be noticed that all of these symptoms point away from the lung; the first three point to the larynx, the fourth to the gastro-intestinal canal, the fifth and seventh to circulatory disturbances and the sixth to skeletal structures.

There is nothing in this group which, when taken alone, would warrant a diagnosis of active pulmonary tuberculosis; but when those symptoms on the part of the larynx are combined with symptoms of Group I lasting more than a few days or lasting a few days and recurring, then we feel quite sure that the cause is not in the larynx but in the lung. Digestive disturbances associated with symptoms of the toxic group are very suggestive, and especially if laryngeal irritation is present. Flushing of the face with cough is especially suggestive and will nearly always be accompanied by toxic symptoms. Chest and shoulder pains, particularly the dull aches, are suggestive but need other symptoms to point to activity.

The symptoms in the last group (Group III) are due to the tuberculous process *per se*. This may not be a happy designation for this group, but it has the recommendation of being suggestive.

Frequent and protracted colds of tuberculous origin are accompanied by other symptoms of Groups I and II, and from their frequency or the fact of their repetition may be considered as being due to a chronic process, the most common of which is tuberculosis.

Spitting of blood should always be considered as being due to tuberculosis unless another cause is obvious. In this I do not mean a streak or a speck of blood, but free, bright blood. This symptom may appear unaccompanied by others; but, as a rule, if of tuberculous nature, will have some symptoms of Group I and II or others of Group III, precede, accompany or follow.

Pleurisy either dry or accompanied by effusion is usually of a tuberculous nature. It is nearly always accompanied by laryngeal irritation, often by flushed face, and usually by some of the symptoms of Group I. It always means active tuberculosis and should be heeded as a sign of such.

Sputum may be a result of the stimulation of the mucous glands of the bronchi by the tuberculous process or consist of the secretions from ruptured tubercles. If due to tuberculosis it is usually accompanied at least at times by laryngeal irritation and other reflex symptoms and some of those belonging to Group I.

It can readily be seen that the most important group of symptoms from the diagnostic point of view is Group III. It is further evident that few of these symptoms occur alone. They are usually so combined as to make the meaning quite plain if carefully analyzed. By eliciting a careful history, and following this group of symptoms

little doubt should remain in the examiner's mind as to the presence or absence of active tuberculosis; and the valuable part is that the diagnosis can usually be made before bacilli appear in the sputum.

Physical Examination. The data obtained on physical examination above all other methods is based upon the observation and skill of the examiner. In it he aims to determine what pathologic processes are present by methods which reveal disturbances in the normal anatomic and physiologic condition.

The changes which are found on physical examination are usually discussed as though they were anatomic disturbances; but such is not the case. They are partly anatomic and partly physiologic, and the physiologic changes, if one understands that part of visceral neurology which pertains to the lung and pleura, are just as definite as the anatomic changes.

Auscultation and percussion have long been depended upon as affording the best diagnostic data in pulmonary tuberculosis. This is partly due to the fact that it is generally believed that the examiner is examining the lung tissue more directly than in any other manner. When one considers all the difficulties and errors which are incident to these methods in early cases of tuberculosis, he is forced to the conclusion that the data obtained through them would be much easier of interpretation if substantiated by data from other methods. This is why other methods have been searched for so diligently.

I desire in the remaining portion of this paper to discuss certain physiologic changes which result from the infection in the lung which furnish this corroborative evidence, or which may be taken as giving primary evidence to be corroborated by the findings on auscultation and percussion.

There has been a tendency in examining chests to direct the attention too much to the changes in the lung. While these are what we wish to determine, yet we must not consider that we can auscultate and percuss the lung alone. The percussion note is made up of vibrations set up in all of the tissue which come in the path of the percussion impulse and is modified by all adjacent structures, even the surroundings of the patient. Therefore percussion examines the skin, subcutaneous tissues, muscles, bony thorax, lung and all adjacent structures which modify the impulse. The tension of the soft tissues as revealed, especially in the degeneration of the subcutaneous tissue and muscles and the increased muscle tone, often make up most of the departure from normal in the percussion note. This is particularly true in percussion over the apices from the second rib upward in early tuberculosis. When active pulmonary tuberculosis is present the scaleni, which are inserted in the first and second ribs, the sternocleidomastoideus, which is inserted in the sternum and clavicle and the pectoralis which is spread out over the surface of the ribs, all show increased tension; and so produce a fixing of the upper portion of the chest

wall. Percussion through this fixed area and through the tense muscles must of necessity produce greater changes in the percussion note and percussion resistance than can possibly be produced by the few tubercles in the lung. Personally I believe this causes the major portion of the percussion changes that we have been ascribing to the infiltration in the lung in early tuberculosis.

This same is true of auscultation though to a lesser degree. The changes on auscultation are not all due to the modifying of the sounds in the lung. The muscles, subcutaneous tissue, ribs and other structures change and modify them, too. One hears a murmur not wholly unlike that due to respiration over contracting muscles. In complete pneumothorax and empyema the chest wall with its coverings gives fair imitation of the respiratory murmurs, although there is no pulmonary tissue underlying. Examiners must not concentrate too much on the lung but must consider all adjoining and modifying structures.

In passing I should like to call attention to an almost wholly unknown and neglected method of diagnosis which depends upon anatomic change for its value and which in my hands has proved of great value. I refer to palpating or feeling the anatomic changes in the lung. Palpation is as accurate as percussion at its best without being subject to so many errors. Different density in the lungs, mediastinum and pleura may be felt by a light palpation— light touch palpation. Infiltration, empyema, cavity, pleural exudate, thickened pleura, the borders of the lungs, the heart and the liver may all be detected by palpation; in fact, everything that can be detected by percussion, and some of it without the error that is incident to the percussion stroke which sets up vibrations extending to adjacent structures. One palpates or feels more directly than he percusses. Aside from this method being of great value in diagnosis, it offers proof of the superiority of light over heavy percussion.

There are certain disturbances in physiologic action in pulmonary tuberculosis which are visible to the eye and recognizable on palpation. I refer to the motor and trophic changes in the muscles, skin and subcutaneous tissue, which are reflexly produced by the inflammation in the lung. These reflexes are of especially great diagnostic import because they affect skin and subcutaneous areas and groups of muscles which are distinctive. Barring the diaphragm there is no other organ, except the heart on rare occasions, which produces reflexes in these structures.

The structures which show the pulmonary motor and pulmonary trophic reflexes are as follows:

1. The pulmonary motor reflex expresses itself in those muscles which receive their innervation from the cervical segments of the cord, particularly the sternocleidomastoideus, scaleni, pectoralis, trapezius, levator anguli scapulæ, rhomboidei and diaphragm.

2. The pulmonary trophic reflex is shown in the skin, subcutaneous tissue and muscles supplied by the cervical segments of the cord, particularly the III, IV and V segments. This means the skin and subcutaneous tissue from the chin to the second rib anteriorly and from the base of the skull to the spine of the scapula posteriorly; and the muscles belonging to the shoulder girdle, and the diaphragm, as mentioned above.

This pulmonary reflex is produced by impulses arising in the inflamed lung. They are carried to the cord by the sensory sympathetic neurons and there transferred to ascending neurons which carry them up into the cervical part of the cord and these again transfer them to motor and sensory spinal nerves which supply the tissues above mentioned as the seat of the reflexes. The cause of these reflexes is identical with those which are so well known in connection with the appendix, gall-bladder and stomach, except that instead of the afferent impulse which is carried to the cord finding efferent motor and sensory nerves in the same segment with which to complete the reflex, in case of the lung, it must be transferred upward in the cord to the cervical segments. This variation is based on embryologic differences.

The motor reflex which shows an increased tonus (spasm) of the muscles may be seen on inspection or detected by palpation. It may also be detected by the effect which it produces in limiting the respiratory movement. On inspection of the muscles themselves, particularly the sternocleidomastoideus, trapezius, levator scapulæ and rhomboidei they may be seen to stand out more prominently than normal and on palpation they reveal an increased tonus or spasm. This increased tonus is also detected in the scaleni. The effect of the reflexes is to shorten the muscles, and this shows in a limitation of movement. This is particularly produced by the scaleni above and the diaphragm below. That the infiltration itself in reducing the elasticity of the tissue of the lung particularly in advanced cases, is also a factor in lessened motion is quite probable; so are pleural adhesions either at the base or elsewhere; but this lessened motion often appears early in the disease when the amount of tissue involved is scarcely sufficient to be considered, and when pleural adhesions do not seem to be present; at a time when the only factor which seems capable of producing it is the reflex muscle tension.

These two symptoms then, the increased muscle tonus, particularly as detected on palpation, and the lessened respiratory movement, are just as much symptoms of physiologic disturbance as are the symptoms detailed above under the discussion of clinical history. As such they are among the most evident, therefore most dependable, symptoms indicative of active inflammation in the lung; and because of their localization in definite groups of muscles their presence suggests pulmonary disease.

The pulmonary trophic reflex shows as degeneration of these same muscles and of the skin and subcutaneous tissue above the second rib anteriorly and the spine of the scapula posteriorly. This is indicative of chronic inflammation and would be of no value in the diagnosis of early tuberculosis were it not for the fact that clinical tuberculosis usually manifests itself long after the lung tissue has been invaded. Chronic inflammation means chronic stimulation, and this results in injury to the neurons in reflex relationship to the parts inflamed. This results in trophic change, lack of nutrition and degeneration. These degenerations, then, which are evident at a glance and more so on palpation, tell at once that the patient under observation has probably had a chronic inflammation in the lung. Tuberculosis is the one chronic inflammation which produces the greatest amount of reflex degenerative change, although chronic infected bronchi, unresolved pneumonia, pulmonary abscess and other chronic infections produce some. If the history gives no evidence of other conditions, or if the degeneration is marked, the evidence is strong of tuberculous infection being in the underlying lung. Degeneration in these tissues when symptoms suspicious of active tuberculosis are noted, now that we know the tendency for old infections to become reactivated and furnish foci from which the disease may spread, offers valuable diagnostic suggestions; and if accompanied by spasm in the muscles of the shoulder girdle practically makes a diagnosis of a reactivated tuberculosis.

Diagnosis is a process of reasoning. It is not made on one thing alone. Relationships between cause and effect must be seen and appreciated. Data must be carefully considered and correlated.

From our discussion we can see how advantageous it would have been had clinical observation kept pace with laboratory research during the period of development of our knowledge of tuberculosis; and with our knowledge brought to its present state, the one outstanding cry is for more thorough clinical study. It now offers the greater and apparently the more fruitful field. The patient should be studied more intently and his body reactions should be recognized and interpreted with greater accuracy. Without belittling in the least the magnificent work produced by the laboratory I wish to assert with emphasis that no laboratory method alone or no combination of laboratory methods will ever give the clinician a knowledge equal to that which comes from observing and analyzing the patient. Looking into the future we have an increasing confidence that clinical observation and research will be prosecuted with greater zeal and that it will produce a better balanced science of medicine and one which will be better able to satisfy the requirements of the patient.

PSEUDO-RUBELLA.[1]

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During the last ten years of practice among infants and young children it has been the fortune of the writer to encounter, at more or less considerable intervals of time, isolated cases of a febrile eruptive malady of infancy which have so closely resembled each other in general characteristics as to suggest the definite symptom-complex of a mild infection resembling, but apparently differing from, rubella in several important features.

This pseudo-rubella, as it may be called for the present, seems to be confined to infants between the age of eight or ten months and twenty months to two years, and in every instance observed has occurred in private practice in children who have in the majority of the cases had older brothers and sisters to whom a disease of the contagious character of rubella could easily have been communicated. In not one of the 10 cases observed has the attack been preceded by a similar affection or by rubella in the other children of the family, nor has any instance of communication of the disease or of rubella to other children been observed. The resemblance to a mild rubella has been so striking that this diagnosis always has been most carefully considered, and in each case efforts were made to trace possible exposures to this contagion but without success. While this failure is not remarkable, the absence of communication of a similar disease or of rubella is certainly noteworthy.

These cases have always been observed singly and unexpectedly, never during the prevalence of an epidemic of rubella, and have recovered so promptly that little opportunity has been offered for exhaustive study other than careful noting of the clinical features; and it is therefore with the hope that others may have wider opportunity of observation that the writer ventures to present this purely clinical paper.

The characteristics of rubella are well known. Most writers speak positively of the absence or short duration of prodromal symptoms; of the usually slight degree of fever, which may range, however, from normal to 103° or 104° F. and of the prompt appearance of the rash, frequently the first distinct evidence of the disease. D. J. M. Miller[2] has called attention to the fact that a febrile pre-eruptive stage lasting three or four days or even up to six or seven days might occur, with prompt fall of temperature after the eruption appeared, and this has been confirmed by others, including

[1] Read before the American Pediatric Society, Washington, May 10, 1916, and not previously published.

[2] Archives of Pediatrics, January, 1905.

the writer; but, as these cases certainly are exceptional, it would seem more reasonable to attribute them to a delayed appearance of the rash, rather than to a prolonged prodromal stage.

The eruption of rubella appears as small, round, rosy-red macules or maculopapules, first behind the ears, on the scalp and face, and thence spreads rapidly downward over the body; the spots become larger and in some areas coalesce to form patches of the so-called "bat-wing" pattern. The enlargement of the postauricular and postcervical lymph glands, and frequently of the axillary and inguinal groups, and occasionally of isolated glands over the abdomen and chest, is one of the most distinctive features of rubella. Desquamation is very variable, sometimes is entirely wanting; but usually can be detected by close observation in the form of fine powdery scales.

The onset of pseudo-rubella is abrupt. The infant, previously in perfect health, is found usually toward evening to be feverish, fretful, may refuse his bottle, or may even vomit once or twice. The temperature is elevated, 102° or 103°. If seen at this time, examination shows normal fauces, a clean or only slightly frosted tongue, with a normal or only slightly feverish odor to the breath. The pulse is somewhat accelerated, in keeping with the rise of temperature, but of good quality and not suggestive, while the heart sounds are clear. The lungs are negative; there is no cough nor coryza, no lacrymation nor conjunctival irritation, no abdominal symptoms; the last stool of perfectly normal color and consistency. The spleen and the liver are not enlarged. The external ears and surrounding tissues are not tender to touch, and the speculum shows perfectly normal drumheads. Under these conditions a positive diagnosis is impossible. The possibility of a latent intestinal disturbance, however will prompt the administration of a laxative like castor oil, with the result on the following day of a good clearing out of the bowel showing normal intestinal contents modified only by the changes resulting from the hasty clearing out of milk feces that have not had time for complete digestion—a normal castor oil stool. On the second day the febrile elevation continues, 101° to 102° in the morning. Physical examination yields nothing new except the observation that the postcervical chains of lymph nodes are palpable and seem to be slightly tender. The postauricular glands are not affected, but in some of the cases the inguinal nodes have been found slightly enlarged. The axillary glands have not been involved.

The evening temperature is fairly high—103° to 104°, but the baby usually takes food better and is grateful for water. The diagnosis, except for a possible mild rubella, seems no clearer than at first. The third day is very much a repetition of the second, the morning temperature usually somewhat lower, averaging about

101°, while the evening temperature may reach 104° and over, but no more conclusive symptoms have made their appearance, except for the possibly greater prominence of the lymph nodes.

The urinary examination shows no abnormality. The pulse is still elevated, but the baby seems brighter despite his fever, and shows no signs of toxicity. There have been no changes in the mouth or fauces, no enanthem, and no abnormal physical signs in the rest of the body.

The diagnosis is therefore still in doubt; and prompted by the enlarged postcervical glands, one is tempted to speak of rubella and to look for a rash without success. The fourth day still shows fever about 102° in the morning, with no new symptoms; but toward evening, with the temperature usually not so high as on the preceding evening, a few discrete pale reddish macules, about the size of the head of a pin, may be observed variously about the neck, on the face, under the ears or above the clavicles.

On the fifth day the temperature is about 101°, the rash has come out rapidly since the evening before and covers more or less thickly the face, neck, chest and shoulders, and is spreading downward. It is more discrete than a typical rubella rash, not raised above the surface but in some areas on the face has grouped or coalesced into roundish patches of the size of a very small coin. This tendency to coalescence is also noticed about the loins and in some cases about the thighs. The arms and legs are but sparsely invaded, and the palms and soles are usually spared. The color is pale pinkish, even slightly violaceous. The temperature keeps falling, often to below 100° by evening, and the pulse comes down. The baby is brighter, takes his bottle better and passes a good night.

The following day the temperature and pulse are practically normal. The rash is still present, but looks less intense. The enlarged glands are noticeably smaller and less sensitive. There have been no catarrhal symptoms, no changes in the stools. Except for the rapidly fading rash and still enlarged glands, the baby is well. An occasional transient concentration of the urine, and exceptionally a passing trace of albumin without casts have been noted, but the urine has always cleared up rapidly.

In a day or two the rash has disappeared, leaving phantom traces of discoloration for a few days. The glands have been reduced to almost impalpable size and soon cease to be noticeable. No desquamation has been observed in any case.

The resemblance to rubella is therefore quite striking, especially in the characteristic appearance of the rash, the enlargement of the postcervical glands and the febrile course; but there are a number of points of difference which must be carefully weighed.

Contagion.—Rubella is decidedly contagious, prevailing in epidemics and rarely seen sporadically. It is also generally accepted that second attacks are exceedingly rare. None of the infants of

the series here reported, all of whom were of well-to-do families, had been known to have been exposed to rubella, nor did any of the cases occur during or shortly before or after an epidemic prevalence of this disease. While susceptible children in the same household have in a majority of the cases been in contact with the patient before the appearance of the rash, and even during the whole course of the illness, no instance of a secondary case has occurred either in the same family or among other possible contacts. The cases have occurred sporadically, usually widely separated in time, most of them in Philadelphia, two of them at an interval of a month during the same summer at Cape May, N. J., these latter, however, in two families unacquainted and not living near each other.

Only one of the infants of this series, who had had "pseudo-rubella" at the age of two years, is known to have had an attack of rubella subsequently, at the age of nine years; but, for the other cases, it may be pointed out, the more rigid rules of the Board of Health of Philadelphia, which now quarantines rubella equally with true measles, may well account for an escape from rubellous infection up to the present time.

Age.—The general consensus of opinion, gleaned from an exhaustive study by Griffith[3] in 1887, seems to be that rubella occurs especially between the ages of five and fifteen years, though it has been seen in children under two years (Griffith), and Scholl[4] reported a case in an infant a few days after birth, the mother having had the disease two months before her confinement. All the children in the series here reported were under two years of age.

Invasion.—Many of the cases of rubella collected by Griffith in the monograph already quoted showed no prodromes at all. In a large number, however, slight symptoms were observable for not more than twelve hours before the rash made its appearance. His conclusions, from a comparison of numerous published reports, are that the symptoms in a normal case are malaise, often slight cough, suffusion of the eyes with some lacrymation, probably some coryza, sometimes pain in the limbs, drowsiness, at times hoarseness, sore throat often, enlargement of the glands at the back of the neck and behind the ears, possibly an elevation of temperature of 1° or 2°, occasionally nausea, and some edema of the face.

In the series forming the basis of this study the invasion has lasted invariably three full days or somewhat longer from the onset of fever to the first appearance of the rash and the rapid decline of temperature. There has been no cough, no suffusion or congestion of the conjunctivæ, no coryza or other catarrhal symptoms, no angina, no enanthem.

Eruption.—While the rash of rubella is rose-tinted in color, of a distinctly brighter hue than the darker red of true measles, the

[3] Medical Record, July 2 and 9, 1887.
[4] Trans. Med. Assoc., Alabama, 1881, p. 528.

enanthem in the cases of this series was paler, less rosy and even in several instances with a slightly violaceous tint. It was less liable to coalesce into larger areas especially where folds of the cutaneous surfaces occur, and was therefore more discrete, and spread more slowly to lower parts of the body. It had little or no elevation above the surface, and in no case presented an appearance simulating that of the scarlatiniform type of rubella.

Allowing for the long intervals of time between the individual cases observed, it has seemed that the rash has faded more rapidly and has left less pigmentation than does rubella. Desquamation has been observed in none of the cases.

Symptoms of the Eruptive Stage.—The absence of angina and enanthem and of the catarrhal symptoms so frequently found in rubella leaves the eruption and the adenitis as the only features of the eruptive stage, since the fall of temperature is very prompt as soon as the rash appears; while in rubella fever is usually an important symptom of the eruptive stage and in a considerable number of cases an elevation of from 99.5° to 100° has continued for a week after the rash has entirely vanished.

Tenderness and enlargement of the lymph nodes, while invariably found in all the cases of this series, was never so widespread or so marked as in rubella or in "the fourth disease," as described by Dukes, who states that the enlargement is universal in both diseases. In the pseudo-rubella cases enlargement was chiefly confined to the postcervical chains; but it is important to emphasize that enlargement and tenderness were present very early in the prodromal stage and rapidly subsided as soon as the eruption appeared.

The Fourth Disease.—From the "fourth disease" of Dukes pseudo-rubella is distinguished by its long prodromal period as compared with that of a few hours (Dukes), by the slower progress of the eruption, by the characteristics of the rash, the absence of throat symptoms and its marked difference in general appearance from scarlet fever, which the "fourth disease" is considered to resemble so closely as to cause frequent confusion of diagnosis; and, finally, by its apparent lack of contagiousness and the absence of desquamation, both of which features are marked in the "fourth disease."

It is therefore evident that enlargement of postcervical lymph glands, fever, and a rash are the only symptoms common to true rubella, pseudo-rubella and the "fourth disease," and that while a diagnosis of rubella would have been the most natural one to make in the cases here reported, sufficiently sharp distinctions have been noted in the clinical picture to warrant the suggestion that they were not rubella, and certainly not the so-called "fourth disease."

The conclusion therefore seems reasonable that this symptom-complex constitutes a hitherto undescribed mild infection, non-contagious, or only feebly contagious, to which young infants are

peculiarly susceptible and older children not at all or only rarely liable.

If, as the writer believes, these cases are not true or modified rubella, it is important that the existence of a pseudo-rubellous affection of young infants should be recognized, and by reason of its non-contagiousness should not be subjected to the quarantine that properly is enforced by health authorities against true rubella.

CLASSIFICATION OF RALES: A PLEA FOR SIMPLIFICATION.

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The writer has taught physical diagnosis for many years. He is impressed with the difficulties encountered in teaching students to identify the adventitious sounds heard in auscultation, commonly called *rales*. He has examined most of the text-books in use in the leading American universities and finds an astounding divergence in the matter of nomenclature. The variation, so far as the student is concerned, depends to a very great extent on the early educational environment of his teachers or of those who have written the text-books that are put into his hands for study.

It is quite desirable that the student come into contact with men who have themselves been taught in different schools. This gives the student a little broader grasp of his subject than he would get otherwise. However in respect to this part of the nomenclature of physical diagnosis the difference in teachers may bring confusion to the student.

Seldom do we find two authors whose classification is the same. Every writer has apparently been conscious of the difficulty and has tried to make a classification which will clarify the situation. They have all failed to do this. My own effort may meet with the same failure, but if calling attention to the difficulty may result in some sort of coördinated effort to remove obstacles for the medical student I shall be content.

He may be spared the supreme memory effort of mastering such a list as the following, taken from the authors I have had at hand: Dry, moist, sonorous, sibilant, mucous, submucous, crepitant, subcrepitant, wheezing, whooping, mucous click, crowing, whistling, piping, squeaking, hissing, humming, high-pitched crackling, bubbling, small bubbling, gurgling, snapping, musical, coarse, fine, resonant, non-resonant, consonating, non-consonating, flapping, cardiopneumatic, laryngeal, tracheal, cavernous, euphonic, pleural, vesicular, latent, crumpling, crackling, metallic groaning, hollow,

metallic tinkling (*Gutta cadens*), bronchopulmonary, fistula rale, crepitous, indeterminate, frémissement cataire, Hippocratic succussion.

Our first classification came from Laennec, as we all are aware, and it is today superior to the classifications found in most of the text-books. He did not use the word *rale* but the French word *rhonchus*. I quote from the translation by Forbes[1]—Rhonchi (rales).

1. Moist crepitus rhonchus or crepitation (very large).
2. Mucous rhonchus or *gurgling* (large, middling, small).
3. Dry, sonorous rhonchus or snoring.
4. Dry, sibilous rhonchus or whistling.
5. Dry, crepitous rhonchus, with large bubbles or crackling.

Those who came after Laennec in their effort to supplement and clarify the work of the master have gone further and produced the almost Rabalaisian collection I have mentioned above.

Professor G. Andral in his notes on the fourth and latest French edition of Laennec has the following to say regarding rhonchi (rales): "Since Laennec hardly anything has been added to the excellent description given by him of the different rhonchi." Surely it is commendable that study of such an important contribution should go on, that a form should be determined and some sort of agreement reached as to terminology to which we shall all agree. It is within the province of constituted medical associations to aid in clarifying matters of this kind.

It would seem important that medical men who speak the English tongue adopt a standard terminology.

The diagnostic value of the signs and the importance of their differentiation are not to be gainsaid. Who will deny that the determination of a different type of rale speaks for a difference in pathology? Yet how frequent is it that we read in medical papers, "Rales were found at the base?" The authors who write thus evidently are choosing words which all understand and prefer not to enter a discussion as to classification. Perhaps they are wise.

In a survey of the literature we find two tendencies. One school, among which that of Austin Flint[2] stands out conspicuously, has attempted to establish a nomenclature based on anatomical considerations. Austin Flint's classification is as follows: Laryngeal and tracheal rales; bronchial rales; vesicular rales; cavernous rales; pleural rales; indeterminate rales.

Flint uses the term "so-called" as applied to the *subcrepitant* rale in the chapter on classification of rales and attributes great diagnostic importance to this rale. One gets the impression that he accepts the term against his will. Indeed, his idea in departing

from Laennec's original classification is set forth on page 140, "The term *subcrepitant* gives rise to confusion and there is no advantage in retaining it as the name of a distinct sign. Very fine bubbling expresses more correctly the characters of the sign. The moist rales are often called *mucous rales*. The name is obviously inappropriate, since not only are the sounds produced by other liquids than mucus, but other liquids are best suited for their production, especially in the large and medium sized tubes."

One of the difficulties in classification comes from the limitation of the words "mucous rales." If we take it in the narrow sense of a rale produced by a mucous liquid, all that Flint says is true. However if we consider the word as applying to a rale produced in a tube lined with mucous membrane we are justified, perhaps, in preserving it. Flint's subclasses describe vividly the acoustic qualities used by Laennec's *sonorous* and *sibilant*. Yet he avoids the words.

Da Costa the elder[3] uses a strictly anatomical classification: Bronchial; vesicular; cavity.

His subclasses are made by acoustic qualities and are of the simplest. All of the types of Laennec's main headings are here preserved, namely, *sonorous*, *sibilant*, *mucous*, *crepitant*.

The younger Da Costa[4] puts forth a classification based partly on anatomical and partly on auditory qualities. This is fatal to understanding and to good pedagogics. Here, in the writer's opinion, is the source of most of the confusion which exists.

We have another classification which is partly based upon the physical properties of the apparatus producing the sound and partly on the auditory perception of the sound itself.

In explanation of dry rales Sahli[5] says they may have their origin in *viscid fluid*. This shows how artificial is the term and impossible from the standpoint of clearness. In justification of the term "bubbling," Sahli says: "The term 'bubbling' was employed because it was formerly supposed that moist rales arose from the bursting of air-bubbles in fluid secretion. Of course, we know now that the contents of the bronchi are not sufficiently fluid for such an explanation, and so we suppose that the rales arise from *membranes* of *secretion* being formed in the bronchial lumen and then torn apart again, partly by movement of the air and partly by movement of the lungs." If the term *moist* does not mean moisture or fluidity of tube content, if a dry rale may have its origin in *viscid fluid* are we justified in further burdening medical literature with either of these terms?

Norris and Landis[6] say in explanation of a classification purely

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[3] Medical Diagnosis, 1898.   J. B. Lippincott & Co.

[4] Principles and Practice of Physical Diagnosis, 4th edition.   W. B. Saunders Company, Philadelphia, 1919.

[5] Treatise on Diagnostic Methods, Trans., 4th German ed.   Kinnicutt & Potter, 1905, W. B. Saunders Company.

[6] Diseases of the Chest and the Principles of Physical Diagnosis.   W. B. Saunders Company.

auditory in character: (Sonorous; sibilant; crepitant; subcrepitant; bubbling.) "Genetically all rales are moist but sometimes they are classified as 'moist' and 'dry.' These are undesirable terms, however, and should not be used. Further, the term 'dry' as applied to rales seems paradoxical, for it is impossible to conceive of a 'rale' that does not, to some extent at least, depend on moisture or increased turgescence for its causation."

I heartily agree with this conclusion.

Upon the classification moist or dry, Latham[7] makes this illuminating statement: "Call it *rale* or *rattle* or *crepitation* or what you will, but pray do not add 'mucous' to it by way of specific difference, for this term must always imply that the sound is produced by air passing through mucus whereas it is produced equally by air passing through mucus, blood or any fluid whatever. Besides, it is beyond the truth to say that the quality of the fluid through which the air passes can be distinguished by the quality of the sound that results. The sound will indicate the situation and quantity of the fluid and no more."

We are indeed fortunate for this, for most of us believe that the situation and quantity of the fluid may be estimated by the extent and quality of the rales heard after our ears are trained to recognize them. In listening and learning we must teach our students to see the structure of the region examined and to picture the mechanism of the production of the rale heard rather than to identify a certain auditory quality for which he must endeavor to find a name. If we insist on an anatomical classification this power will come to the student.

Richard Cabot[8] has departed furthest from the classic nomenclature of Laennec. He has done this without utilizing the anatomical classification of Flint. All of the classical terminology has been abandoned with the exception of *crepitant*. Nowhere do we see mention of *mucous, subcrepitant, sonorous* or *sibilant*—terms certainly as worthy as *bubbling, crackling* and *musical*. Cabot even mentions "complicated chords from rales which vary in pitch." One reads and fears that tomorrow may bring forth the necessity of adding harmonics to an already full junior year.

Of all the authors cited, Sam J. Gee[9] has, perhaps, adhered more closely to the original of Laennec in the matter of classification. In his foreword he says: "The sense of words has not been perverted nor have new words been introduced to denote signs already well denominated. Much of the difficulty of teaching auscultation and percussion to students is due to neglect of these plain rules." Gee utilizes but four categories: Crepitant; mucous; sonorous and sibilant; doubtful.

[7] Lectures on Subjects Connected with Clinical Medicine. Philadelphia, Borrington, 1847.

[8] Physical Diagnosis, 6th edition. Wm. Wood & Co., 1915.

[9] Auscultation and Percussion, 6th ed., London.

In starting out to write this paper I was thoroughly convinced that any departure from the classical terminology was to be deplored. Since examining and tabulating the classifications from various sources I am convinced that there is no need to sacrifice the advantages of an anatomical classification to this end. If we take three simple heads: (1) Crepitant or vesicular; (2) mucous or tube; and (3) cavernous we shall be able to place every rale we hear excepting pleuritic friction sounds, which are perhaps best excluded from this category.

It may be that I may be charged with perverting the meaning of the word "mucous." It is surely within a tube lined with mucous membrane that these rales have their origin. Whether fluid or tenacious, the basis of the mechanism which produces them is mucous; whether they are due to turgescence of the lining of the tube, or to muscular contraction in the wall, our term applies. We can utilize the classical *subcrepitant* and the onomatopoetic pair *sonorous* and *sibilant* as subdivisions of the *mucous*. Nearly all of the half a hundred of varieties described by the authors named and others would be subvarieties of the mucous rale.

Of the other two, one (*crepitant*) stands alone and needs no comment or word of explanation. The other (*cavernous*) I should perhaps include within the category of mucous rale also. This would be a further and a desirable simplification. We should then have but two categories: (1) Vesicular or crepitant rales; (2) tube or mucous rales. This shortening involves no departure from Laennec's form other than placing *sonorous* and *sibilant* as subheads of mucous and the addition of the corresponding anatomical words.

I feel sure that teachers and students would rejoice if but two great classes of rales were to be remembered.

THE DIAGNOSIS OF PRIMARY LUNG TUMORS.[1]

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UNTIL comparatively recently the lungs have been an unexplored surgical domain. Improvement in method of anesthesia and in the technic of thoracic surgery have enabled the surgeon to invade the lungs with rapidly increasing success. The time is not far off when thoracic surgery will be just as common and the thorax invaded by the surgeon with the same ease as the abdomen is today. The development of this hitherto untrodden surgical field imposes upon the internist the duty of recognizing intrathoracic lesions that

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[1] Read at a meeting of the Yorkville Medical Society, February 20, 1920.

may be amenable to surgical treatment much earlier than was previously necessary or customary.

We shall confine our remarks in this paper to the medical diseases of the lungs which are amenable to surgical treatment. Essentially such lesions consist almost entirely of lung tumors.

Tumors of the lungs may be either secondary or primary. We shall discuss the secondary tumors first as they are much more common and comparatively easy to recognize, but hopeless from the therapeutic standpoint. However, they are apropos in this discussion because their clinical features throw a good deal of light upon the primary lesions of the lungs. The diagnosis of these secondary metastases of the lungs does not present many problems. Nevertheless it is surprising how often the condition is overlooked. The most important diagnostic feature of the secondary metastatic lung tumors is, of course, the etiological factor. This is the history of a previous removal of a primary lesion, in the breast, in the stomach, in the eye or other organ; or, as is not infrequently the case, the actual but unrecognized presence of the primary lesion at the time the patients present themselves for examination.

Besides the history of this etiological factor the patient complains of progressive cough and expectoration, which may or may not be blood tinged, of dyspnea, cyanosis, pain in the chest and loss of weight. At the same time there may be symptoms of other metastases such as pains along the arm and forearm from axillary nodes or pain in the back and along the extremities as evidence of spinal metastases.

The examination of the chest may reveal areas of localized crepitant and subcrepitant rales or signs of fluid in one or both chests. The character of the fluid on aspiration is of extreme importance. A bloody fluid in the chest is very suggestive of metastasis in the lung, but the fluid does not become bloody unless the metastases are very extensive, and consequently the presence of a serous fluid in the chest does not exclude malignancy. The roentgenographic examination may show scattered shadows in one or both lungs, with more or less definite outlines, which are quite characteristic of metastases.

This usual picture is, of course, easy to recognize, but the most important element in the syndrome, however, is the scar of the operation or the history of the presence of the primary lesion. At times, however, the clinical picture of the secondary metastasis occurs so early in the course of the disease that it entirely masks the primary lesion as the following case indicates:

About a year ago a middle-aged woman was admitted on our medical service at the Lenox Hill Hospital complaining of severe pain, cyanosis, cough and expectoration. She had been treated about six months previous for heart disease, and for about four months before that for intractable neuritis of the left upper

extremity because of severe pains extending along the left arm and forearm. The examination showed the dyspnea to be due to fluid in both chests, which was more extensive on the right side. The left border of the heart extended to about five and a half inches to the left of the median line, but there was no evidence of any lesion of the heart. The most striking point in the examination, however, was the presence of a small adherent nodule, about the size of a walnut, in the left breast, with large adherent nodes in the left axilla. Upon exploring the left chest with the needle the fluid was found to be bloody in character. The pathology in this case was therefore very apparent. The so-called neuritis was due to secondary metastatic nodes in the left axilla from a primary carcinoma of the breast. The dyspnea, cyanosis and pleural effusion were all the result of the lung metastases, and these signs resembling the classic picture of myocardial insufficiency, assumed the important role in the syndrome. We corroborated our clinical ideas by roentgenographic examination and when the patient died a few weeks after admission, by an autopsy.

Primary lung tumors are much less common than secondary ones. The tumors may be benign or malignant. We can dismiss the benign tumors of the lungs with a few words as most of them are only discovered at the autopsy table and they give no clinical manifestations whatever. Dermoid cysts, however, merit more attention because these are the only benign tumors that may give clinical manifestations. They usually occur in the mediastinum, behind the sternum, and may exist there for years without any clinical disturbance. When, however, the tumor grows in size the only evidence is that of pressure in the mediastinum: dyspnea, cyanosis, cough and expectoration, or symptoms of pressure on the sympathetic nerves, such as pupillary changes. A definite diagnosis can only be made when the tumor finally ulcerates into a bronchus and hair or sebaceous contents of the cyst are expectorated. A dermoid cyst in the thorax may also be suspected when, after years of constant observation, the mediastinal tumor may be shown to be present without making any progress. Recently we have had under observation a patient who had a cyst about the size of a child's head in the right thorax which evidently came from the diaphragm and grew so rapidly that it occupied the lower half of the chest, displacing the lung upward. This mass gave the signs of consolidation which persisted for months and which showed in the roentgenographic shadow with a well-defined outline. There was no evidence of free fluid in the pleural cavity and the diagnosis of a tumor was readily made, principally on the basis of the roentgenogram and just as readily removed.

The most common type of primary lung tumors are the malignant ones. In spite of the fact that they are considered to be comparatively uncommon, we believe they are much more frequent than

we are in the habit of regarding them. The infrequency of these lesions is based upon autopsy statistics. Autopsy findings do not tell the whole truth, for the statistics are only of relative value. It is surprising to know that Dr. Sidney Yankauer in an extensive series of bronchoscopic examinations found that 12 per cent. of his cases had primary malignant tumors of the lungs, most of which were unsuspected. Pathologically, malignant tumors are of three types: carcinoma, sarcoma and endothelioma. The latter type of tumor is considered as a form of carcinoma or as an intermediate type between sarcoma and carcinoma. The carcinomata originate either at the pleural surface or at the hilus of the lungs; sarcomata usually begin at the hilus, while endotheliomata, which are very slow growing tumors, originate on the surface of the lungs. From the clinical standpoint the primary origin of the tumor is of great importance for the diagnosis of primary lung tumors, for the diagnosis must be made early and the primary location recognized. We therefore distinguish two clinical types of primary lung tumors: (a) Those that originate at the pleural surface, and (b) tumors that originate at the hilus of the lung and usually from a bronchus.

The early diagnosis of a primary lung tumor, which is the only useful diagnosis in these days of progressive thoracic surgery, cannot be made on one examination alone. The case must be studied for weeks or months at a time, as the progress of the case while under observation is of diagnostic importance. Besides, these tumors usually grow very slowly. The symptoms may be classified into three groups: (1) General symptoms; (2) symptoms of the pleural type; (3) symptoms of the hilus type.

The patient in whom we have a right to suspect a lung tumor usually comes to the physician complaining of cough, pain in the chest and dyspnea of long duration. It is quite evident that this syndrome does not suggest any definite lesion. These symptoms may be due to subacute bronchitis, pulmonary tuberculosis, cardio-renal disease or primary lung tumor, and with close study of these generic symptoms we may verify our supposition regarding this possible lesion. The cough is usually dry in the pleural type, while in the hilus type it may be accompanied by profuse, thick, purulent sputum and only occasionally by blood-tinged sputum. It is rare indeed to see the prune-juice sputum as described in text-books. The pain may resemble that of pleurisy or it may be substernal or supraclavicular. It does not necessarily have any relation to the primary site of the lesion. The dyspnea is a very important sign. Persistent and marked dyspnea, with a disproportion between the dyspnea and the physical signs, is an extremely suggestive sign of lung tumor. The patient may be suffering for months from cough, pain, dyspnea and expectoration, and these may be the only persistent physical signs with a small area of localized bronchitis and an inordinate amount of dyspnea. In such a patient, after we have

eliminated tuberculosis by repeated and thorough physical examination, by repeated sputum examinations, by tuberculin tests and by a
complement-fixation test for tuberculosis we must then make all
efforts to eliminate a primary lung tumor.

The physical signs are the characteristics by which we may be
able to differentiate the type of the tumor. The signs of the
peripheral type are largely pleural. Occasionally there is a friction
rub, but the most characteristic sign is the occurrence of one-sided
pleural effusion. The size of the effusion is not an indication of
the size of the primary tumor. I have seen a small mass, the size
of a walnut, give repeated pleural effusions of 2000 c.c. The effusion
is invariably one-sided and the character of the fluid may be hemorrhagic, but it need not necessarily be so. Only about 50 per cent.
of pleural effusions produced by primary lung tumors are hemorrhagic in character. As a rule it is serous in type, with the characteristics of a transudate. Occasionally on centrifuging the fluid
we may obtain the characteristic large, highly granular cells which
are believed to be pathognomonic of lung tumors, but we have rarely
been successful in finding them except in one case in which the
diagnosis was made without them. Recently the technic devised
by Dr. Mandlebaum of Mount Sinai Hospital has made it easier to
find these cells in the centrifuged fluid as well as in the sputum.
Dr. Mandlebaum's method consists in embedding the centrifuged
material in paraffin and then making serial sections. We have seen
a chylous effusion in a case of primary lung tumor originating at
the left apex of the lung, which was probably due to pressure on the
thoracic duct. Of course, a pleural effusion may be just as suggestive
of pulmonary tuberculosis, but the frequent recurrence of the fluid
on the same side, especially when tuberculosis has been eliminated
and when the fluid is bloody in character, is particularly suggestive
of lung tumor.

Even when the pleural effusion is not present we may be able to
diagnose a primary lung tumor by the localized bronchitis, with
pain and inordinate dyspnea. When the tumor is large enough we
may be able to make out a small area of consolidation on physical
examination. Of course, if the case is followed long enough we
may get all the signs of metastases: enlargement of the mediastinal
area of dulness, glands, cachexia, etc., but the patient is then beyond
therapeutic aid.

The hilus type is much more common and presents an entirely
different picture. The patient suffers for weeks or months from
what seems to be chronic bronchitis, and usually tuberculosis can
be definitely ruled out. The sputum may be mucoid or purulent
and only later does it become prune-juice in color. If the tumor
begins near a bronchus the findings may be only those of a localized
bronchitis, with consolidation later on. Usually in the hilus type
the signs are those of severe dyspnea, with signs of compression of

a large bronchus, such as diminished breathing on auscultatory percussion and later on actual dulness and diminished breathing. It would seem, however, from the study of pathologic specimens of primary lung tumors, that we should get signs of massive consolidation. This is masked by the fluid, and when the fluid is removed we may get the signs of consolidation. But when these signs are present there is usually no diagnostic difficulty.

The hilus type of primary malignant tumor grows much more rapidly than the pleural type. The proximity of the tumor to the mediastinum is the reason for the occurrence, very early in the disease of pressure symptoms and metastases. The most common pressure symptoms are those of recurrent laryngeal paralysis, a one-sided dilated pupil from paresis, and finally paralysis of the sympathetic nerves; dilated veins over the sternum and local edema of the infraclavicular region; palpable left supraclavicular lymph nodes and finally enlarged axillary nodes, and increased areas of mediastinal dulness with myocardial insufficiency from pressure. Cachexia, which is a classic characteristic of the mediastinal type of malignant tumors and of malignant growths in other parts of the body, is absent in primary lung tumors until very late in the disease, and this symptom is therefore of little value for an early diagnosis.

The examination of the chest fluid holds out a helping hand, but unfortunately the grasp is not a very tight one. When we are most in need of aid it is usually of no value. When the diagnosis is evident these examinations are of corroborative help.

The characteristics of a typical specimen are only present in those cases with extensive involvement of the lung or of a hilus type which has perforated into the lumen of a bronchus. At first the sputum is not characteristic, but later on it may be found tinged with blood and still later it may resemble prune-juice, which is not due to the presence of blood and occasionally it has a characteristic greenish hue. Rarely we may find on microscopic examination proof of the tumor itself. Large polyhedral granules with faint vacuoles are believed to be almost pathognomonic, but they are rarely found when most needed. Centrifuging the fluid may bring out the characteristic granular cells, but this is rather a rare find. Dr. Mandlebaum, of Mount Sinai Hospital, has been able to find these cells more frequently by embedding centrifuged specimens in paraffin and making sections of them. It must be remembered, however, that sputum examinations are not of very great value. The finding of a few characteristic cells may be just enough diagnostic evidence to tip the scales in favor of a primary lung tumor. The diagnosis of a pleural effusion is usually not of great value. A hemorrhagic effusion is only indirect evidence of a malignant mass. Occasionally the lung puncture and examination of the aspirated material may show the tumor cells.

The nature of the tumor can only be surmised. The pleural type is more likely to be endothelial and then carcinomatous, while of the hilus type the most common tumor is usually sarcoma and less frequently carcinoma.

Examination of pathologic specimens of primary lung tumors seem to indicate that these masses show definite shadows on roentgenographic examination. Extensive involvement of the lungs by malignant tumor certainly does show very interesting pictures. But the condition is then quite advanced and the roentgenographic evidence is then merely corroborative. In early cases the roentgenogram does not show the definite evidence that we usually lack and that we are inclined to expect. The roentgenographic shadows of the lungs showing the primary lung tumors occur very late. We have watched two cases over a year before the roentgenogram showed a definite shadow in the lung. A mass in the mediastinum shows much more clearly and earlier than one in the pleura. Consequently when these shadows occur it is difficult to ascertain the primary lesion by study of the roentgenographic pictures. We had a man under observation about two years ago who gave a definite picture of primary lung tumor with metastases. The roentgenogram showed the mass in the mediastinum but no mass in the lung. Seven or eight plates were taken but none showed the mass in the lung, which we believed to be the primary tumor. At postmortem examination it was shown that we were correct in assuming the primary lesion to be in the lung and the secondary metastasis in the mediastinum, although the mediastinal shadows showed much earlier and more definitely than those in the lung. The recent method of roentgenographic examination after inflation with oxygen, devised by Drs. Stewart and Stein, is exceedingly helpful, in the roentgenographic study of primary lung tumor. By this method we may show masses in the lung much earlier than by the ordinary method. A case recently under our observation illustrates the advantage of this method. The patient had several pleural effusions in the chest in the course of a year and a half, several of which were bloody. Fourteen roentgenograms showed normal lung markings. We finally inflated the chest with oxygen after removing the fluid and the roentgenogram showed a definite mass about the size of a walnut at the right base on the pleural surface, which was corroborated at operation. We believe this was one of the first cases in which this method was used for the determination of a primary lung tumor. The mass was verified at operation and a lobectomy of the lung was successfully performed.

In the hilus type of tumor bronchoscopic examination is of distinct value. We believe in cases in which primary lung lesion is suggestive a bronchoscopic examination should always be done. In competent hands this method gives more evidence than any other and is practically devoid of danger. Even in cases of chronic

bronchitis where tuberculosis can be ruled out we believe broncho-scopy is indicated.

The value of bronchoscopy was never brought out so forcibly as several years ago, in a patient, on the surgical service at the Lenox Hill Hospital, who suffered apparently from bronchiectasis, for which she was operated upon a number of times in the course of two or three years. She would have periodic attacks of coughing, with profuse expectoration. Repeated operations during her stay in the hospital were without avail.

When she died an autopsy revealed a pedunculated benign ade-noma which acted like a ball valve, causing interrupted obstruction of the bronchial tree, with retention of secretion. When the secretion had accumulated an attack was brought on and the coughing kept up until the fluid was expectorated, with relief of the symptoms for a few days. The mass found at autopsy could readily have been seen and just as readily removed through the bronchoscope.

The definite diagnosis of primary lung tumor depends upon the clinical findings. When the principal findings are those of mediasti-nal symptoms and a mediastinal mass the differential diagnosis is between different types of mediastinal tumors, mediastinal Hodg-kin's disease and aortic aneurysm. The differential diagnosis between other types of mediastinal tumors and Hodgkin's disease cannot be made on any difference in the clinical features in the lungs. Mediastinal Hodgkin's disease can only be recognized by the presence of other glandular enlargements and the characteristic blood picture and morphological picture of a removed gland. Aortic aneurysm can be differentiated by the clinical picture, the positive Wassermann and the pulsating mass on fluoroscopic examination.

In the pleural type and in the type where there is no evidence of a mediastinal mass the difference lies between a tumor and pulmonary tuberculosis. Pulmonary tuberculosis can be ruled out by careful and repeated negative sputum examinations, by the absence of cachexia, by the negative tuberculin reaction, by the negative complement-fixation test and by the finding of a tuberculous lesion. Tuberculosis usually occurs in the upper part of the lung and travels downward, while primary lung tumors are much more liable to begin at the base of the lung. Fever and night-sweats may occur in both conditions with equal frequency. Not infre-quently a primary lung tumor begins with evidence of primary infection, as the following case indicates. A young woman, aged about thirty-six years, was admitted to our medical service of the Lenox Hill Hospital with a lobar pneumonia. She had been ill for several weeks with a condition that began with sharp pain in the right side of the chest, dyspnea, high temperature which ran the course of a classic lobar pneumonia with consolidation. But the temperature never subsided nor did the consolidation ever clear up.

Repeated examinations of the sputum and complement-fixation tests for tuberculosis gave no evidence of tuberculosis. Repeated chest punctures gave no signs of fluid. Finally after about five or six weeks' observation with persistent temperature and apparently an unresolved pneumonia we obtained a clear serous fluid from the right chest, and we began to be suspicious that the lesion was a lung tumor. On taking a very careful history again it was brought out that about two years before the patient had a small nodule, the size of a walnut, removed from the left breast. We communicated with the surgeon who operated upon her and the pathologist who examined the mass and were told the mass proved to be a benign tumor. In a few weeks skin metastases and liver, abdominal and general metastases occurred, and the etiology of the condition was clear. The so-called pneumonia was evidently a pulmonary metastasis from a malignant tumor of the breast.

In spite of the apparently clear distinction between pulmonary tuberculosis and primary lung tumor the diagnosis of an early primary lung tumor is extremely difficult to make, and in doubtful cases an exploratory thoracotomy should be done. The tumor is then within the scope of modern surgery, and if the tumor proves to be a pleural one it can rapidly be removed with success.

The following case will illustrate the difficulty of differential diagnosis:

A man, aged about fifty-five years, was admitted to our service at the Lenox Hill Hospital with a one-sided pleural effusion which was of a serous character. Tuberculosis was definitely ruled out by repeated negative sputum examinations, by repeated negative tuberculin tests, by negative physical signs and numerous examinations and by negative complement-fixation test. We observed this man for about a year and a half, examining him repeatedly for tuberculosis and primary lung tumor. About fourteen roentgenograms were taken in the course of a year, all of which were negative, although he was aspirated a number of times, only two pleural effusions were bloody in character. After careful study we made the diagnosis of a primary malignant tumor of the lung which we finally demonstrated after oxygen inflation by the Stein and Stewart method to be about the size of a walnut. An exploratory thoracotomy showed the mass at the base just as we had proved clinically. It seemed to be a malignant tumor the size of a walnut and a lobectomy of the lower lobe of the right lung was done by Dr. Franz Torek. The patient made a stormy recovery and finally died about seven months later of chronic nephritis. The tumor turned out to be a cartilaginous tuberculous mass.

Conclusion.—The diagnosis of a primary lung tumor is one of the most difficult pulmonary lesions to recognize early. This can only be done with a fair degree of certainty. If we wait until we can do so positively the patient is beyond our therapeutic reach. Conse-

quently when the condition cannot be recognized definitely an exploratory thoracotomy should be performed whenever there is a reasonable suspicion of a primary tumor of the lung. If such a lesion is present it can be removed at the time when the operative risk is at a minimum and the chances for recovery are at their height.

Clinically we may recognize two distinct types of primary lung tumor, the pleural and the hilus type. The pleural type is most amenable to surgical treatment.

A reasonable suspicion of the presence of the pleural type of primary lung tumor is based upon the occurrence of a one-sided pleural effusion, with or without bloody fluid, in the absence of definite signs of tuberculosis. The roentgenograms of the chest taken when the pleural cavity is inflated after removing the fluid is one of the best methods to demonstrate the mass in the lungs.

The hilus type is not so amenable to treatment, and the most important indications of its presence are the persistence of chronic bronchitis in the absence of tuberculosis, with evidence of blood-tinged sputum and the subsequent evidence of a mediastinal mass with pressure symptoms. In these cases bronchoscopic examination is of the greatest diagnostic value and gives the earliest evidence.

Finally, I believe that careful study of many cases of recurrent pleurisy and chronic bronchitis will reveal that primary lung tumors are much more common than we have heretofore believed.

INTUBATION AND VISUALIZATION OF THE DUODENUM IN SUSPECTED LESIONS OF THE PYLORUS, DUODENUM, AND GALL-BLADDER.

By I. O. PALEFSKI, M.D.,

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THE technic and the diagnostic significance of this procedure were described previously.[1] Its purpose is to determine whether defective filling and distortion at pylorus and the first part of the duodenum, is due to ulcer, pericholecystic adhesions, pressure from neighboring organs or caused reflexly from the intestines or other abdominal organs. From the writings of Smithies,[2] Carman[3] and Cole[4] it appears that this differentiation is not always possible. The experience of Lockwood is of interest. He states:[5] "Over four-fifths of duodenal ulcers that I have seen

[1] Jour. Am. Med. Assn., December 4, 1920. Med. Rec., April 18, 1914.
[2] Jour. Am. Med. Assn., November 30, 1918. [3] Ibid., March 28, 1914.
[4] Lancet, May 2, 1914.
[5] New York State Med. Jour., December, 1917.

diagnosed by the roentgen ray have turned out nothing more than chronic appendicitis. The picture may be perfect, the photograph may be clear-cut; but the diagnosis derived from inference of disturbed gastric function and distortions of the cap may be alto-
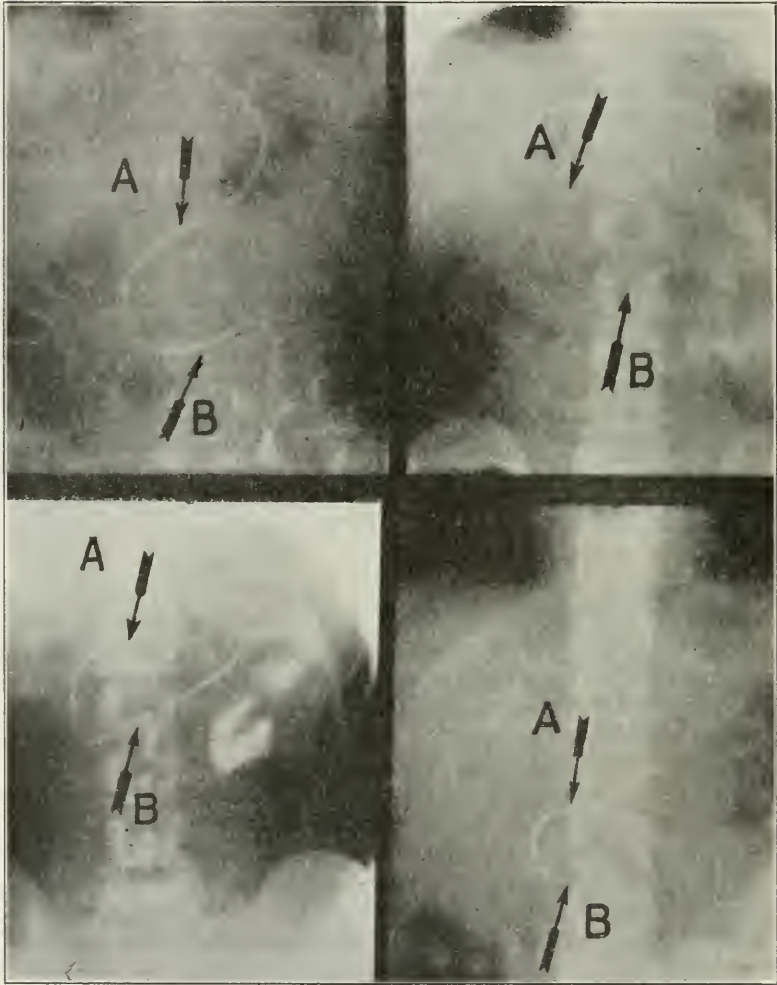
Fig. 1.—Curve of the duodenal tube in the normal duodenum. *A*, lesser curvature; *B*, duodenum and jejunum; normal distance between *A* and *B* is 7 to 9 cm.

gether valueless. My remarks are suggested by the results obtained from a variety of sources." Indeed, it appears to me that many of these roentgen-ray errors are preventable by using the fluoroscope, by making more exposures and by repeating examinations. It must be conceded that in a large number of cases the roentgen-ray

diagnosis of lesions about the pylorus, duodenum and gall-bladder is not corroborated even when made by a skilful roentgenologist. Experience has shown that defective filling, distortion, spasm and altered gastric evacuation are no more characteristic of duodenal ulcer than of periduodenal cholecystic adhesions and that the latter is usually taken by the roentgenologist for the former. Employing both clinical and roentgen methods, I have learned to depend chiefly upon roentgen-ray findings in gastric lesions and upon intubation and visualization of the duodenum in duodenal ulcer and gall-bladder disease.
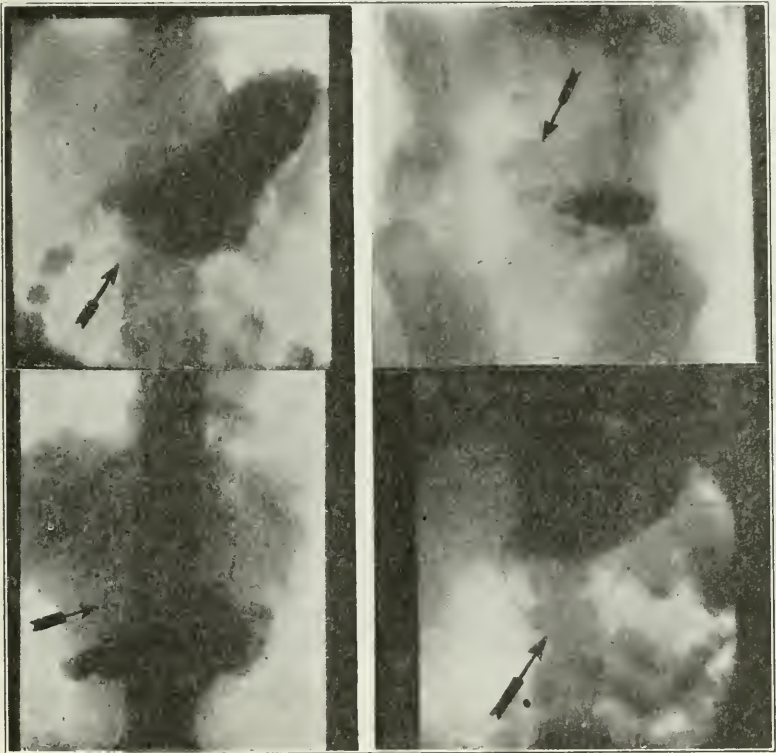
FIG. 2.—Variations in the curve of the duodenal tube in the normal duodenum in four patients. (Note arrows.)

Duodenal intubation and visualization is a clinico-roentgen procedure of twofold purpose: (1) The examination of duodenal juice for its physical, chemical, microscopical and bacteriological properties; a change in the normal color and transparency; the persistent presence of blood in any form; an increased amount of mucin and number of epithelial cells and bacteria in duodenal juice signify infection and inflammation situated in the duodenum, biliary ducts

or gall-bladder.   (2) A roentgen study is made of the course the
duodenal tube assumes from the stomach to the jejunum.   In
stomachs of normal size and position it forms a horseshoe curve;
the tubing in the third part of the duodenum is about 7 to 9 cm.
below that running along the lesser curvature (Figs. 1, 2, 4 and 6); in
peripyloric and periduodenal cholecystic adhesions this position is
altered.   The tube then appears either twisted, kinked or angulated
(Figs. 8, 10, 11 and 12).   Ordinarily these adhesions may escape detec-
tion or show roentgen signs indistinguishable from duodenal ulcer.

Fig. 3.—Double filling defect of the first part of the duodenum due to duodenal
ulcer discovered shortly after appendectomy.   Patient, H. F.   Male, aged twenty-
eight years.   Referred by Dr. H. Finkelstein, N. Y., June, 1917.   (See Fig. 4.)

The diagnostic significance of their presence lies in the fact, as em-
phasized by Smithies,[6] that these are usually associated with chronic
cholecystitis.   The detection of periduodenal adhesions, therefore,
should arouse the suspicion of the presence of chronic gall-bladder
disease.
    The technic of this procedure is rather simple, although at times
it may require two or three hours for its completion.   My modified

[1] Loc. cit.

duodenal tube,[7] owing to its small size and heavy weight, is best adapted for this examination. It is introduced to the 20-inch mark and the patient is given a glass of cool water to drink and then assumes the right posture. In the absence of obstruction the tube passes into the duodenum in thirty minutes and with the patient in the Trendelenburg position, reaches the jejunum in about one hour or longer. Specimens of duodenal juice are aspirated at short intervals and then the tube is injected with a suspension of barium, one-half glass of which is also taken by mouth. Roentgen-ray
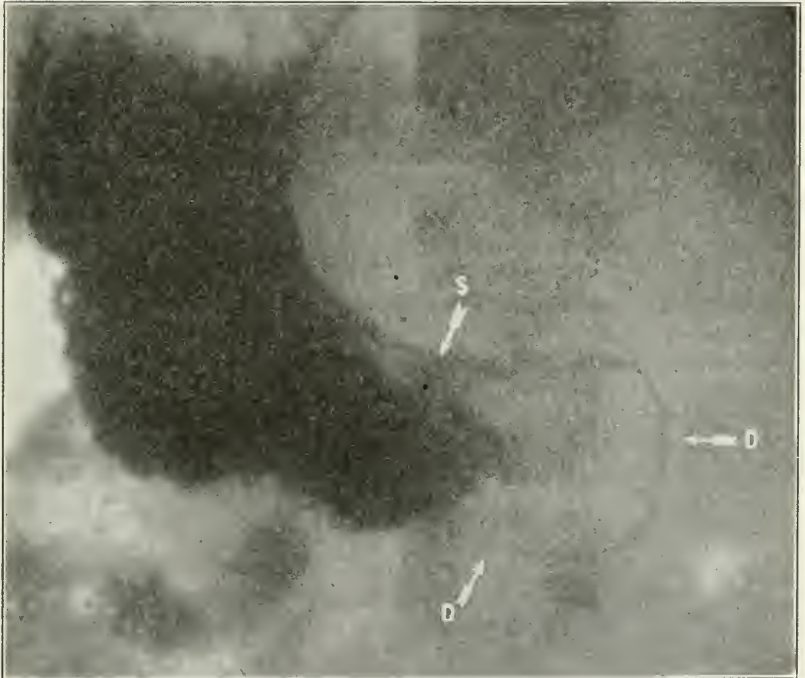
Fig. 4.—Patient, H. F. Note normal horseshoe curve of the duodenal tube in duodenal ulcer. Blood in the duodenal juice. Symptoms and filling defects disappeared since medical treatment, three years ago.

exposures are then made in the erect and prone, the latter being more diagnostic. Care must be taken to place the roentgen-ray tube at right angle to the patient and the latter flat against the screen holding the film. The duodenal tube is then slowly removed and cleansed. I have used this method in the following group of cases:

Prepyloric Ulcers and Adhesions. Ulcers situated at the antrum, not involving the lesser curvature, may either escape detection alto-

[7] Obtainable from the Kny-Scheerer Corporation, 56 West 23d St., New York.

gether or cause suspicion by only one or more minor roentgen signs,
such as incisura or intensified gastric peristalsis. In a number of
patients these ulcers do not cause pronounced symptoms, except
gastric distress, distention and eructation. On the other hand, peri-
pyloric cholecystic adhesions may produce marked gastric distortion
simulating typical penetrating gastric ulcer when surgical inter-
ference is urgently advised. The duodenal tube is of diagnostic

Fig. 5.—Defective filling of the duodenum in chronic appendicitis. Patient,
R. S. Female, aged twenty-two years, referred by Dr. M. Schmerzler, Brooklyn,
January, 1919. Exploratory laparatomy by Dr. H. Haubold, Harlem Hospital,
New York. (See Fig. 6.)

aid in this group of cases. Its passage into the duodenum is delayed
or prevented, owing to pylorospasm. Specimens of gastric con-
tents aspirated at frequent intervals may show occult blood in the
ulcer. In adhesions the distorted curve of the duodenal tube is
readily observed.

Duodenal Ulcer. Many a patient suffering from duodenal ulcer
is regarded as neurasthenic on the strength of negative roentgen-ray
findings. I have seen instances in which fairly large callous ulcers

of the cap showed no roentgen evidence whatsoever. On the
other hand, defective filling of the duodenum, in my experience,
is less frequently due to duodenal ulcer, as is generally supposed,
than to periduodenal cholecystic adhesions. A case with gastric
symptoms showing high gastric acidity one hour after an Ewald
meal, delayed gastric evacuation after a mixed meal, blood in duo-
denal contents and a normal horseshoe course of the duodenal tube
may safely be regarded as duodenal ulcer whether or not there is

Fig. 6.—Patient, R. S.   Note normal horseshoe curve of the duodenal tube.
Visualized appendix.   (See arrow.)

defective filling of the duodenum. It may be of interest to recall,
at this junction, the emphasis by Rehfuss[8] of the frequent presence
of bile, and blood in duodenal ulcer, in specimen of gastric con-
tents obtained by the fractional method "at the phase of tryptic
regurgitation" I found this, by roentgen-ray observation, to be due
to the passing of the metallic end of the tube beyond the pylorus.

[8] Jour. Am. Med. Assn., November 9, 1918.

The specimen is thus aspirated directly from the duodenum. It should be remembered that the tests, except the roentgen ray and the fluoroscope, for the localization of the tube, are not always dependable.

Chronic Cholecystitis with Periduodenal Cholecystic Adhesions. This group includes a large number of cases presenting a chain of symptoms simulating either ulcer, chronic appendicitis, intestinal stasis, neurasthenia or, in the female, ·pelvic disturbances. In

FIG. 7.—Defective filling of the duodenum in chronic cholecystitis, with periduodenal cholecystic adhesions simulating duodenal ulcer. Patient, M. G. Male, aged forty-one, referred by Dr. M. Weitzen, N. Y., June, 1917. Exploratory laparotomy by Dr. William H. Luckett, Harlem Hospital, N. Y. (See Fig. 8.)

many of these there is also roentgen evidence of duodenal ulcer. It is often a surprise to the clinician and surgeon when on exploratory laparotomy no ulcer is found, but instead a thickened gallbladder and periduodenal cholecystic adhesions. These cases can now readily be recognized by duodenal intubation and visualization. A case with gastric symptoms showing tenderness in the right hypochondrium, normal or subnormal gastric acidity, delayed gastric evacuation after a mixed meal, a distorted course of the duodenal tube with or without defective filling of the cap may safely

Fig. 8.—Patient, M. G. Note deflected course of the duodenal tube in periduodenal cholecystic adhesions. The tube in the third part of the duodenum is above that at the lesser curvature. (See arrows D and S.)
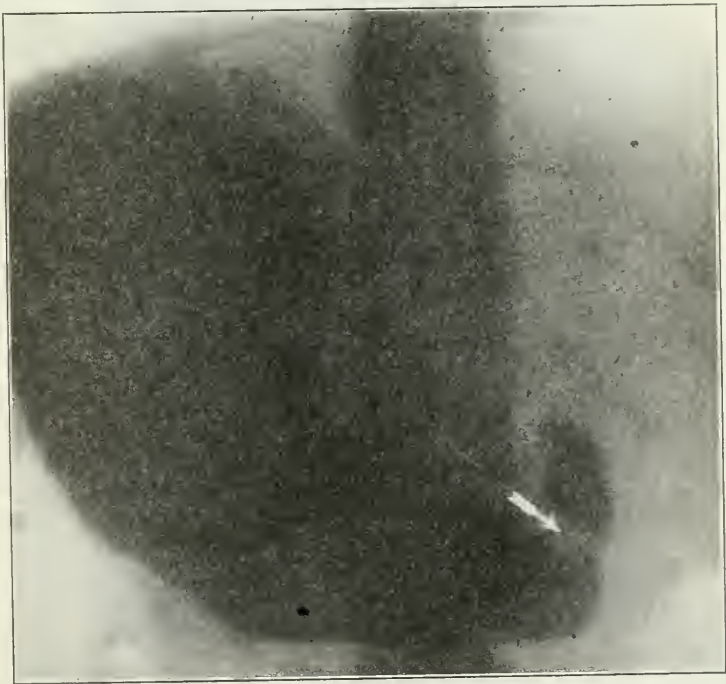
Fig. 9.—Normal pylorus and duodenum in periduodenal cholecystic adhesions. Patient, S. R. Female, aged twenty-two years. Exploratory laparotomy by Dr. William H. Luckett, June, 1917. (See Fig. 10.)

FIG. 10.—Patient, S. R. Note angulation of the duodenal tube in the duodenum due to periduodenal cholecystic adhesions. (See arrow.)
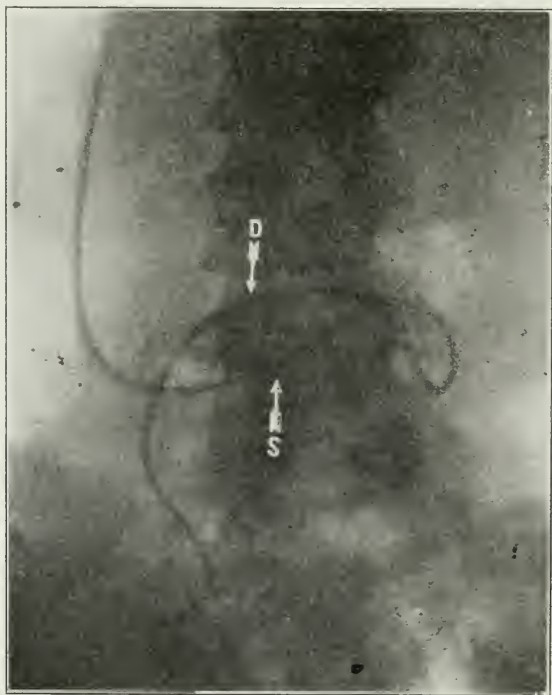
FIG. 11.—Perigastric periduodenal adhesions. Patient. R. F. Exploratory laparotomy by Dr. William H. Luckett, Harlem Hospital. Note twisted course of tube. The duodenum (D) is above the lesser curvature (S).
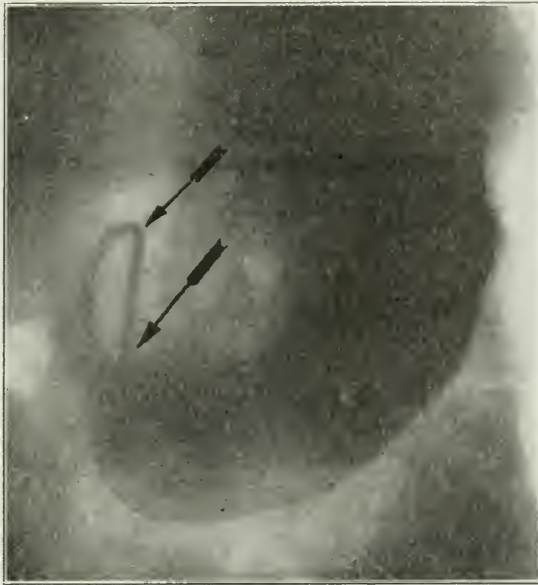
FIG. 12.—Postoperative periduodenal cholecystic adhesions causing biliary colic and jaundice. Patient, R. Female, aged forty-eight years. Exploratory laparotomy by Dr. C. Goodman, Beth Israel Hospital, N. Y. Note twisting of the tube in the second part of the duodenum, the latter being internal to the first part. (See arrows.)

FIG. 13.—Jejunal obstruction following gastro-enterostomy caused by perijejunal adhesions. Patient, S. G. Female, aged thirty-one years. Exploratory laparotomy by Dr. C. Goodman, Montefiore Home and Hospital. (See Fig. 14.)

FIG. 14.—Patient, S. G. Note twisted curve of duodenal tube.

FIG. 15.—Patient, S. G. Note normal course of the tube in the jejunum after separation of the adhesions.

be regarded as chronic cholecystic adhesions (Figs. 6, 7, 8, 9). Most of these cases also show gastric hypermotility six hours after a barium-zoolak meal, turbidity, increased mucin, epithelial cells and bacteria in the duodenal juice. There is usually a history of constipation.

Postoperative Adhesions. Duodenal intubation and visualization offer a practical method of detecting postoperative adhesions after surgery upon the stomach and gall-bladder. In some cases adhesions do not evidently cause pronounced symptoms, while in others the symptoms are suggestive of interference with the patency of the common bile duct or with gastric evacuation (Figs. 12, 13, 14 and 15). In recurrent symptoms after gastro-enterostomy the duodenal-tube is allowed to pass through the anastomosis and outline the jejunum. In perijejunal adhesions the course of the tube in the jejunum is twisted (Figs. 13 and 14).

The conclusions drawn in this paper are based upon an experience of several years on a considerable number of patients, including about 400 established cases. It is not intended that this method should distract from the diagnostic value of the older and well-established methods, but when combined with them at least 90 per cent. of duodenal ulcers and no less than 75 per cent. of gall-bladder disease should be detected even in their incipiency. I must emphasize, however, the importance of proper technic.

THE TREATMENT OF EMPYEMA WITH GENTIAN VIOLET.

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(From the Henry Ford Hospital.)

Our conceptions of the etiology, pathology and treatment of empyema have undergone a marked change as the result of observations made during the past two years. It may be a question whether our influenza experience has brought out striking advances in the therapy of that disease, but there can be no doubt that in the treatment of postinfluenzal empyema we have made tremendous strides. Whether these lessons learned in the treatment of postinfluenzal empyema are applicable to other forms of empyema the future must decide.

The treatment of empyema following influenza by the older orthodox surgical methods was followed by such an appalling mortality that many felt we were dealing with a disease quite different from the conventional postpneumonic empyema of the past. Also, postinfluenzal empyema is a complication of bronchopneumonia

and presents many differences when contrasted with an empyema following lobar pneumonia, from which we have gained most of our knowledge of empyema in the past. Moschcowitz,[11] however, pointed out that empyema in the past was not a benign condition, the figures at Mt. Sinai Hospital in New York from 1904 to 1914 showing a mortality of 28 per cent. He collected further statistics which show that the death-rate in empyema before the two great influenza epidemics varied from 18.9 per cent (Lilienthal) to 55 per cent (Lavrow). This high mortality was not generally appreciated, however, until empyema was seen *en masse* in the great army hospitals during the past two years as a complication of influenzal bronchopneumonia. The marked fall in the death-rate which followed the policy of delaying operation and of carrying out first a series of preliminary aspirations suggest the interesting query whether these newer methods of treatment would have lowered the empyema mortality in the past.

During the past winter a large number of persons suffering from influenza were treated at the Henry Ford Hospital, where many of these patients developed empyema. It is the purpose of this report to discuss the results obtained in treating these empyema cases, and particularly a group treated by repeated aspirations and intra-pleural instillations of gentian violet.

Many differences of opinion prevail regarding the cases to be considered as empyema. Hartwell[7] in his discussion of empyema uses the term to indicate "a purulent exudate within the general pleural space." "Local collections of pus," he states, "walled off by adhesions are intrapleural abscesses or interlobar abscesses," and as such he excludes them from his discussion. Moschcowitz (*l. c.*), on the other hand, states that "nearly every empyema is an encapsulated one." Aside from these differences in opinion based upon anatomical considerations there are differences in terminology dependent upon the character of the pleural effusion, many observers limiting the term empyema to cases yielding only frank macroscopic pus. Graham,[4] however, in his summary of reports from the various Base Hospitals notes that the exudate most commonly found is a slightly turbid serofibrinous fluid. In our group of cases all patients showing a turbid pleural fluid containing microörganisms are classed as empyema, the fluid in question varying from a slightly turbid serofibinous exudate to a thick, creamy pus.

Objection may be raised to the inclusion in our discussion of certain cases as postinfluenzal empyema, on the ground that they were simply cases of streptococcus pneumonia complicated by streptococcus empyema. As certain of these cases were not observed until after the onset of the empyema, and as the symptoms of influenza show much variation, this objection has some weight. On the other hand these cases of empyema occurred during the height of the influenza epidemic, presented a similar clinical picture, ran the

same clinical course and had bacteriological findings identical with those cases of influenza observed from their onset. Because of this similarity and the lack of definite evidence to the contrary all the cases of empyema occurring during this epidemic have been considered as a single group. Also it must be emphasized that at the present time we have no definite criteria, either clinical or pathological, by which postinfluenzal streptococcic empyema can be differentiated from empyema following a primary streptococcus bronchopneumonia occurring during an influenza epidemic, or in fact from an empyema complicating a measles bronchopneumonia.

The study of our series of cases, although small, brings out some points of interest. In all there were admitted to the hospital 312 cases with the clinical diagnosis of influenza; 40 of these cases, or 12.5 per cent, developed empyema, and of these 17 died, a mortality of 42.5 per cent. This mortality is higher than that reported in a summary of 25 army camps collected by Graham, which was 30.2 per cent, but not so high as that reported from some of the Base Hospitals—for instance, Camp Funston with 84 per cent and Camp Wheeler with 65 per cent. These statistics, however, like many of those published, lose much of their value because of a failure to distinguish between the mortality of empyema and that due to bronchopneumonia. Graham (*l. c.*) has also pointed out that in the army statistics much of the discrepancy is due to differences in definition of the term empyema. In those camps in which the term empyema was limited to cases showing frank pus the mortality was the lowest, while in the camps including also cases of serofibrinous effusions the mortality was much higher. The latter classification was used in our series and doubtless accounts in great measure for the high mortality. The differentiation made by Graham agrees with the observations of many writers, and our cases also show that the serofibrinous exudation corresponds in time to the presence of an acute pneumonic process, and consequently the period in which most deaths occur.

The conclusion of Moschcowitz (*l. c.*) that when a patient dies with an empyema in the acute stage the cause of death is the pneumonia and not the empyema is shared by most observers. Fifteen of our 17 deaths occurred in the presence of an acute demonstrable pneumonia, 10 of them within one week after admission to the hospital. Eleven of the fatal cases showed a serofibrinous exudate, 6 showed frank pus. One of the latter, however, died from streptococcus peritonitis following ulceration of the bowel and one other patient was a case of neglected empyema admitted *in extremis.*

The disastrous experience following too hasty operative intervention in empyema was so uniformly noted in the influenza epidemic as to constitute the most important single observation made on this subject during the past two years. Rodman[14] noted in his work at Camp Bowie that the mortality was 45 per cent in the cases

in which the method of early operation was employed. Later, when he aspirated until frank pus appeared, the mortality dropped one-half. Stone[15] reported a mortality of 61.2 per cent in 85 patients operated upon immediately following the establishment of the diagnosis. Among 190 patients operated upon after a series of preliminary aspirations the mortality fell first to 12.6 per cent and a later series showed a still lower rate of 9.5 per cent. Following a series of such experiences reported from various parts of the country the method of preliminary aspiration rapidly became the method of choice, and its value was emphasized particularly in the report of the Empyema Commission[4] and in a more recent article by Moschcowitz (l. c.). A number of methods of closed drainage also made their appearance; the method of Mozingo,[10] irrigation with Dakin's solution through a trocar; the method of Phillips,[13] irrigation through a catheter, and the method of Harloe,[6] who inserted a catheter into the chest through which the pus was aspirated at various times, and which was clamped off during the intervals. Each of these three methods gave excellent results in the hands of their originators. A similar treatment was employed by Manson,[9] who treated a series of cases by repeated irrigation with chlorinated soda through a catheter. He treated 43 patients by this method; all were cured and no secondary operation was necessary. In discussing the excellent results obtained by many observers who employed first aspirations followed later by operation it must be emphasized that their low mortality was due partly at least to the fact that they were treating the more resistant patients of their series, the others having already succumbed to an acute bronchopneumonia.

Many scattered instances are reported in which the empyema cleared up under the preliminary aspirations and resort to operation became unnecessary. At the onset of our empyema experience repeated aspiration was performed on the patients with the object of preparing them for a subsequent operation. It was thought at the time that this preparation would be assisted by the use of some bland antiseptic solution capable of destroying bacteria without causing any marked irritation of the pleural surfaces. The solution used for this purpose was an aqueous solution of gentian violet, which has been shown by the investigations of Churchman[1 2 3] to possess a high bacterial value in vitro for most Gram-positive organisms, and also to have a value in the treatment of suppurative processes.

The procedure was as follows: The chest was aspirated by means of a Potain aspirating outfit, the fluid withdrawn and 100 c.c. of an aqueous solution of gentian violet introduced into the chest through the aspirating needle by means of a Luer syringe. This solution was allowed to remain until the next aspiration. At first a dilution of 1 to 10,000 was used, followed later by dilutions of 1 to 5000 and

1 to 1000. Later in the series the first instillations were used in the strength of 1 to 5000, followed rapidly by an increase in strength to 1 to 1000. As this method was followed in a number of the earlier cases by a sterilization of the pleural exudate and clearing up of the empyema the procedure was extended to all the cases coming under observation. The greater number of the cases cleared up under this treatment, there were some failures, and in a few instances it is now apparent that surgical intervention should have been resorted to earlier.

Twenty-seven cases in all were treated in this way. Of this number 14, or 51.8 per cent, were cured; 8, or 29.6 per cent, were not cured by this procedure but later came to operation; 5, or 18.5 per cent, died. Of the fatal cases 3 died of pneumonia present on admission and persisting during treatment, while 1 patient died of peritonitis having its origin in a diphtheritic enteritis with ulcer formation and perforation of the intestine. This mortality of 18.5 per cent, although admittedly high, is mostly a pneumonia rather than an empyema mortality, and compares favorably with the mortality statistics previously quoted and also with those of Ingraham,[8] who reports an operative mortality of 31.8 per cent, and of Gray,[5] whose mortality was 21 per cent.

The character of the fluid obtained in the successful group of cases varied. In 3 instances it was serofibrinous, 2 of these patients clearing up after two treatments and the third after six treatments. A fourth patient showing a similar fluid cleared up after two aspirations without the use of any gentian violet. This recovery was not included in the statistics for this reason. All of these showed a pure culture of Streptococcus hemolyticus in the pleural fluid. Another patient with bronchopneumonia developed a sterile serofibrinous effusion that disappeared with one aspiration, the case resembling one reported recently by McCrae,[12] who describes a turbid pleural effusion in a case of lobar pneumonia that cleared up following one aspiration.

In 6 of the 14 successful cases frank pus was obtained at the first aspiration and the fluid continued to be quite thick and purulent, later becoming thinner and finally disappearing altogether. This group is of considerable interest in showing that cases with frank pus do clear up following repeated aspiration and gentian violet instillations, and that rib resection with open drainage is not the only method whereby such cases can be cured.

In 5 of the cases the fluid was at first serofibrinous but later became markedly purulent and remained so until it cleared up. In all, 11 out of the 14 showed frank pus during the course of treatment, and belong to the group of undisputed empyema cases.

Bacteriological studies of the pleural fluid in the 27 cases treated by aspiration and gentian violet injections showed the hemolytic streptococcus present in pure culture in 17 cases; associated with the

B. influenzæ in 4; associated with the pneumococcus in 2; associated with both the pneumococcus and B. alkaligenes in 1; while in 1 instance the Streptococcus hemolyticus, pneumococcus and B. influenzæ were all found at various times in the fluid; in 2 of the cases the pneumococcus was grown in pure culture. In those cases showing more than one organism in the pleural fluid the bacterio-logical findings varied with different aspirations, one microörganism growing at one time, another at other times and often both together.

The number of treatments employed before recovery varied greatly. While in one instance only one treatment was necessary thirty-eight had to be employed in another case. The average has fourteen to sixteen. There was no appreciable difference between the number of treatments necessary in cases in which frank pus or where serofibrinous fluid was obtained at the first aspiration. These results are of interest in emphasizing that in all cases the fluid after a few aspirations became purulent and that the presence of a sero-fibrinous fluid indicated only that the patient had been aspirated at an earlier stage.

In the successful cases two noteworthy effects of treatment were observed: a gradual lowering of temperature and a diminution in the amount of fluid obtained at thoracentesis. While a decrease in the amount of fluid was usually a good sign, yet this alone without a lowering of temperature did not prognosticate a favorable outcome, as it occurred in a few patients who failed to clear up. This failure of the amount of fluid obtained at tapping to serve as a prognostic index is probably to be explained anatomically—a failure to drain the cavity thoroughly because of inaccessible pus pockets.

A study of the temperature curves in all of the successful cases showed that the treatments very soon reduced the fever. In some instances this fall was rapid and a normal temperature was reached in from two to seven days. Such a reduction was, however not the rule, and the average length of time before a normal temperature was reached was fifteen days, during which time the patients were treated from once a day to once in three or four days. In our experience those patients who were treated frequently, as often as every day in the beginning of the temperature, made, as a rule, the most rapid and satisfactory recoveries. In several instances the patients after a week or longer of normal temperature showed sudden rises of temperature which persisted for a few days but disappeared when treatment was resumed. Several patients also showed com-plications in the form of erysipelas and acute arthritis which com-plicated the picture of the temperature curve and undoubtedly extended the febrile stage.

In contrast to this fall of temperature in the successful cases the unsuccessful ones showed neither rapid nor gradual response to aspiration and gentian violet instillation. In most of these cases this treatment did not produce freedom from fever for a single day.

In one case there were occasionally remissions of one to two days followed by periods of fever lasting from one to two weeks. One other case showed marked reaction to tapping and fever-free periods of a week at times. This patient was later operated upon at his own request.

The absence of microörganisms in the pleural fluid was, of course, a favorable sign, but one which, as a rule, appeared late in the course of treatment. In many patients also the fluid was not wholly sterile at the time of the last aspiration, although the number of microörganisms was very greatly reduced. The leukocyte count, while it steadily fell as the patients responded to treatment, showed such great variations that it could not be used as a very reliable prognostic index.

The result of these observations indicates that definite response to the treatment should appear within two or three weeks of frequent treatments if this method is to result in recovery. If this response is absent, successful results with this treatment are doubtful and thoracotomy is indicated.

Moschowitz (l. c.) in discussing the pathology of empyema lays stress upon the presence of ruptured subpleural pulmonary abscesses and states that irrigation of empyema cavities with irritating solutions such as Dakin's solution results in coughing and choking. In our experience the presence of such communications between the bronchus and the pleural cavity was strikingly shown by the appearance of a violet-stained sputum in 19 of the 27 cases treated. In the first cases noted the question was raised whether the appearance of the dye-stuff in the sputum was not due to penetration of the lung by the aspirating needle. While this possibility cannot be absolutely ruled out, further observation led to the conclusion that it was unlikely. In all aspirations extreme care was used not to penetrate the lung itself; the appearance of the dye-stuff in several cases was instantaneous upon introduction of the gentian violet into the pleural cavity; also in other patients the dye-stuff was coughed up suddenly several days after the intrathoracic injection. In another group of patients the frequent expectoration of thick pus led to the conclusion that a bronchopleural fistula was present.

The duration of the patient's stay in the hospital after the development of empyema is a question that must be taken into consideration in the choice of a method of treatment. This question has not been studied in detail in many of the empyema reports doubtless because of the difficulty in tracing these cases which in the army camps were frequently transferred. Ingraham (l. c.) states that the average stay of his cases in the hospital was 78 days— 22 days before operation and 56 days following operation. Gray (l. c.) found the average number of days in the hospital to be 92 at Fort Des Moines. Tinker and Wattenberg[16] have reported in

their studies on the treatment of empyema some interesting figures. Their series comprise 80 cases—all but 6, however, were operated upon elsewhere and transferred to them for after-treatment. The average stay of the patients in their hands was only 34 days, but as the average length of suppuration before admission was four months their general average was over five months. One of their patients had been suppurating eleven months before coming into their hands and another was under treatment for five months before recovering.

The average stay in the hospital necessary for our cases, which were cured by aspiration and gentian violet instillation, was 76 days, the longest 120 days, the shortest 25 days. The average length of stay in the group unsuccessfully treated and later subjected to thoracotomy was 101 days, the longest 112 days and the shortest 92 days. The patients who were operated upon were discharged from the hospital on the average of 39 days after operation. This indicates that the previous treatment of the patient by aspiration and intrathoracic injection had not, as a rule, rendered the surgical problem more difficult nor delayed the time of recovery. In one conspicuous example a bilateral empyema by means of this treatment cleared up on one side, and the remaining empyema being limited to one side, proved a simple surgical problem. The average length of stay of all patients was 84 days, which compares favorably with the figures above mentioned. This period of time could doubtless have been somewhat shortened by an earlier operation in a few of the cases which failed to improve rapidly after treatment and and who in the light of our experience now should have been operated upon sooner. Our cases also were kept in the hospital on the average of a month with a normal temperature before discharge, a period which doubtless could be considerably shortened.

The cases in this series have been followed closely in order to ascertain the after-results of the treatment. One of the patients died subsequently after discharge from the hospital from what was apparently acute cholecystitis. This patient had responded very readily to treatment, and at the time of her discharge showed nothing abnormal in the chest but the presence of some pleural thickening. Nine of the patients returned to the hospital in response to recall letters and showed only the signs of a thickened pleura on the affected side. All of these persons are at work and consider themselves cured. The physical signs at present do not indicate an excessive pleural thickening and none of them show any recognizable deformity. Four other patients have been followed by letter and have made perfect recoveries. Letters from their physicians of 2 of these state that they have recovered entirely and show only slight signs of a thickened pleura. There have been no relapses. This point has been very carefully studied, and this report has been delayed largely because it was desired to allow a sufficient

time to elapse to be sure the patients were cured. It has now been over four months since the last patient was discharged from the hospital.

Summary. In a series of 27 cases of postinfluenzal empyema, 14, or 51.8 per cent, were cured without operation by repeated aspiration and intrapleural instillations of gentian violet. No relapses occurred and no deformities of the chest developed. The presence of frank pus was no contra-indication to treatment by this method. It is possible that some of these cases would have recovered without the use of gentian violet installations, yet because of the prompt symptomatic response to such injections and the rapid diminution or disappearance of bacteria in the pleural fluid it was evident that the dye-stuff possessed a very definite bactericidal value.

The most valuable indication that a patient is responding to treatment is a lowering of temperature immediately following aspiration, which persists and gradually reaches normal. A diminution of microörganisms or a frequent absence of them in the aspirated fluid is a favorable sign, but only when there is a temperature response to aspiration. Patients who failed to show such reactions to treatment in 15 to 20 days in our experience did not recover by this method. If the aspirations and instillations are not effectual within this time surgical intervention is indicated. This method of treatment should delay the operation only slightly longer than usual while making an attempt to clear up the empyema during this period. Failures were due usually to inability to empty the pus because of extensive pocket formation—a fact demonstrated at operation.

In the great majority of the cases repeated aspiration after thorough cocainization of the skin was performed without any great discomfort. The absence of any drainage tube through the chest wall permitted the patients great freedom of movement, both while in bed and later when they were walking about.

It is difficult to discuss the amount of time necessary for treatment by this method because of the limited number of cases treated. All of the patients were kept under observation in the hospital for a much longer period than necessary. This has lengthened considerably the average duration of stay in the hospital for this series of cases. Many of these patients were up and about the hospital for four or five weeks before discharge, receiving during this time one to two treatments a week. Such patients could be discharged earlier and have the occasional aspirations carried out in the out-patient department.

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THE ADVANTAGE OF SERUM THERAPY AS SHOWN BY A COMPARISON OF VARIOUS METHODS OF TREATMENT OF ANTHRAX.

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Various methods of local therapy of anthrax have been in use for many years past, and are still widely employed either alone or in conjunction with other measures.   If one has the time to consult the literature dealing with the subject, whether it be in periodicals or in text-books, it is at once evident what wide differences of opinion exist as to the most effective method of treatment.   This is unfortunate and is liable to lead one to the conclusion that most all the usual methods give about the same results and it is not therefore a vital matter which one is employed in the individual case.   This view-

point must be changed, as there is now accessible certain indisputable facts which prove it to be incorrect. Almost all the measures of local therapy in common use possess too many disadvantages to be considered locally effective, and they are uniformally without claim to a specific effect once an anthrax septicemia has originated. Some of them have even the danger of increasing the possibility of this latter grave complication (septicemia) supervening.

An ideal method of therapy for anthrax is one which fulfils best the following points: (1) It should be appliable to the various forms and locations of the disease; (2) should have the lowest mortality rate; (3) should be as specific as possible; (4) possess no danger of generalizing the local infection; (5) offer the least amount of scarring and deformity; (6) cause a minimum of pain; (7) entail the shortest absence from employment.

To draw any conclusion as to the method which best fulfils these points, the various measures of therapy in use must be first reviewed and their advantages and disadvantages considered.

Thermocautery is one of the oldest methods of treatment known (Schwartz[1]), and despite its many objectionable features it is still widely employed in many parts of the world. It is an extremely painful procedure, and when the lesion is extensive, especially when on the face or neck, it leads to hideous deformity, and prolonged convalescence if the patient recovers. It destroys rather indiscriminately both dead and living tissue, and unless applied thoroughly, which is surely an heroic measure in voluminous anthrax, it may seal off from free drainage tissue which is still infective.

Moreover, the barrier zone to the infection which nature has established may be in part or entirely broken down and generalization may thus originate. The treatment is not in the least specific, and when an anthrax septicemia exists is of no avail. For all these reasons it should be entirely omitted from the therapy of the disease.

Chemical caustics have been widely used in anthrax. Many writers advocate them as the only method of treatment, but in the majority of instances they are advocated as secondary measures. Among the caustics recommended are chloride of lime, nitric acid, zinc chloride, carbolic acid, bichloride of mercury and caustic potash. Graef[2] has reported a mortality of 5 per cent in 38 cases, and Scharnowski,[3] Bidder,[4] Arnozan Laude and Maranger[5] report successful results. The latter three authors, however, have abandoned the procedure owing to the vivid pain which ensues. That the method is uncertain the experience of Morosof[6] shows, for he has been unsuccessful in 2 cases, although in 1 he gave twenty-eight injections of 3 per cent carbolic acid and in the other seventy-six injections of 4 per cent carbolic acid in the depth of the pustule. Amory and Rappaport[7] report 3 recoveries by combined excision and cautery, but in 1 instance it required twenty days for the bacilli to disappear on culture from the lesion, and in another the patient

recovered only after three months. Whitla[8] mentions 2 per cent iodine for local injection and Chauffaud and Boidin[9] report the use of subcutaneous injections of 1 per cent carbolic acid and a solution of Gram's iodine. They admit that the latter solution is horribly painful and both are equally inefficacious.

Chemical cauterization has many of the same contra-indications mentioned under thermocautery. The possibility of poisonous effects or nephritis originating is an additional danger. Superficially applied these caustics are only palliative, and to be in the least effective the application must be thorough, and with many it should be repeated. Their lack of specificity is evidenced also by the diversity of the chemical solutions recommended.

Surgical intervention in the therapy of anthrax comprises two forms—incision and excision.

Incision has fallen in much disrepute as a mode of treatment, especially in Italy and France. Yet it is still often used, both here and abroad, particularly in instances in which the physician fails to recognize the disease and believes he is treating an ordinary carbuncle. The danger of the method was long ago recognized by the French physicians. Guerin,[10] Faucon,[11] Richard,[12] Chambert[13] and more recently Despres[14] warn of the danger of an erysipeloid or purulent inflammation of the wound setting in following operation. It is characteristic that patients treated by incision commonly develop the more severe types of the disease, and not infrequently die. Verneuil[15] gives interesting statistics on this point: "Among 6 patients so treated all died."

Incision has no place in the therapy of anthrax. It is not only contra-indicated but is actually dangerous. The operation breaks down the barrier zone to the infection and opens wide the blood and lymphatic channels of absorption, at the same time failing to remove the infected focus. As a result, increase in the extent of the local involvement and grave possibility of a generalized infection supervening are to be expected. It is also to be remembered that Marchoux[16] showed experimentally in animals that anthrax bacilli multiply rapidly in blood-clots, as they are not then so susceptible to leukocytic activity. Instead of assisting in the cure the operation further endangers the patient's life.

Excision at the present time is the most commonly used method in the therapy of the disease. It is, however, so frequently combined with thermo or chemical cautery or with serum that it is difficult to tell to which the results obtained are mostly attributable. Courtellement and Weill-Halle,[17] Dudley,[18] Ellitrop[19] and Raymond[20] are among the advocates of the method. Dudley combines the treatment with cauterization and serum, as used at Guy's Hospital, London, while Ellitrop administers anthrax vaccine. Some surgeons, among them Paget and Gosselin[21] and Despres,[22] believe that one should never resort to excision no matter what the location of the

lesion. Picaud[23] and Pratorius,[24] the latter on the basis of his extensive experience with anthrax, advise against excision. Müller[25] and Hiss and Zinsser[26] have found it impossible to prevent the spread of the disease in guinea-pigs by immediate excision of the site of inoculation. Scholl[27] recently compared the results obtained by the surgical and non-surgical treatment in 51 cases: 4 (44 per cent) of 9 cases treated surgically died while only 3 (7 per cent) of 42 cases treated non-surgically succumbed. One patient only recovered after amputation at the shoulder-joint. In conclusion, he states "that in several of the surgical cases a rapid increase in edema, a steady decline in the patient's general condition and death several hours later definitely pointed to the operation as a causative factor."

Excision despite its advantages over incision and thermo or chemical cautery has certain outstanding limitations and disadvantages. Thus in anthrax of the face it will always be objectionable from the esthetic viewpoint. Likewise when the neck is involved, if the disease is at all extensive, excision leaves often an extensive surface devoid of skin, with resulting scar-tissue formation and contracture, and, if skin-grafting is not performed, convalescence is much prolonged. The pain of the operation and possible hemorrhage must also be considered. Probably the most frequent source of danger is the difficulty of accurately defining the area to be excised, especially when the edema and induration are marked, as microscopic sections have at times shown bacilli far beyond the exact limits of the pustule in the edematous zone. To excise less than the entire area involved is to subject the patient to the pain and discomfort of the operation without a compensatory result in the way of a certain cure. On the contrary, as Nature's barrier zone is broken down and the blood and lymphatic channels are opened, the danger, local and general, of disseminating the infection is much increased. Since anthrax in man is primarily a local disease and usually remains thus—any treatment which may tend in the slightest way to generalize the infection is scarcely to be looked on as proper therapy. Once a septicemia exists the treatment is only palliative. Then, again, bacilli may persist in the wound for almost three weeks after operation (Rappaport and Amory's case), and in the presence of blood-clots rapid multiplication may occur. For all these reasons the writer believes excision should likewise be omitted from the routine therapy of the disease.

Various other methods have been advised locally in anthrax, many of which are only palliative measures, and some of which are claimed to be somewhat specific. Among the former may be mentioned wet dressings of various antiseptics, as advocated by Verneuil[29] and pulverization with bichloride, as advised by Savini.[30] All these measures evidently exert their action too superficially to be of any direct curative value and are at best only secondary measures. They may provoke inflammation, as Ricaud and

Launoy[28] have pointed out. The value of the subcutaneous injection of oxygen locally into and around the pustule, as recommended by Thiriar[31] and Theiry,[3] has not been established; moreover, anthrax bacilli grow well in atmospheric oxygen. Ramstedt[33] in 7 cases and Müller[34] in 13 have employed symptomatic treatment and rest with complete success. Such measures, while useful adjuncts to a more specific method, cannot be relied on alone, and it represents an attitude of therapeutic nihilism to allow a disease to take its own course if a remedy of proved value is at hand. The use of steam as advocated by Gucciardello[35] is too severe a measure for routine employment and its specific nature is not proved.

In the second group may be mentioned powdered ipecac, arsphenamine, extract of Bacillus pyocyaneus and normal beef serum.

Muskett[36] reports the successful treatment of 50 cases with ipecac paste locally. Both he and Washbourne[37] have experimentally found ipecac to destroy readily anthrax bacilli. This treatment, while not to be relied on alone, owing to what impresses one as a too superficial action, is a useful supplementary measure to a more specific mode of therapy.

Fortineau[38] uses extract of Bacillus pyocyaneus on the basis of antagonism existing between that bacillus and anthrax. He reports 32 cases, with 1 death. Further reports are necessary to establish the value of this local method. It has not been proved to be effective in anthrax septicemia, and the question of its value in the more virulent types of the local disease is still to be settled. It is not usually accessible for use, which is another disadvantage.

Arsphenamine has experimentally been proved of value by Shuster and Laubenheimer,[39] Laubenheimer[40] and Becker.[41] Each reports a recovery in septicemic cases with the drug. The results are encouraging but the treatment is in its experimental stage.

Normal beef serum has been advocated by Kraus, Penna and Cuenca.[42] They report a total of 415 cases with 4.3 per cent deaths. In the last 180 cases treated there were 11.6 per cent deaths, or 3.4 per cent, omitting intestinal cases. Lignieres[43] denies the value of beef serum in anthrax and reports experiments to prove his contentions. Kolmer[44] has also recently shown that while beef serum contains some antibactericidal properties it is without demonstrable protective and curative value in experimental infections in mice and rabbits.

Hutyra[45] has proved that immune anthrax horse serum gives higher protection in test animals than normal serum. In a recent article[46] in current literature the value of beef serum is again repudiated. Therefore Kraus's contention must still be accepted with reserve until such a time as normal beef serum has been shown to be experimentally and practically as effective as anthrax serum. In the absence of immune serum, normal serum may be tried until the former is obtained.

Anti-anthrax Serum. The credit for the original production of this serum is due to Marchoux, of France, and Sclavo, of Italy, both investigators publishing their work in 1895. Marchoux succeeded in immunizing sheep to anthrax by use of attenuated cultures, according to the method devised by Pasteur, Chamberland and Roux, and then by hyperimmunization with virulent cultures, in increasing doses at intervals of a week, obtained a serum possessed of both prophylactic and therapeutic properties.

Marchoux[16] showed that an immune sheep serum of (1–200 titer) was curative for rabbits in doses of 7 c.c. when it was inoculated at the same time or seven hours after the subcutaneous inoculation of $\frac{1}{3}$ c.c. of virulent anthrax culture. It was likewise effective in preserving life in 10 c.c. doses when it was injected twenty-four hours after the virus.

Sclavo,[47] working along somewhat similar lines to Marchoux, using, however, larger animals, at first goats and later asses, succeeded in producing a potent serum for use in human cases of the disease. As recently prepared, 10 c.c. of the serum thus obtained protects a rabbit from 0.5 c.c. of fresh virulent broth culture. Sclavo immunizes his animals over a long period of time, often as long as two years. Sobenheim[48] has modified the original methods of immunization further by employing simultaneous inoculations of anti-anthrax serum and culture, the latter being at first attenuated and later highly virulent, and given in increasing amounts until the animals (sheep) could withstand enormous doses. The serum was injected on one side of the animal's body and the virus on the opposite side. The serum obtained thus had the usual prophylactic properties for experimental animals (rabbits) in 10 c.c. doses, and also protected non-immune sheep (2 out of 5 animals) inoculated with a virulent anthrax culture in doses of 40 c.c. given from ten minutes to six hours after the cultures. Sobenheim used his method of immunization with complete success in a herd of 2700 cattle without any deaths or ill-effects attributable to the inoculations and with the complete disappearance of any further cases of anthrax among them.

Sclavo serum has been used extensively in Italy and South America both prophylactically and therapeutically in cattle and also in the treatment of the disease in man. It has, however, been very little employed in this country, and it is only in the last few years that the serum treatment of anthrax has come at all into use in the United States. The more frequent employment of immune serum in human cases of the disease is in no little part due to the fact that for the last few years the Bureau of Animal Industry in Washington has been preparing and has been distributing on request a very potent anthrax serum.

The credit for the perfection of this very potent serum is due to Dr. A. Eichhorn,[49] formerly chief of the bureau, and his collaborators.

In an attempt to find a more satisfactory method of immunization than those now in use they resorted to combined immunization with potent anthrax serum and carefully standardized spore vaccine, and found this method to possess marked advantages over the older Pasteur method. (The Pasteur method possessed certain hazards either in that the vaccine was too weak to protect or too virulent to be safely used[50]). During the progress of the work repeated occasions arose to treat a considerable number of afflicted animals with the serum thus produced, and remarkable recoveries were obtained in a very high percentage of the cases, including some of the more severe types. Comparative tests were made of this serum and several of the European makes and the American product was revealed to be twice as potent. The serum has been shown to have great therapeutic value in malignant pustule in man. Later by an improved technic, modelled along that which Banzoff used for diphtheria antitoxin, success was attained in fractioning and separating off the globulin content which contains the concentrated antibodies. This globulin serum has also proved its potency both in numerous tests on laboratory animals and practically in larger animals—cattle and horses.

The Bureau of Animal Industry has been furnishing state and city hospitals with the serum upon request for several years past, but in a recent communication from the bureau the writer learns that it is not their intention to continue this practice, inasmuch as several of the biological firms are now prepared to furnish such a product.[50]

Statistical Study of Anti-anthrax Serum. Picaud[23] believes that anti-anthrax serum has an incontestable efficacy, and to prove this refers to statistics of Pagliani.[51] In Italy from 1890 to 1900 there were recorded 24,052 cases of anthrax with 5812 deaths, or 24.16 per cent. On the contrary, statistics of these late years during which serum was used show 160 cases with 10 deaths, or 6.25 per cent, and in these 10 cases Pagliani states that the serum was employed too late to expect anything of the treatment. In 130 cases observed in Argentine Republic and treated by Sclavo[23] serum the mortality is considered by the writers as reduced to zero, the few cases that happened to die being attributable to secondary infection. In 1903 Sclavo[52] reported 164 cases treated by serum with only 6.09 per cent of fatalities. Legge[53] collected 12 cases of anthrax treated by serum in England between 1904–1905. Of these, 4 were treated by serum alone, 3 recovered and 1 died; while of 8 treated by serum plus excision, 6 recovered and 2 died. Of the fatal cases the serum was not administered until the day of death in one case and in the other case not until twenty-four hours before death, the dose being only 20 c.c. in the latter.

Herley[54] has reported 8 cases of anthrax treated by Sclavo serum with 1 death, excision being performed also in all but 1 instance.

Royer and Holmes[55] have reported 15 cases of anthrax, 4 of which were treated without serum with 1 death, and 7 by Sclavo serum plus surgical intervention with 1 death. These 11 cases comprised the more serious in which the lesion was located on the face or neck, while in the remaining the extremities were involved 3 out of 4 times. Schwartz[1] has collected a series of 68 cases occurring in New York state. His statistics show 17 cases treated by serum and rest with 5 deaths and 12 recoveries, and 28 cases treated by serum and excision, in one of which excision was close, with 26 recoveries and 2 deaths. Page's[56] statistics from English cases of anthrax threated with serum show an apparently higher mortality than in untreated cases. In the earlier group of cases the apparently high mortality was due to use of too small doses (10 to 20 or 30 c.c.), and in the later group the serum was often administered *in extremis*.

Pied,[57] in 1913, states that up to that date he found reports of 7 cases of anthrax with generalized blood infection which had recovered following serotherapy and 2 in which serum was used without success. Bandi,[58] in 1904, reported 2 remarkable cases of recovery in patients with an anthrax septicemia following energetic serum therapy. The first patient had been ill four days with a lesion on the forearm treated by thermocautery, and although the latter was thoroughly applied the process rapidly advanced, and when Bandi was called the man was comatous, with a temperature of 104° and a cloud of albumin and casts in the urine; 150 c.c. of serum was given immediately intravenously and 50 c.c. more the same evening. One and a half days later the temperature was normal, the patient conscious, the blood culture negative, the urine cleared up and the edema confined to the pustular zone. The second case was very similar and equally remarkable. Becker,[59] Bissell[60] and Graham and Detweiler[61] have each reported a case of malignant pustule with septicemia which recovered following the use of anti-anthrax serum. In the case of Graham and Detweiler excision was performed on the fourth day of the disease but failed to control the malady. In fact, within twenty-four hours afterward the blood culture became positive. On the sixth day 80 c.c. of anthrax serum and 100 c.c. of chloramin-T (Dakin) were given intravenously and complete recovery ensued.

Sclavo, Buron and Jager and Becker[62] have also demonstrated that anthrax serum is an efficient means of cure of even an anthrax septicemia in which the mortality by any other method is 100 per cent. All agree that under the influence of serum intravenously the bacteria rapidly vanish from the blood stream.

Rappaport and Amory[7] have reported a severe facial case with marked edema recovering rapidly after 80 c.c. of serum intravenously. Armour[63] cites an interesting case in which serum was not used until the seventh day of the disease, when the patient was in danger of suffocation. Within four days the patient was convalescent. A total of 60 c.c. of serum was given.

Mendez[64] has reported 1073 cases of anthrax with a death rate of 4.19 per cent treated by means of a serum he prepared himself by a method similar to that of Sclavo, the fatalities being due in the few fatal cases to the use of serum in moribund patients, to edema of the glottis, to myocarditis, to atheromata or to alcoholism.

Legge[53] in his very thorough article has examined the details of all published cases he could find up to January, 1905, treated by serum, namely, 67 in number. Of these, 56 were treated by serum alone and 11 by serum and some other treatment with a total death rate of 9 cases. In 44 of the 56 cases in which details would allow conclusions, marked improvement had taken place not only in the general symptoms but in the arrest in the further development of the pustule and in diminution of the edema by the third day. The average duration of treatment in these 44 cases was eight days. In none was it more than fourteen days. No visible scar or only a slight scar was present in all cases except 2, in which there was some loss of tissue, despite the fact that the face and the neck were involved in 35 of the 44. In 7 of the 9 fatal cases the patients were in a serious condition with widespread edema when the serum was administered and in all death occurred within thirty hours, usually in twelve, after the serum was given. Moreover, the doses of serum used in fatal cases were small, usually 20 to 30 c.c., and only one dose was given, and that apparently subcutaneously. In only 2 cases was the dose repeated a second time.

Cicognani[65] reports some remarkable facts in connection with the serum treatment. In Santa Croce, in Italy, a town of 5000 inhabitants with 36 tanneries, where Cicognani has adopted the serum treatment exclusively, the workers now insist on having this treatment to the exclusion of every other, and since operative interference is unnecessary, present themselves when there appears the smallest pimple suggestive of anthrax. Cicognani remarks on the rapidity with which improvement in the general condition occurs, often within a few hours, and the pustules dry up within a few days, while convalescence is much shortened. Lockwood and Andrews[66] and Stretton[67] have each reported a successful case treated by serum. In each instance the lesion was on the face and excision was contraindicated from an esthetic standpoint. The writer[68] has previously reported 2 cases and has since treated 5 more successfully by Eichhorn serum. The recovery in all instances was extremely rapid; convalescence was established within a few days after serum treatment was begun. The pustule in all instances rapidly dried up in a minute and a almost invisible scar was the only remains of the disease. The specific influence of the serum was so marked as to leave no question in the minds of the observers of the value of the treatment. The lesion was not excised in any of the 6 cases. Ascoli,[69] of Milan, uses serum often as the only treatment in doses of 5 to

15 c.c., sometimes repeating the injections five or six times in the same day. Sclavo[70] has lately stated that doses of 10 to 50 c.c. of serum are too small and that 60 to 80 c.c. is a minimum. Many authorities advise 40 c.c. Pagliani[51] has drawn certain conclusions in regard to treatment by anthrax serum: (1) The serum even in large doses is absolutely innocuous; (2) it is well supported even if given intravenously; (3) it may save the patient when the prognosis is hopeless; (4) it arrests rapidly the local process and reduces to a minimum the destruction of tissue.

Modat[71] believes in the efficacy of the serum treatment of anthrax and uses doses as high as 60 c.c., repeating the injection in twenty-four hours in doses of 20 to 30 c.c. and continuing this until the disease is controlled. Modat states that veterinarians sometimes use as much as 500 c.c. to 600 c.c. of serum at one dose in anthrax infections in horses. He quotes the work of Cuica in Bucharest, who has prepared an immune serum and relies on it exclusively in therapy. This writer has reported 40 cases, in 6 of which serum was not used, with 100 per cent mortality, the remaining 34 all recovering under serum therapy.

Dr. Douglass Symmers,[83] director of the Laboratories at Bellevue Hospital, reported recently "that within the past few years some 15 cases of anthrax have been treated in that hospital with specific serum and the results have been very gratifying; that while as one readily understands, all of the cases which had become septicemic with anthrax bacilli when first seen died, those which came under the serum treatment early were speedily cured, good results being apparent within forty-eight hours and recovery taking place within a week or ten days." The method of treatment followed has been to give 40 c.c. of Eichhorn serum intravenously every four hours, and at same intervals to inject 10 c.c. into the skin surrounding the pustule. Excision which was formerly used as a routine with serum or alone has been abandoned.

The reported cases of anthrax in New York City in the last few years have been as follows:

Year.	Cases.	Deaths.
1915	13	9
1916	4	3
1917	16	9
1918	15	4
1919	14	9
1920	12	1

During the early years of this period, 1915, 1916, 1917, serum was little, if at all, used. During the following years it began to be more employed but was combined usually with other methods of treatment, mostly excision. Finally, during 1920 serum has been fairly uniformly used and excision has been given up by many hospitals.

Hubbard and Jacobson[85] summarize the treatment in the 34 cases that have occurred in New York City during 1919 and 1920. The table is as follows:

	No. cases.	Recoveries.	Deaths.
Anti-anthrax serum only	14	12	2
" " " and incision	5	4	1
" " " and excision	4	3	1
" " " and chemical cautery	2	0	2
Chemical cauterization and incision	2	1	1
Anti-anthrax serum, excision and chemical application	1	1	0
Chemical application	1	1	0
" " yeast	1	1	0
No treatment recorded	4	0	4

Hubbard and Jacobson comment upon therapy thus: "As 14 cases recovered without operation and 9 recovered with operation it would be logical, to judge from the observed cases, that it was best not to operate. Again, out of the 14 that received only anti-anthrax serum 2 died. Out of the 12 that received serum aided by other treatment 4 died. The method which seems most successful is that of administering anti-anthrax serum, 10 c.c. by local infiltration every eight hours and 40 c.c. intravenously every four hours."

Comment on Serum Therapy. From the review of the statistics just quoted I believe certain conclusions may be drawn. From the standpoint of mortality in very large series of cases, anthrax serum has evidently the lowest death-rate of any treatment. Still there are very low mortality rates reported in fairly large but isolated series of cases by other methods, such as those of Kraus and his collaborators with normal beef serum, of Graef with caustic potash, of Muskett with powdered ipecac, and of Fortineau with extract of Bacillus pyocyaneus. Mortality alone however is not the only factor to be considered in selecting the ideal method of therapy for anthrax; other points previously referred to must also be considered.

At first, offering as it did a new method of therapy, anthrax serum was used like diphtheria antitoxin in the more desperate cases, often very late in the course of the disease, and this fact accounts for many of the early non-successes. Relatively few failures have occurred with immune serum which cannot be traced to either of the following facts: (1) To its use too late in the course of the disease within twelve to twenty-four or thirty-six hours of death; (2) to the employment of too small doses (20 to 30 c.c.); (3) failure to repeat the injections frequently, say every six to twelve hours; (4) use in persons with chronic disease, such as alcoholism, syphilis, chronic nephritis, myocarditis, etc.

The number of recoveries in cases that are considered hopeless is a most important comparative test of any measure of therapy. In anthrax septicemia immune serum has given the highest number of successes. In internal anthrax it should always be used, as it is

the only instrument of treatment worthy of the name, and we have yet to see what may be accomplished with a potent serum used properly. It is to be recalled that Mitchell[72] has seen cases presenting all the symptoms of pulmonary anthrax recover under serum therapy.

Immune serum therapy fulfils best the points mentioned as requisite for an ideal method of therapy. It offers the least pain, a minimum of scarring and is appliable to all forms and locations of the disease. It entails a shorter absence from employment than any other method with the exception possibly of excision. The serum is specific and is the only safeguard we have against generalization of the infection.

In this country we are especially fortunate in having accessible for the past few years a serum possessed of strong therapeutic properties as that prepared by the Bureau of Animal Industry. On the basis of the experimentally proved prophylactic value of this anthrax serum, as well as its incontestable efficacy in the treatment of the disease in both man and animals, there is now no longer any excuse for failure to utilize it in the treatment of all forms of anthrax, but especially of malignant pustule, in which the mortality can probably be reduced to a negligible one by early diagnosis and prompt serum therapy.

The specific action of the serum upon the course of the disease will rarely be questioned by those who have had an opportunity to employ a reliably potent preparation. Examples have been cited above which illustrate this, and they might be multiplied if space allowed. The prompt subsidence of constitutional symptoms, sometimes within twenty-four hours, and the rapid improvement in the local lesion, often within a few days, are the rule and not the exception. Statistics adverse to serum therapy are impossible to find if Page's[56] reports be excluded.

An argument that has been advanced against the use of serum is the expense of the treatment. Thus $30 has been quoted as the cost of production of the amount of serum required for the initial dose. Eichhorn[73] states that at present the serum sells at the rate of 5 cents per c.c., so in this case the initial dose should not cost any more than from $5 to $10. At this rate the entire cost of the treatment for an average case would not exceed by much the figure previously given by some writers as cost of the initial dose.

General Administration of Serum. The esential aim in the administration of serum is threefold: (1) To bring about a subsidence of the local lesion; (2) to counteract whatever toxemia may exist; (3) most important of all, to anticipate and prevent the development of an anthrax septicemia, or to try to control the blood infection if it exists when treatment is begun.

An outline of a method of administering anthrax serum, including the dosage and interval between doses in the various types of the

disease, may be of practical use, as the writer has been unable to find any such plan in the literature reviewed. It is perfectly logical that a severe or septicemia case requires larger and more frequent doses than a mild case.

At the beginning of treatment a blood culture should always be taken. The result gives one an index of the severity of the case and of the extent to which serum must be pushed. During the interval elapsing before the result of the blood culture is known, usually twenty-four hours' treatment must be energetically pursued in all cases, even the mild and moderate ones, because occasionally constitutional symptoms may be misleading as to the existence of a septicemia. Whether in all cases in this interval of twenty-four hours it would be best to follow the method of Symmers,[83] to give 40 c.c. every four hours, remains for later studies to show. The writer believes, however, that at present the following may be submitted as a tentative plan:

In Absence of Anthrax Septicemia. 1. In mild cases of the disease with little constitutional disturbance and a small well-circumscribed lesion with little edema the serum need not be given more often than every eight to twelve hours and commonly not more than three or four injections of 50 c.c. each (Eichhorn[74] recommends 50 c.c.) intravenously in the first twenty-four hours are required. The subsequent injections may be given at twelve to twenty-four hours' interval, depending on the progress of the case, commonly not more than six injections being required, the last few intramuscular or subcutaneous. Local serum therapy, as described below, should be used every twelve to twenty-four hours.

2. In the moderate cases, with medium-sized lesion and a moderate degree of edema and induration associated with definite constitutional symptoms, the serum should be administered for the first twenty-four hours by intravenous injections in doses of 50 to 80 c.c. (Eichhorn[74] recommends 50 to 100 c.c.) every eight hours, the subsequent treatments and frequency being in accordance with the progress of the case, commonly not more than six to eight injections being required, the last two or three intramuscular or subcutaneously. Local serum therapy should be employed for the first few days every twelve hours.

3. In severe cases, with large, voluminous lesions and extensive edema with or without marked constitutional disturbance but with negative blood culture, the serum should be administered by an intravenous route, either in small doses frequently repeated, 40 c.c. every four hours, or in larger doses at less frequent intervals, 80 to 100 c.c. (Eichhorn[74] recommends 100 to 200 c.c.) every six to eight hours for three or four more injections until the disease is controlled, when the intramuscular or subcutaneous route may be used in part and the doses reduced to 50 c.c. at intervals of twelve to twenty-four hours. Local serum injections should be given every six to eight hours for the first few days.

In Septicemic Cases. In such instances with a lesion as just described we have to deal with a most fatal disease, and it seems to be the consensus of opinion that the use of serum must be in unusually large doses and frequently given, the treatment being energetically continued until after the blood culture is negative. In such cases the injections would appear to be indicated every three or four hours intravenously in doses of 100 to 150 c.c. (Eichhorn[74] recommends 200 to 300 c.c.), and this treatment is continued until the septicemia is checked or the patient succumbs. Salvarsan may yet prove a useful adjunct in these desperate cases. The injection of serum locally should also be given every four to six hours.

In internal anthrax it would seem that a similar method of therapy to that used in septicemic cases would be in order. Anthrax serum should likewise be used intraspinally in anthrax meningitis.

Local Serum Therapy. It is evident in the review in the first part of this article that while many writers advocate diverse methods of local therapy, i. e., cauterization, incision, excision, injection of chemicals, application of steam vapor, etc., a considerable number have combined these measures with serum therapy, evidently not trausting to them alone to bring about a cure. Since the only danger of the disease, rare cases of suffocation excepted, is the dissemination of the infection into the blood stream, the question of the advisability and necessity of these measures comes up. The prime essential in successful treatment is evidently to guard against blood infection, and this may be accomplished by (1) the general (intravenous and intramuscular) and local administration of immune serum, and (2) by avoiding the use of any local measure of therapy which might tend to generalize the local disease.

The measures of local therapy in common use are so severe and have so many disadvantages, such as pain, scarring, disfigurement and danger of disseminating the infection, to which attention has been called in detail above, under their appropriate headings, that the writer[68] in treating his own cases hesitated to resort to any of them. The only measure recommended which seemed to have no disadvantages and be of some therapeutic value, but probably more palliative than curative, was the application of wet dressings of powdered ipecac. This was therefore tried. In order to obtain an additional and more active and probably effective measure of local therapy it was decided to try the effect of the injection of serum into the lesion itself.[68]

It was considered probable that the introduction of the serum into close contact with the pustule would not only possess great advantages over other local methods previously advised but would actually be an additional precaution against an anthrax septicemia thus originating and might well have a decidedly beneficial influence upon the evolution of the lesion. As previously reported,[68] the method consisted in the injection of 2, 2.5, or even 3 c.c. of serum

at each of three or four points equidistant from one another at the various sides of the pustule. The needle is best inserted into the red indurated border of the pustule just beyond the blanched zone, the serum being directed toward the base of the eschar and injected so as to circumscribe the lesion. The injections are given once, twice or three times in the twenty-four hours, depending on the severity of the case, and not more than 7 to 10 c.c. are injected at one time. Commonly four to six injections suffice. A 5 c.c. glass Leur syringe and a fine-gauge needle are used in giving the treatment. The method has proved practically successful as the most desirable measure of local therapy. The writer has reported 2 cases previously and has subsequently treated 5 cases, all terminating in recovery despite the fact that the pustule was located either on the face or neck in all instances.

Local use of serum theoretically seems logical. The serum is then supplied in a most concentrated form at the site of the infection. The importance of this fact has been previously expounded on by Flexner[75] in relation to various bacterial inflammations situated in locations in which they receive a diluted and modified lymph secretion, as in massive inflammations, abscess formations and infections of serous cavities. While anthrax is not mentioned by Flexner in this excellent treatise[75] on *Local Specific Therapy of Infections*, the similarity to a massive inflammation and abscess formation is obvious. As examples of previous local use of serum in infections certain facts may be cited. Speiss[76] has shown that incisions infected with virulent streptococci have been controlled in the rabbit more surely by the application of the corresponding antiserum locally to the wound than by injecting it intravenously. Romer[77] has shown that pneumococcus keratitis is benefited by the direct instillation of antipneumococcus serum into the eye. Likewise, Netter[78] has recently succeeded in preserving vision by the injection of anti-meningitis serum into the vitreous chamber of the eye in a case of epidemic meningitis complicated by suppurative choroiditis, a complication always resulting in loss of vision.

The character of the local inflammation in anthrax is of a peculiar type.[79] The serous discharge from the pustule during the first several days of the disease and often until the end, especially in fatal cases, is characteristically poor in leukocytes. The pathological anatomy of the lesion, as shown by Cornil,[80] Wagner[81] and Straus,[82] shows a very definite tendency for segregation of the anthrax bacilli in the center of the pustule, in which they are intertwined in a compact network practically free of leukocytes, the latter being distributed most densely as diffuse infiltration at the margins of the lesion and in the subjacent cellular tissue. In the more malignant cases and in the early stage of the disease, phagocyte activity is not much in evidence. Since the serum has been shown to have a marked effect in facilitating phagocytosis (Mar-

choux[16]) it is evidently logical to supply it in a concentrated form at the site of the pustule. In this way the normal resistant processes are strengthened, phagocytosis is increased and the inflammation is more quickly terminated.

The writer is glad to say that Symmers,[83] of Bellevue, has recently adopted the local serum therapy of anthrax as described above and reports very satisfactory results. Graham,[84] whose experience with anthrax has been quite extensive, in a recent article also endorses local serum therapy, and comments on the success that has attended its use when combined with the intravenous administration of serum.

Summary. 1. The various measures of therapy in use in treatment of malignant pustule have been reviewed. Statistics have been quoted showing comparatively the mortality with different treatment.

2. The disadvantages of the various measures of local therapy in common use have been discussed and attention has been drawn to the dangers that many of them possess.

3. The history of the development of anti-anthrax serum has been outlined. All the available statistics and facts relative to serum therapy of the disease in the foreign and domestic literature have been quoted so that conclusions might be drawn as to the value of the method. With marked uniformity reports of those who have used immune serum are favorable to the method.

4. The advantages of serum treatment over the other methods have been outlined.

5. A plan of dosage and interval between doses in the various forms of the disease has been tentatively given.

6. Local serum therapy has been described as a method of local treatment to replace the older and more dangerous measures. Its practical application and theoretical basis have been discussed.

Conclusions. 1. The measures of local therapy of anthrax in common use should be abandoned, owing to the disadvantages or even dangers they possess. These disadvantages include scarring and disfigurement, pain, danger of secondary infection being introduced, liability of spreading the disease locally or into the circulation, prolongation of convalescence and, but most important of all; their lack of any specific effect upon the course of the malady and their uselessness when the pustule is voluminous and when a septicemia has originated. The pustule is best left to its own evolution rather than to employ the more radical measures, owing to their tendency to disseminate and generalize the local disease, while the palliative measures exert their effect entirely too superficially for any direct curative value.

2. The value, both prophylactic and curative, of anti-anthrax serum must now be regarded as established by statistics. Its well-nigh specific nature in the therapy of the disease must be recognized

by the profession. The mortality from malignant pustule will be reduced to a minimum by prompt recognition and early serum treatment.

3. No case of anthrax septicemia should be considered beyond hope until intensive serum therapy has failed.

4. The serum prepared by the Bureau of Animal Industry or according to their method has been proved of marked potency, being according to certain reports twice the strength of the European preparations.

5. As originally described by the writer, the local injection of anthrax serum into the pustule is apparently the most effective means of local therapy and should always be used as a supplementary measure to the general administration of serum.

6. Anthrax serum fulfils best the points requisite for an ideal method of treatment of anthrax: (1) It is appliable to all forms and locations of the disease; (2) yields on average the lowest mortality rate; (3) is a specific measure; (4) is a safeguard against generalization of the local disease if used in time; (5) offers the least amount of scarring and deformity; (6) causes a minimum of pain; (7) demands on an average the shortest absence from employment.

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RECURRENT ADENOMYOMA OF THE UTERUS.

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ADENOMYOMATA of the uterus comprise an interesting and important group of uterine tumors not only from their immediate clinical and pathologic aspects, but also from the fact that they may be potential foci for such complications as ectopic pregnancy or subsequent malignancy. The work of Cullen, which indicated a source for adenomyomata from the mucosæ of the derivatives of the Müllerian ducts, and particularly the endometrium, has supplanted the earlier conception of von Recklinghausen and his followers, who claimed that the glandular elements in such tumors arise from the Wolffian ducts. Subsequently further investigations have confirmed the observation of Cullen, and, in addition, as a factor of significance, it has been shown that portions of mucous membrane very similar to and apparently allied with endometrium may occur in places other than their normal position. In his monograph on *Adenomyomata of the Uterus*, Cullen cites the finding of normal uterine mucosa upon the serosal surface of the cervix and suggests the probability of origin for the epithelial elements in these tumors from such aberrant patches. Prior to the efforts of von Recklinghausen, in 1896, adenomyomata of the uterus received scant investigation, and it is greatly due to the stimulus of those studies that after exhaustive research the later views of Cullen and his associates were established. True it is that many worthy observers yet hold with the earlier hypothesis of von Recklinghausen, while still others, as, for example, Ries, are conciliatory, granting that since the Müllerian and Wolffian ducts are so intimately associated embryologically the adenomatous portions of these tumors might arise from either organ. Nevertheless the definite procedures pursued by Cullen demonstrated with sufficient conclusiveness that the epithelial structures in adenomyomata of the uterus arise directly from the uterine mucosa.

The incidence of adenomyoma of the uterus varies within narrow limits. In a series of 3388 hysterectomies for myomatous growths of the uterus (1906–18) at the Mayo Clinic, McCarty reports 211, or 6.43 per cent, of adenomyomata, while in 1283 myomata of the womb Cullen has found 73, or 5.7 per cent, of adenomyomata, exclusive of cornual nodules. The statistics compiled at the Magee Pathological Institute of Mercy Hospital at Pittsburgh showed 47, or 4 per cent, of adenomyomata were present in 1200 uteri removed because of myomatous growths. The condition presents a clinical

picture so closely resembling that produced by other myomatous growths of the uterus that preoperative differential diagnosis is difficult. . In the Mayo Clinic series no case was diagnosed as such prior to the pathological analysis of the specimen. The age incidence of adenomyomata uteri enjoys a wide range in that the tumor has been found in a patient nineteen years of age, and also in some sixty years of age, with, however, the most frequent occurrence between the ages of thirty and fifty years. The association of pregnancy and collateral pelvic pathology with the finding of adenomyoma apparently have no significant interpretation. Any attempt to classify or group adenomyomata of uterus clinically would be futile. Therefore the anatomical grouping described by Cullen is here accepted as the working basis: Group I. In which the uterus maintains a normal contour, *i. e.*, adenomyoma diffusum benignum. Group II. Subperitoneal or intraligamentary adenomyomata of uterus. Group III. Submucous adenomyomata of uterus.

In the literature numerous instances of the association of carcinoma and adenomyoma as separate tumors within the same uterus are quoted, but few allusions are made presenting a definite tendency toward malignant change within the gland structures of the adenomyoma. This feature is prominently introduced in the case at hand and its presence lends an enhancing interest in view of the triple recurrence of the pathological and clinical findings. Hartmann and Lecene report the occurrence of a benign diffuse adenomyoma of cervix which manifested all the local symptoms and signs of cervical malignancy. Littlewood and Stewart recount the paired findings of adenomyoma and adenocarcinoma in the same uterus but as distinctly separate neoplastic processes. Cullen also details the possibility of multiple pelvic lesions in company with adenomyoma, and quotes instances of definite malignant development within the epithelial structures of the tumor. Von Recklinghausen is concerned with only 2 occurrences of carcinomatous change within the adenomyomatous tissue in his extensive series, while Meyer narrates 1 of doubtful validity.

The following case was admitted to the service of the late Dr. X. O. Werder, to whom I am indebted for the clinical records:

CASE HISTORY. The patient, a single woman, aged forty-three years, entered Mercy Hospital, December 4, 1917, complaining of irregular, profuse and painful menstruation, with a mildly irritating intermenstrual watery discharge. At times she would not menstruate for five to six months, but recently has been bleeding every three weeks. The menses were profuse, exhausting and lasted five to seven days, being accompanied by severe pains in the back and general weakness. Her general appearance and nutrition were good. There was no weight loss and the important functions, aside from the menses, were normal. The hemoglobin was 70 (Sahli) and the erythrocytes numbered 4,300,000. Bimanual pelvic examination

revealed a firm mass about the size of a small orange occupying the vagina and protruding by means of a narrow pedicle through the cervix from within the uterine cavity. The exposed surface of the tumor mass was necrotic. The uterus was symmetric and not enlarged. The tumor was removed by vaginal myomectomy. After removal the specimen consisted of several irregularly torn fragments of tumor tissue removed from the uterus. The larger fragments showed partial covering by intact endometrium but elsewhere there was superficial necrosis. Some of the smaller and thinner plaques appeared as though they might have been portions of a cyst wall. Throughout the larger masses, numerous small, oval, honey-combed areas of pin-head size were observed, some of which contained a pearly, mucoid material. Microscopical sections of the mass from the uterus showed a dense, waving and interlacing fibromuscular structure, through which were irregularly distributed abundant gland structures. These varied markedly in size and shape, some being small or oval, while others were dilated, cystic and of irregular contour. Although a few tortuous spaces were noted, presenting for the most part empty lumina, nevertheless some of the cavities contained a homogeneous, mucoid material. The lining epithelium was of a tall columnar type and uniform throughout. Where the glands were dilated the parenchymal cells were to a degree flattened. Nuclear figures were not observed and there was no evidence of invasive qualities or atypical growth. It was noteworthy that not a few of the acinar structures were surrounded by a richly cellular stroma of concentric arrangement, as is seen in normal endometrium. Occasional mitotic figures were observed in the nuclei of these stroma cells. Still other alveolar elements were inserted directly between the muscle fasciculi of the tissue and displayed no accompanying stroma. The pathological diagnosis was adenomyoma uteri.

Fourteen months later (February 1, 1919) the patient again sought the hospital, with a return of all the clinical symptoms which preceded the first operation, and, in addition, a definite metrorrhagia with its resultant secondary anemia. Pelvic examination disclosed a large firm mass the size of a fetal head tightly wedged in the vaginal cavity. A vaginal myomectomy was repeated and by virtue of the firm impaction of the mass in the vagina it was necessary to remove it piecemeal. The tumor, as in the case of its predecessor, hung into the vagina from within the uterus by means of a slender fibromuscular pedicle.

Several variously sized pieces of tissue from the uterus, portions of which were discolored and superficially necrotic, were removed at the second operation. The surfaces of the tissue elsewhere were of a pale pink or red, moist, glassy appearance and in places showed a normal mucous membrane. On section through the fragments islands of pearly gray tissue were encountered which at intervals showed microscopic cyst cavities of varying size and containing a

gelatinous gray or brownish material. The tissue was edematous and could be easily crushed between the fingers. Microscopical sections of the tissue presented a dense, though edematous, fibromuscular structure, throughout which were scattered islands of glandular tissue. The alveolar structures varied greatly in size and shape, some being tortuous and at times contained a mucinous material. The acinar epithelium was of columnar type and occasionally surmounted a cone-like shaft of stroma which projected into the lumen in the manner seen in intracanalicular fibro-adenoma of the breast. However, at no place was there any reduplication of the lining epithelium, no nuclear figures were observed, and there was no violation of the basement membrane nor papillary formation by parenchyma. For the most part the glands lay in a concentrically arranged, moderately cellular stroma which now presented rather marked myxomatous change. The pathological diagnosis was adenomyoma of the uterus.

Three months following this operation (May 2, 1919) the uterus was found to be slightly enlarged. Eight months subsequent to the second operation (September 24, 1919) the patient returned, complaining of almost continuous bleeding. Pelvic examination showed the uterus to be considerably enlarged but quite regular in contour. Abdominal hysterectomy was advised and executed, there being removed an enlarged uterus, amputated above the cervix, and the attached adnexa of both sides. The uterus was opened through the posterior wall and measured 13 x 9 x 5.5 cm. When reconstructed, the serosal surface was smooth, regular and yielded no evidence of tumor within the organ. The myometrium was very thick, especially at the fundus where it varied from 2.7 to 3.3 cm. in thickness. Toward the cervix it measured 1.7 cm. The uterine wall was tough, with apparently an increased fibrous connective-tissue content, and the blood channels therein were tortuous and thick walled. On opening the uterus three distinct tumor masses were found. The largest one occupied almost the whole of the posterior wall of the organ and had been cut through; the second, a smaller one, about the size of an English walnut, nestled high in the fundus; while the third, which formed a symmetrical bulging of the uterine wall, presented itself upon the anterior surface. The uterine cavity was large and lined throughout by a thick intact endometrium of healthy appearance, which was carried in unbroken continuity over the projecting tumor masses. The large polypoid mass on the posterior wall projected well into the uterine cavity and for a distance at its juncture with the myometrium was sharply demarcated, but for the greater part merged almost imperceptibility with the muscular coat. On the cut surface this tumor measured 7.0 x 3.8 cm. Its surface presented a variously nodulated contour and was covered by an intact mucosa which dipped into the mass to meet the irregularities of conformation. Section through the tumor mass

revealed a variegated appearance. At places the tissue was quite firm, gray, smooth, glassy and not easily crushed, while other areas displayed numerous thin-walled cysts containing a clear straw-colored fluid. The latter structures varied markedly in size and radiated in a cluster-like manner from a central fibrous core, to which they were attached by a slender pedicle. These grouped cystic clusters gave this portion of the tumor an appearance not unlike that of hydatidiform mole. The small cysts could be easily ruptured and the linings were smooth. This peculiar cystic formation gave the mucosal aspect of the tumor its peculiar appearance. At places the endometrium dipped into and over irregular cavitations in the tumor, the walls of which were composed of a thick, pale
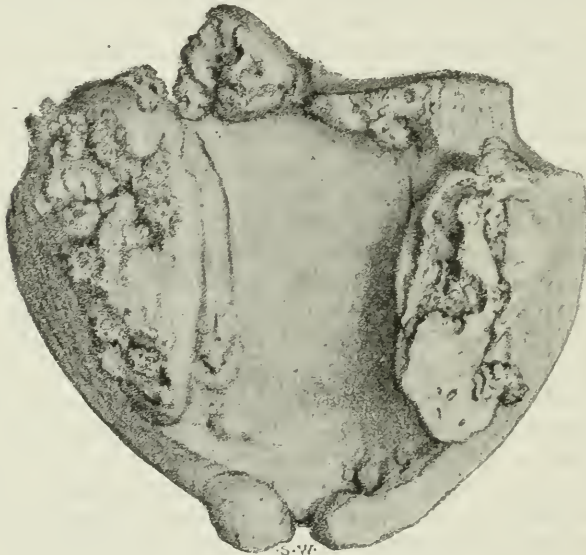
Opened uterus, showing three tumor masses.

membrane. On opening such membranous sacs their inner lining in turn was observed to be studded by inward projecting, lobulated, cauliflower masses. No more than a thin watery fluid was found in such cavities. At one point on the surface an oval, sessile bulging was noted which contained two small typical cauliflower masses. These hung from a narrow base into the otherwise smooth, empty cyst. At the juncture of the tumor mass with the myometrium several rather large channel structures were observed, and these, too, presented the characteristic fungoid papillary projections into the otherwise smooth-lined cavities. It is noteworthy that these papillary ingrowths were somewhat more easily crushed than the remainder of the neoplastic tissue. The smaller nodule in the fundus was about the size and shape of an English walnut. Its mucosal

covering was complete and the component tissue was of soft consistency. This mass also presented the characteristic cysts with a pale membrane comprising the cyst wall and the typical polypoid cauliflower projections into the cyst cavities, as noted in the larger mass. Several cysts in this instance were filled with a chocolate-colored fluid. The nodule was not sharply defined against the underlying uterine musculature, although it did not invade the myometrium to any great depth. The oval sessile symmetrical elevation on the anterior wall was quite firm and was covered by an intact endometrium. On section through the compact uterine wall a pearly, opalescent area, implanted directly into the surrounding opaque myometrium, was encountered about 3 mm. beneath the mucosal surface. No definite cysts could be determined in this area, and it was indistinctly differentiated from its environs.

Microscopic analysis of the tumor tissue of the uterine wall showed a compact fibromuscular structure in large whorls. Gland structures of varied size and shape were quite regularly and abundantly scattered through the tissue. Some of the cysts were elongated or stellate. In the greater number the lumina were empty, but occasionally there was contained in them a homogeneous material. Not infrequently the irregular stellate acini presented definite bulgings into the lumina, due to the projection of a slender shaft of stroma tissue. These papillæ were almost invariably surmounted by a single layer of columnar epithelium and imparted a picture not dissimilar to that presented by an intracanalicular fibro-adenoma of the breast. In the majority of instances the lining of the glands was of a tall, columnar-cell type, fairly uniformly arranged and occasionally showing definite cilia. The cell nuclei were, as a rule, quite large and vesicular. Nevertheless in some instances, and particularly where the glands were most tortuous, the lining epithelium manifested a definite tendency toward proliferation or showed a papillary ingrowth into the lumen. At rare intervals mitotic figures were observed in the nuclei of the epithelial cells. In no instance did the mucosal cells violate their basement membrane or exhibit high invasive qualities. It is of interest to note that many gland structures were surrounded for varying widths by a more or less concentrically arranged stroma very like that seen about the normal endometrium, while the remaining glands, devoid of supporting stroma, were inserted directly between the muscle fasciculi. Nuclear figures were seen quite frequently in this stroma tissue. The sections displayed no evidence of an inflammatory reaction. The "flowing in" of the endometrium deep into the interstices between the muscular whorls was well demonstrated in the sections.

The triple recurrence of a supposed benign growth is of sufficient import to merit painstaking investigation, and to the clinician is the occasion of no slight misgiving. The clinical diagnosis of the condi-

tion prior to the first and second operations were sarcoma uteri. It is interesting to note that at the present time, three years after the beginning of the condition and fifteen months subsequent to the hysterectomy, the patient enjoys improving health and manifests no evidence of metastatic involvement. The materials furnished by the earlier operations consisting only of projecting tumor tissue afforded an opportunity for no more than a purely speculative study as to the true intra-uterine status. As above stated the recurrence of a neoplastic process signifies grave possibilities to the surgeon, and so, too, to the pathologist when attempts at complete surgical removal have been made. However, in this instance the failure to extirpate the foci of growth would probably explain the repetition of the pathological state. Nevertheless over and above this are presented certain gross and microscopic characteristics of unmistakable significance. With the two earlier specimens a very definite picture of adenomyoma was portrayed. The tissue masses were evidently of the usual fibromyomatous character covered in places by a healthy mucous membrane and containing numerous gland structures of innocent nature. The third specimen presented an enlarged but symmetrical uterus which, when opened, revealed three distinct tumor masses. The large area on the posterior wall and the smaller one high in the fundus were quite similar in structure. In general they were seen to be made up of a peculiar combination of cysts and fibromuscular tissue. The latter, however, was somewhat more easily crushed than in the normal myometrium. The cysts were formed of a thin membrane lined by smooth endometrium and usually containing a clear or brownish-tinged fluid. From the walls of several of these cysts, projecting clusters of cauliflower appearance jutted into the cavity. These projecting clusters could be easily crushed between the fingers and were strangely suggestive of tissue met with in carcinoma uteri. Throughout the irregularities of conformation in the tumor the endometrium persisted in unbroken fashion. Microscopical analysis corroborated previous diagnoses of adenomyomata of the uterus, but here and there the reduplication of the lining epithelium of the glands or papillary projection into the gland lumen were strongly suggestive of early malignant neoplasia even though no definite invasive characters were as yet manifest. In addition the extreme irregularity of the glandular acini and the occasional finding of nuclear figures in the alveolar epithelium gave added weight to the view. The difficulty in making a diagnosis of early carcinoma requires no more comment than to allude to the extreme caution with which one approaches the interpretation of differential stages in papilloma simplex, recurrent papilloma and carcinoma of the larynx. The dividing lines in the process of neoplasia are most delicate and rest more or less upon accessory factors gleaned in ways other than from the microscope alone. Certainly, on this occasion, the microscopical analysis of

several of the gland structures, in addition to very suggestive appearances in portions of the gross specimen, lend weight to the possibilities of very early malignant change despite the fact that such is contra-indicated by both the mass of the general pathological findings and the clinical progress of the patient.

By virtue of the fact that adenomyomata were so intimately grouped with other myomatous growths of uterus it was not until the searching efforts of von Recklinghausen, in 1896, that these tumors received special attention. The champions of this author's views that the glandular elements in such tumors arose from the Wolffian duct were numerous. It is quite possible that the work of this group stimulated Cullen to a more exhaustive study of these growths with the resultant production of his monograph on *Adenomyomata of the Uterus*. Subsequent publications recording the discovery of myomatous tumors with glandular inclusions in various portions of the pelvis and lower abdomen give greater prominence to the far-reaching conclusions of Cullen. Firmly of the opinion that the gland structures in adenomyomata arose from Müllerian duct mucosa, particularly endometrium, the latter observer demonstrated clearly the direct continuity of such structures in the endometrium with those in the tumor mass. The peculiar "flowing in" of the uterine mucosa between the fasciculi of myometrium in the third specimen herein described coincides with the opinion expressed. Other features supporting this view are the characteristic stroma of normal endometrium accompanying many of these glands and the fact that the parenchymal cells possess cilia. Beyond clearly defining the origin of adenomyoma, Cullen is also concerned with the distribution of these tumors in the body, their clinical manifestations, complications, prognosis and treatment. Ries in his article concerning "Nodular Forms of Tubal Disease," assumes the middle road, not attempting the differentiation of one embryonal development from the other, and suggesting that because of the intimate association of the Müllerian and Wolffian ducts during their development it is reasonable to accept the theory that either organ may participate in the formation of adenomyomata.

In discussing adenomyomata of the recto-vaginal septum, Cullen remarks that the histopathology in such tumors is exactly identical with that seen in similar growths occurring in the uterus and that the glands appear as uterine endometrium out of place. The discovery by Cullen that normal uterine mucosa may at times be found upon the serosal surface of cervix could well be explanatory of the development of these tumors in such extra-uterine sites quite independent of the possibilities of migration from the uterus directly. Sir John Bland-Sutton details the finding of an adenomyoma of the uterus involving the rectum. This tumor presented the characteristic microscopic picture of an adenomyoma and probably represented an original growth in the uterus which subsequently

became subserous by extension and thereafter involved the rectum. Further studies of adenomyomata of the recto-vaginal septum were reported by Curtis and Jessup, both of whom portrayed typical features of such growths in their descriptions.

In 1916 Cullen described a tumor occurring in the round ligament in which were numerous cysts. Of the latter some contained a clear fluid while others were filled with a chocolate-colored material. The tissue, the writer asserted, was suggestive of adenomyoma. Almost simultaneously there appeared in another journal an article written by the same author, dealing with an adenomyoma of the round ligament and incarcerated omentum in an inguinal hernia, in which he felt assured that the tumor was a true adenomyoma. One of the earlier reported cases of adenomyoma uteri was that reviewed by Hellier, in 1913, wherein he noted the absence of sharp demarcation of outline about the tumor, so characteristic of this neoplasm, and observed the typical gland arrangement so similar to that of endometrium with the accompanying stroma of uterine mucosa in abundance. Gough and Stewart cited the triple location of adenomyoma in a patient who presented the tumor in the uterus, Fallopian tube and sigmoid colon. In each instance the macroscopical and microscopical findings were analogous and the mucous structures in the neoplasms were very much similar to those of normal endometrium. The reason for the implantation of the growth in so distant a locus as the sigmoid colon is open to conjecture, although, as before noted, the finding of tumor containing uterine mucosa far removed from the uterus is now not uncommon. The occurrence is apparently somewhat akin to the findings of the observations of Leitch, who investigated an adenomyoma beginning in the posterior wall of the uterus, which migrated or was extruded through the serosal surface and attached itself to the sigmoid colon. Later the glandular elements in the tumor infiltrated the wall of the colon. Among other observers who have described typical adenomyomatous growths in places far removed from the endometrium was Schwarz, who, in the course of relating the details of an adenomyoma of the recto-vaginal septum, noted that these tumors, or at least tissue like endometrium, did occur in the ovaries. Concerning this feature there is little information given. However when the relationship of the sex gland and the Müllerian duct structures during the embryological development of the female is understood the discovery of uterine mucosa in the ovary may lose its perplexing attitude. In this regard it is interesting to note that Casler described a peculiar diffuse uterine tumor in which the stroma of endometrium was abundant, but at no place were parenchymal structures observed. At a subsequent laparotomy upon the same patient the left ovary was removed and on pathological analysis presented a stroma-gland arrangement analogous to that of normal uterine mucosa.

The greater portion of the evidence gleaned from the work of

recent investigators lends support to the opinion of Cullen as to the derivation of the glandular elements in adenomyoma uteri. Were more details of information required to firmly establish such views they are furnished through the reports of two rather curious cases. Bell performed a hysterectomy on the second day of the normal menstrual period. Pathological examination of a large tumor mass contained within the uterus demonstrated a characteristic adenomyoma save that the glands were dilated and filled with a dark blood clot indicating that the alveolar structures were participating in the menstrual phenomenon. The utilization of a specificity allotted only to derivatives of the Müllerian system is strongly suggestive of the direct origin of the glandular structures quite aside from the repeated proof furnished by histological study. So, too, Doederlein and Herzog recount the occurrence of a true pregnancy within one of two loculi in an adenomyoma of the uterus. Truly the continuity of the mucous surface lodging the fertilized ovum with that of the endometrium cannot be doubted, for otherwise there is no explanation for the ectopic implantation of the germinal cells. Fortunately the observers were able to demonstrate the communication between the endometrium and the dilated gland cavity containing the placenta. The wide range of distribution of adenomyomas containing uterine mucosa has been recently published by Cullen. The writer indicated that tumors composed of unstriped uterine muscle and containing uterine mucosa were to be found in the uterus, the rectovaginal septum, tubes, round ligaments, utero-ovarian ligaments, utero-sacral ligaments, sigmoid flexure, rectus muscle, umbilicus, and that quantities of uterine mucosa may occasionally be found in the ovaries.

Little further comment need be made upon the association of carcinoma of uterus with adenomyoma. There is no indication that there might be any direct relationship between the two conditions even though the incidence is more than occasional. Cullen denoted the moderate frequency of such paired findings while MacCarty estimated 5.5 per cent of the uteri removed for myomatous growths at the Mayo Clinic presented concurrent, independent malignancy of the cervix or body. Littlewood and Stewart reported the finding of the paired condition in a uterus, each occurring separately. Hartmann and Lecene related an interesting observation wherein a patient presenting all the local manifestations and physical findings of a cancer of the cervix was found on later pathological analysis of the surgically removed specimen to have been suffering from a benign diffuse adenoma of the cervix. Nor should there be any particular surprise that malignant neoplasia may occur in the acinar structures of adenomyomata. On the other hand it is rather remarkable that this pathological change has not been noted more frequently than has been reported at this time, for the tissues involved possess proliferative tendencies.

Concerning the clinical symptoms produced by adenomyomata, little may here be said other than that they are in general quite comparable to those produced by other myomatous growths of uterus. Cullen maintains that careful observation will yield features which will render possible a true differential diagnosis. On the other hand, MacCarty reports that not one of the 211 adenomyomatous uteri in the immense series of hysterectomies for myomatous growths of uterus was diagnosed as such before operation.

The writer wishes to express his appreciation to Professor Oskar Klotz for suggesting the study, and for his generous advice and helpful criticism.

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REVIEWS

INFECTIONS OF THE HAND. By Allan B. KANAVEL, M.D., Assistant
Professor of Surgery, Northwestern Medical School, etc. Fourth
edition. Pp. 500; 185 illustrations. Philadelphia and New
York: Lea & Febiger, 1921.

THE reader should need no introduction to this book, the first
edition of which came out some years ago. This, the fourth edi-
tion, is a result of a thorough revision with additions. The text
has been supplemented with the knowledge obtained from the
war upon gas bacillus and streptococcic infections as well as
permitting the addition of a chapter upon the restoration of function
in infected hands.

Experimental and anatomical studies are made, upon which
the deductions are founded. Much emphasis and space is given
to the pathological anatomy, for it is only by understanding and
appreciating the underlying pathogenesis that a surgeon can
correctly treat the hand infections.

The book covers the subject completely, thoroughly describing
by text and illustration every condition and complication. A
chapter on diagnosis and treatment in general shows into what
group a particular case will fall and directs the student to the
proper place in the book for the detailed treatment.

No surgeon should be without this excellent work and every
hospital should have one available for reference, both for the sur-
geon and the intern.   E. E.

MOUTH HYGIENE. A TEXT-BOOK FOR DENTAL HYGIENISTS. Com-
piled and edited by ALFRED C. FONES, D.D.S., Professor of Pre-
ventive Dentistry in Columbia University. Second edition. Pp.
334; 218 illustrations and 8 plates. Philadelphia and New York:
Lea & Febiger, 1921.

THE dental hygienist is the most recent professional addition to
the ranks of those ministering to the health of the community.
Special training schools have been established in several univer-
sities and many states have enacted laws to govern the practice of
dental hygiene. The young women who take up this work are

destined to play an important part in the prevention of disease.
The establishment of this work on a professional basis is largely
due to the pioneer efforts of Dr. Fones, whose ideas have been
largely adopted as a foundation for the courses of instruction that
are being given. In his book, aided by several eminent collabor-
ators, he has set forth the dental and allied subjects that are essen-
tial for the education of the dental hygienist. The principal matters
covered are: anatomy of the head, functions of the teeth, mal-
occlusion of the teeth, inflammation, pyorrhea alveolaris, dental
caries, dental disease in relation to general health, principles and
technic of dental prophylaxis, and the broad field of service of
the dental hygienist, especially in relation to hospitals, industrial
clinics and public schools.   R. H. I.

Roentgen Interpretation. By George W. Holmes, M.D.,
   Roentgenologist to the Massachusetts General Hospital and
   Instructor in Roentgenology Harvard Medical School, and
   Howard E. Ruggles, M.D., Roentgenologist to the University
   of California Hospital and Clinical Professor of Roentgenology,
   University of California Medical School. Second edition, thor-
   oughly revised, pp. 228; 184 illustrations. Philadelphia and
   New York: Lea & Febiger, 1921.

In the second edition of this splendid little volume the authors
have made a number of corrections of defects that appeared in
the first and, in addition to this the text has been thoroughly
revised and new material and illustrations added. The simple
expedient of placing arrows on the illustrations to indicate the
lesions under discussion has greatly enhanced the value of the book.
Very often a lesion that is quite apparent on a negative becomes
just as obscure on a reproduction and in studying an illustration
the reader has no little difficulty in locating just what the illustra-
tion portends to show. This is particularly true of line fractures
and early bone and pulmonary disease. The indicating arrows
relieve the reader of this difficulty and as a result the book is studied
with much more satisfaction.

No pretension is made to present a finished treatise on any one
subject. The purpose of the authors is to present the essentials
of roentgen interpretation; this they have done concisely and well.
For more detailed and specific information the reader is referred
to the list of the most recent literature that is found at the end
of each chapter.

Among the important new material in this edition is a brief
description of some of the rarer forms of bone pathology, namely,
Madura foot, parasitic cysts, yaws, Koehler's disease and chloroma.
                                                          J. D. Z.

Evolution of Disease. By Professor J. Danysz, Chef de Service, Institut Pasteur, Paris; translated by Francis M. Rackemann, M.D., Assistant in Medicine in the Harvard Medical School. Pp. 194; 1 illustration. Philadelphia and New York: Lea & Febiger, 1921.

In Part I of this engaging little book "the various stages in the development of acute infectious diseases" have been traced and in Part II a theory of immunity, anaphylaxis and anti-anaphylaxis propounded, which if correct should have an extremely valuable application in the comprehension and therefore intelligent treatment of many chronic non-contagious diseases. Far be it from the present reviewer to pass judgment on the merits of a theory arising from such a source and involving problems of such scope and importance; but he can at least recommend to readers the perusal of a concise, interesting and suggestive treatment of the subject.

E. B. K.

Medical Electricity, Roentgen Rays and Radium, With a Practical Chapter on Phototherapy. By Sinclair Tousey, M.D., Consulting Surgeon to St. Bartholomew's Clinic, New York City. Third edition. Pp. 1337; 861 illustrations, 16 in colors. Philadelphia and London: W. B. Saunders Company, 1921.

In the first part of this book the author discusses the different kinds of electrical currents that are used in treatment, their modes of production, physiological and pathological effects, and the methods of applying them in diagnosis and therapy. In this part electrophysics is dealt with very thoroughly and at great length. No fault can be found with the quality of the text dealing with the physics of electricity, but there is entirely too much of it. It is easily appreciated why it is necessary for the specialist in this field to be familiar with the principles of electrophysics; it is quite as readily understood that this speciality can be intelligently practised without knowing, for example, how to measure the potential of a condenser or determine the horsepower wasted in the form of heat by the passage of a current of electricity through a wire. We do not argue that it is not an advantage to possess this purely technical knowledge, but it must be borne in mind that the primary interest of the physician lies in the diagnosis and treatment of disease and not in the construction of electrical machinery.

The chapter on electrodiagnosis is well done, as is also the one on electrical accidents and their prevention. The same thing, however, cannot be said about that part of the text that is concerned with the application of electricity in disease. There are doubtless many things in it that are of value despite the fact that in not a few instances rather extravagant statements are made in

extolling the virtues of this therapeutic agent. A claim of apparent cures in cases of angina pectoris by rubbing a vacuum electrode over the entire chest and applying electric vibratory massage to the abdomen, falls hardly within the bounds of conservatism.

In revising the text on Roentgen Rays, the author has failed to bring it up to date. As a whole this part of the book lacks balance. For instance, fifty-four pages are devoted to radiography of the teeth and about three-fourths of a page to the x-ray diagnosis of gastric ulcer and carcinoma, while the discussion on the duodenum is exhausted by two short paragraphs in which appears the remarkable statement that "radiographs, as a rule, do not show this part of the intestine at all, or only as a shadowy outline making a curve around the pylorus, with its concavity toward the left."

The last chapter is devoted to a discussion of radium, its physical properties and physiological effects. This chapter contains much useful information.   J. D. Z.

A LABORATORY COURSE IN SERUM STUDY. By HANS ZINSSER, M.D., J. G. HOPKINS, M.D., REUBEN OTTENBERG, M.D. Second edition, revised. Pp. 184. New York: The Macmillan Company, 1921.

THIS course outline of immunology for medical students has received but few important alterations since the first edition of five years ago. Most of these changes are in the form of alterations in the plan of experiments.   E. B. K.

OPERATIVE SURGERY. By JOHN J. MCGRATH, M.D., F.A.C.S., Professor of Surgery, Fordham University, etc. Sixth edition. Pp. 863; 369 illustrations. Philadelphia: F. A. Davis Company, 1921.

THIS work is preëminently for the student and practitioner, and for the man learning his surgery. The text is arranged well and the subject-matter presented in a very readable manner, based on an anatomical or regional plan. Before describing the procedures the author gives a very complete practical outline of the anatomy of the part; preserved in a style and manner that robs it of its dry detail nature. Many of his anatomical points are further impressed upon the reader by illustrations.

The operative procedures are thoroughly and clearly outlined and illustrated, and should be clearly understood and readily followed by the operator.

The size of the book precludes any possibility of its being an extensive reference book on operative surgery. It does not attempt to describe every operation, but it does furnish the student reader a most complete and ready operative surgery for daily use.   E. L. E.

VITAMINES—ESSENTIAL FOOD FACTORS. By BENJAMIN HARROW, Ph.D., Associate in Physiological Chemistry, College of Physicians and Surgeons, Columbia University. Pp. 213; 8 charts. New York: E. P. Dutton & Company, 1921.

A WORK couched "in terms of our everyday tongue" and designed to give the layman a working knowledge of nutrition. In chapters I–VIII the author builds for the reader a knowledge of the physiological chemistry of food. Chapters IX–XIV deal solely with vitamines and to the physician seeking fundamental knowledge of vitamines these chapters are recommended. For those who wish to delve into the subject more deeply, the appendix offers food tables and an extensive bibliography. The physician who has occasion to supply information to his patients, on foods or on vitamines, will do well to recommend Dr. Harrow's book, for the author has not taken any knowledge of the reader for granted. The only adverse criticism to be offered is that the title is too limited, as less than one-half of the book is devoted to vitamines.

E. T. C.

A TEXT-BOOK OF PATHOLOGY. By ALFRED STENGEL, M. D., Sc.D., Professor of Medicine, University of Pennsylvania, and HERBERT FOX, M.D., Director of the Pepper Laboratory of Clinical Medicine, University of Pennsylvania. Seventh edition, reset. Octavo of 1111 pp., with 509 text illustrations, many in colors, and 15 colored plates. Philadelphia and London: W. B. Saunders Company, 1921.

THE seventh edition of this text-book appearing after an interval of six years may be taken as sufficient evidence of its continued popularity. During the twenty-three years that have elapsed since the appearance of the first edition the number of pages has increased from 851 to 1111 and the text figures from 372 to 509. It is to be regretted, however, that neither author is actively engaged in the study of this subject as his major interest, and this may account in part for the fact that many of the illustrations of the first edition are still to be found in the just appearing edition, and that those borrowed from other sources constitute more than half of the total number of illustrations. As "replacements and additions of illustrations to the extent of about a hundred have been provided," this condition will perhaps be still further improved in the next edition.

The terminology of the section on bacteriology contains several peculiarities; for instance, the streptococcus intracellularis meningitidis would hardly be recognized by many younger students of bacteriology. Bacillus typhus is surely a more common designation of this organsim than bacillus typhi abdominalis. The authors

showed a pecular preference for bacterium and mycobacterium, over the customary term of bacillus. One regrets the omission of *B.* edematiens in the section on anaërobes and of Rickettsia prowaczeski in the designation of typhus."

One notices with pleasure the inclusion of concise paragraphs on Lethargic Encephalitis, Trench Fever, Influenza, Noguchi's Leptospira Icteroids and similar "novelties." The sections on nephritis and tumors of lymphatic tissue, rewritten for this edition and of particular interest to the senior and junior authors respectively, are for both these reasons of particular value.   E. B. K.

SYPHILIS AND VENEREAL DISEASES. By C. F. MARSHALL, M.D., F.R.C.S., and E. G. FFRENCH, M.D., F.R.C.S., Lt.-Col. R.A.M.C. (retired). Fourth edition. Pp. 422; 96 illustrations (6 in color). New York: William Wood & Company, 1921.

IT is as great a pleasure to welcome the fourth edition of this book, whose premier volume appeared fifteen years ago, as it is interesting to see how far superior it is to the flood of similar literature, the apparent outgrowth of the War's stimulating experiences. This volume owes its worth, not alone by right of prior domain, but because of its clear presentation, its sane attitude, and its concise style. This edition has been greatly strengthened by having E. G. Ffrench as co-editor, adding materially in both experience and authoritativeness.

There is but one criticism, and that pertinent to all such efforts, *i. e.,* the impossibility of incorporating in so small a volume the entire field of venereal diseases; and yet we can frankly say that this is by far and away the most concise, readable, instructive and trustworthy treatise on these conditions that it has been our privilege to review. It is a splendid type of book to put in the student's hands, feeling confident that he will not be advised in error when following its teachings.   A. R.

THE WASSERMANN TEST. By CHARLES F. CRAIG, Lieut.-Col., M. C., U. S. Army, Professor of Bacteriology, Parasitology and Preventive Medicine, and Director of Laboratories, Army Medical School, Washington, D. C. Second edition. Pp. 279; 3 colored and 10 half-tone plates. St. Louis: C. V. Mosby Co., 1921.

THIS book has been enlarged, carefully reëdited and brought up to date. The author touches upon the history of the Wassermann reaction; considers its specificity; discusses its underlying principles; gives detailed methods of its application, both for the

blood-serum and the spinal-fluid tests; and elaborates in a mature manner upon its interpretation under various conditions, involving duration of syphilitic infection and thoroughness of treatment. The author's modification of the test and that of the U. S. Public Health Service are given. The importance of considering iso-hemolysins within the different blood groups (Moss's classification), where the anti-human hemolytic system is employed, is emphasized. Colloidal gold, protein tests and cell counts on spinal fluids, with methods, are mentioned in conjunction with the Wassermann test, as they have bearing on the diagnosis of syphilis. The book throughout bears the authoritative stamp of the writer's rich experience. Especially valuable is the conservative interpretation of the Wassermann reaction in the light of available data in the different stages of syphilis and following treatment—an interpretation unbiassed by any pretext of placing personal skill in diagnosis, or the efficiency of any particular system of treatment in the foreground. The book is a safe guide for the laboratory worker, and yet admirably meets the needs of the clinician who wishes to be able to interpret the laboratory findings in syphilis, and to correlate them with his clinical observations.   J. C. S.

TYPHUS FEVER, WITH PARTICULAR REFERENCE TO THE SERBIAN EPIDEMIC. By RICHARD P. STRONG, Professor of Tropical Medicine, Harvard University Medical School; GEORGE C. SHATTUCK, Medical Secretary, League of Red Cross Societies; A. W. SELLARDS, Assistant Professor of Tropical Medicine, Harvard University Medical School; HANS ZINSSER, Professor of Bacteriology, Columbia University; J. GARDNER HOPKINS, Bacteriologist of the American Red Cross Sanitary Commission to Serbia. Pp. 273; 26 full-page illustrations. Cambridge, Mass.: Harvard University Press, 1920.

THE campaign against the appalling typhus epidemic in Serbia, 1915—"one of the most severe which the world had known in modern times"—is described by Dr. Strong in an interesting and vivid manner. Perhaps, due to its occurrence before this country was thoroughly alive to the situation in Europe, this epidemic did not receive in this country the attention that its importance warranted. It is, therefore, correspondingly surprising to read that during the six months of 1915 in which the epidemic was at its height, typhus admissions to the military hospitals alone often reached 2500 per day. With a mortality varying between 30 and 70 per cent there was a total of over 150,000 deaths in Serbia alone, and to meet this terrible situation there were just 350 Serbian doctors available, with totally inadequate material supplies. The story of America's part in the organization of the International

Sanitary Commission and in the prosecution of the campaign which quickly brought the epidemic to a successful termination must be entered as one item to our credit in that difficult period before our tardy entrance into the war. The loss from typhus of 126 of the 350 Serbians and of 5 volunteer American doctors points to another chapter in the glorious history of the medical profession's combat with disease.

The history of previous epidemics and the etiology of typhus are discussed in detail. The mass of evidence points toward Rickettsia as the most probable cause, and its transmission by lice is regarded as of the greatest practical importance, though not yet definitely excluding droplet and other forms of infection.

The valuable clinical observations by Shattuck, based on 42 carefully studied case reports, with autopsy notes in 20 laboratory examinations by Sellards and bacteriological reports by Zinsser and Hopkins, add to the thoroughness of the presentation. Numerous illustrations and the pleasant format of the Harvard University Press complete the value of this contribution to epidemiological literature.   E. B. K.

GRAPHIC METHODS IN HEART DISEASE. By JOHN HAY, M.D., F. R. C. P., Honorary Physician, Liverpool Royal Infirmary; Honorary Consulting Physician, Ministry of Pensions. Second edition. Pp. 178. London: Joint Committee of Henry Frowde, Hodder and Stoughton, 1921.

THE first edition of this book was published in 1909. Since that time the use of graphic methods in studying heart disease has so far extended knowledge of the subject that it became necessary for the author to rewrite rather than revise most of the book. This has been done and the subject-matter brought abreast of present-day knowledge and beliefs.

The most of the book is devoted to the technic of the use of the polygraph and the interpretation of tracings. A chapter on the electrocardiograph has been added.

The material presented is well chosen, the tracings are excellent and the legends accompanying them fully explanatory. There are a few faults, mostly of minor type. For the sake of completeness, some attention should have been devoted to the rare abnormal rhythms such as auriculo-ventricular rhythm, ventricular escape and sino-auricular heart block. The classification adopted, which groups sinus arrhythmia and paroxysmal tachycardia together as disturbances of stimulus production, but classes extrasystoles as disturbances of excitability seems of rather doubtful utility.

The book may be heartily recommended to anyone desirous of beginning the use of the polygraph, likewise to those who wish to acquire proficiency in the reading of polygraphic tracings.

C. C. W.

PROGRESS

MEDICAL SCIENCE

SURGERY

UNDER THE CHARGE OF

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Trasplantation of the Ureters into the Large Intestine in the Absence of a Functionating Urinary Bladder.—COFFEY (*Surg., Gynec. and Obst.*, 1921, xxxii, 383) says that it was found in experimental work that the bile duct when implanted directly into a dog's small intestine always dilates, while a bile duct which has been transplanted and made to run immediately under the mucosa for a distance does not dilate. A ureter implanted directly into a dog's intestine always dilates and sooner or later the kidney is destroyed by pressure and infection. A ureter which has been transplanted and made to run immediately under the mucosa does not dilate as a rule. The author explains the dilatation universally found in direct implantation. The small intestine as well as the large is practically always found in a state of rotundity and partial distention, which he calls static intra-intestinal pressure. His second proposition was—how has Nature prevented this intra-abdominal pressure from reaching the inside of the normal duct? Dissection of the duodenum showed that the common duct passed through the wall of the intestine down to the mucosa and ran for a distance under the loose mucosa before emptying into the bowel. With a fountain syringe attached to a rubber bag and with a thin flap of rubber cemented over the inside of the tube's entrance, these same principles were demonstrated in a purely mechanical way. The modifications in technic and clinical application were devoloped by Charles H. Mayo.

Acute Intestinal Obstruction.—FINNEY (*Surg., Gynec. and Obst.*, 1921, xxxii, 402) says that early diagnosis is the most important factor. The shortness of the interval of time elapsing between the onset of the symptoms and the operation plays a most striking part. In 21 cases with operation within twelve hours from the beginning of symptoms, there were 20 recoveries and 1 death. The effect of the time element

can be still more strikingly seen in the steady increase of mortality with lengthened interval since the mortality of his entire series was 36 per cent. The author is impressed with the difficulty of definite diagnosis, for intestinal obstruction in many cases may be simulated by typhoid fever, Henoch's purpura, certain infections, appendicitis, acute pancreatitis, the twisted pedicle of a tumor, lead colic, renal colic, gallstones, mesenteric thrombosis, and diaphragmatic pleurisy. It is comforting to note, however, that most of these conditions demand operation almost as imperatively as bowel obstruction. Post-operative intestinal obstruction is often masked by the symptoms usually present in the first few days after operation. In cases of doubt it is safer to operate. The determining factors are the intestinal character of the vomitus, the failure of lavage and enemata to relieve the vomiting and an increasing pulse-rate with restlessness and thirst. The passage of the stomach tube in doubtful cases of this type may prove to be a means of avoiding reoperation if used with due intelligence. It is safe to say that approximately one-half of the cases of intestinal obstruction occurring in hospital and private practice have their origin in adhesions resulting from previous operative procedures. There has been no satisfactory explanation for some of the phenomena observed. It is probable that the two most potent factors are the presence of a persistent low grade inflammatory process, and the presence of some foreign body, such as unprotected gauze drains. Prevention of sepsis, careful handling of tissue and discontinuance of packing and repacking have helped much. Moreover, not much aid can be hoped for from artificial sources, such as the application to the peritoneal surfaces of ointments or membranes and the like. Paralytic adynamic ileus in some degree is probably of more common occurrence than is usually believed to be the case. Differential diagnosis between paralytic and mechanical obstruction is not always easy. These cases do not always look sick—abdominal pain is not marked, pulse rate is not much increased. Regurgitant vomiting is early pronounced but does not persist. After several days, in favorable cases, vomiting reappears— a sign of reëstablished gastro-intestinal activity. The pathology of this condition is still in doubt. The character of the anesthetic however, does not seem to play an important part, while infection is generally believed to be the most constant etiological factor but in the author's series the picture in a well developed case is rather that of a true paralysis of the sympathetic nervous system.

High Tracheotomy and Other Errors—The Chief Causes of Chronic Laryngeal Stenosis.—JACKSON (*Surg., Gynec. and Obst.*, 1921, xxxii, 392) says that the most frequent cause of chronic laryngeal stenosis is high tracheotomy. The classic distinction between a high and low tracheotomy with reference to the isthmus of the thyroid gland is a relic of the days when too much respect was held for this structure. This distinction should be abandoned. There should be taught only one tracheotomy and that should be low. The trachea should always be incised lower than the first ring, except in those rare cases in which laryngoptosis renders this impossible without entering the anterior mediastinum. The cricoid cartilage should never be cut, unless laryngoptosis places all the rings of the trachea below the upper

border of the manubrium. If, in an emergency, a high incision of the trachea has been made a cannula should not be worn in it. As soon as the patient's breathing has been resumed a low incision should be made and the cannula inserted therein.

Suprapubic Drainage of the Bladder.—MOTHERSILL AND MORSON (*Brit. Med. Jour.*, 1921, p. 418) state that acute retention of urine has been relieved by puncturing the bladder with trochar and cannula for a considerable period. More recently, a process has been refined to facilitate drainage and prevent any leakage into the prevesical space or upon the external abdominal wall. In certain suitable cases the insertion of the self-retaining tube invented by M. DePezzer fulfils its purpose of draining the bladder from above the pubes without leakage or discomfort. This method of drainage can only be adopted when a good distention is to be obtained and no previous operation has been performed. When hematuria is present, the operation is contra-indicated because the DePezzer tube is readily blocked by clots. So simple a procedure reduces shock, a most favorable factor in subjects requiring suprapubic drainage prior to prostatectomy because of deficient excretion of urea. The subsequent prostatectomy is without the difficulty caused by the scarring of the abdominal wall.

Treatment of Syphilis.—MACCORMAC AND KERMAWAY (*Brit. Med. Jour.*, 1921, p. 415) says that the syphilis is but one process whether it involves skin, mucous membrane, nerve or other tissue. The principles upon which treatment is based vary in accordance with the duration of infection. When infection is recent, primary or secondary, two objects are in view: cure of the disease and prevention of communication to others. A severe and lengthy course of treatment should be undertaken. The authors by extensive tabulation have shown that six injections of salvarsan, (Novarsenobenzol used) 0.9 gm. per dose are often insufficient. The "10 injections" series proved satisfactory. At conclusion of these salvarsan courses, mercury was administered intramuscularly for three months. The condition of the Wassermann reaction was determined. If positive, the course was repeated from the beginning. If negative Wassermann was obtained, mercury either in pills or by injections is continued until two years have been completed. The Wassermann reaction was investigated every three months. The authors admit that such a course is severe and long but justifiable when balanced with the serious results of failure and delaying of cure, for as time passes the disease becomes fixed. In late stages of disease active forms of medication such as salvarsan and mercury, by inunction and injection are preferable to other methods. Ten intravenous injections of salvarsan were given followed by three months of intramuscular mercury. Repetition of this course is generally necessary.

Renal Decapsulation for Chronic Nephritis.—KIDD (*Brit. Med. Jour.*, 1920, p. 378) reports several cases of far advanced chronic nephritis, where this procedure has given favorable results. The technic of the operation is described. He believes that the lymphatics are unblocked by decapsulation and that another route is set up for drainage of lymph from the kidney for the lymphatics of the kidney run up from the ureter under the capsule through the kidney where they receive

the lymph of the kidney substance and then to the glands in the vascular pedicle of the kidney. Possibly in these cases of chronic nephritis the lymphatics become blocked either by excess of lymph or by fibrinous deposit and the nephritic poison cannot be drained away from the kidney substance. The author has noted that clear lymph seems to flow from the kidney sponge almost immediately after decapsulation.

Chronic Duodenal Obstruction.—KELLOGG AND KELLOGG (*Ann. Surg.* 1921, lxxiii, 578) say that chronic duodenal obstruction occurs more commonly than is realized and can often be diagnosed from the history and physical signs. The obstruction may involve the first or second portions of the duodenum only, due to ulcer, or gastroptosis or adhesions, or the entire duodenum, most frequently caused by compression between the vertebral column behind and the superior mesenteric artery in front, especially when there is traction in the direction of the pelvis from the drag of a distended and ptosed cecum and colon. The physical signs of obstruction in the first portion are those of pyloric obstruction. When the second and third portions are involved it can often be made out by percussion and succussion. The symptoms are those of epigastric discomfort and toxic manifestations. With a competent pylorus, cramp-like pains predominate. When incompetent, regurgitation of bile is frequent. Symptoms are often suggestive of ulcer, gall-bladder or appendicular trouble; in operating for these conditions with negative findings, the duodenum should be carefully examined. Medical treatment, consisting of abdominal support, nutritious diet and anti-constipation measures is beneficial in the majority of cases. Surgical treatment in obstruction of the first and second portions consists of freeing of adhesions, gastropexy or duodeno-duodenostomy. In the third portion, the procedure of choice is duodeno-jejunostomy. Duodeno-jejunostomy is indicated in vicious circle after gastro-enterostomy, accompanying gastro-enterostomy when the duodenum is obstructed, in obstruction of the third portion not responding to medical treatment. The author describes the technic and cites cases with a general summary of symptoms and results. Total number of reported cases is 58, with no mortality. In the author's series of 41 cases, only 1 was unimproved.

Enterostomy in the Treatment of Acute Intestinal Obstruction.— SUMMERS (*Surg., Gynec. and Obst.*, 1921, xxxii, 412) says in serious cases surgeons make a primary enterostomy as a life-saving measure or do a combined operation, making an enterostomy in the distended coils after successfully removing the cause of obstruction. The field has been still further broadened by including peritonitis ileus in the indications for operation. Formerly, Nealton's injunction to open the first coil of distended intestine for enterostomy procedure had been regularly followed. In 1910 Bonney advised opening the jejunum for this purpose, for it is the segment of toxicity when the vomitus becomes feculent. The positive proof of the value of this procedure in the circumstances is that drainage of the jejunum causes immediate cessation of vomiting. MacKinnon, in 1917, recommended strongly the simple modern drainage of the intestine by introducing a large-sized catheter and fastening it into position by a double purse-string suture. The catheter comes away in a few days with quick subsequent closure

of the abdominal wall. The author advocates jejunostomy when the vomitus is frankly feculent.

Injury to the Bile Ducts and Methods of Repair.—SWEETSER (*Ann. Surg.*, 1921, lxxiii, 629) says that interference with the normal flow of bile is due to a stenosis of the ducts following deep ulceration, pressure by adhesions and division of the common duct (intentional or accidental) during operation of cholecystectomy. The anatomical abnormalities and the presence of abnormal adhesions, congenital and acquired, must be carefully noted and guarded against in right upper abdominal surgery. The methods devised for restoring the bile stream to the intestine have been varied in order to meet the conditions encountered. In most cases the ends of the ducts are widely separated and the intervening space filled with dense scar-tissue. Simple approximation is no longer possible. Therefore, other means must be employed to bridge the hiatus. The tissues which lend themselves best to a successful and permanent anastomosis are those which normally are bathed in bile and consequently are immune to its irritation. When the mucous membrane of the bile duct, stomach or duodenum can be brought and held successfully to the proximal end of the duct, the result has been permanent in the majority of cases. Splinting with a soft rubber tube aids the process of repair. Failures have been due to stenosis or ascending cholangitis with abscesses in the liver. Attempts to bridge the gap with autogenous grafts have all failed in experimental animals. No human cases are recorded. An attempts was made by Murphy to utilize the biliary fistulous tract, but the patient died in eight months.

The Wassermann Reaction.—RAY (*Amer. Jour. Syphilis*, 1921, v, 320) says that in spite of the multitude of modifications and newer methods for the serodiagnosis of syphilis, the classical Wassermann reaction or a technic which departs from it only in minor details stands today as the only reliable laboratory test for syphilis. A series of 580 reactions, performed with crude and cholesterinized extract each with 2 methods of fixation namely, the one-hour incubator and the four-hour ice-box methods is analyzed with the following conclusions: A positive reaction with cholesterinized antigen alone should be given no specific significance in untreated cases presenting no clinical manifestatations of lues and giving a negative history. The four-hour ice-box method of fixation, while increasing the sensitivity of the cholesterine antigen as compared with the one-hour fixation in the water-bath magnifies the non-specificity except in treated cases, congenital syphilis and in some cases of neurosyphilis, where it has a decided advantage. On the other hand, with the crude extract, the four-hour ice-box method of fixation, while increasing the sensitivity does not impair but rather augments the specificity. The cholesterinized antigens possess a specific sensitivity exceeding that of crude in all cases of syphilis under treatment, congenital syphilis and in some cases of neurosyphilis. The great value and importance of lumbar puncture in all cases of syphilis is emphasized. A spinal fluid examination including cell count, globulin estimation, colloidal gold and Wassermann reaction is imperative before prognosis can be given in spite of the fact that treatment has produced a Wassermann negative of the blood.

THERAPEUTICS

UNDER THE CHARGE OF

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AND

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The Tonsillar Route of Infection in Pulmonary Tuberculosis.—ZWALUWENBURG and GRABFIELD (*Am. Rev. Tuberc.*, 1921, v, 57) have described a shadow which they believe represents a thickening of the pleura over the apex of the lung, and they have studied its relationship to tonsillar and cervical gland tuberculosis. They state that such apical pleuritis was seen in 10 per cent of the rœntgen-ray examinations made. Such apical pleuritis occurs most frequently in cases showing tuberculosis deposits in the faucial tonsils (93 per cent). With cervical gland tuberculosis this lesion is recognizable in 59 per cent of all cases and probably occurs in a larger number, being obscured by the shadows of pulmonary tuberculosis, 71 per cent in this group showing either this lesion or frank tuberculosis of the lung or both. Cases without tuberculosis of the tonsil show an apical pleuritis in only 11 per cent of the cases. It is suggested that a common route of infection may lie through the tonsil and cervical lymphatics to the apical pleura and thence into the lung. If this hypothesis is accepted it offers a singularly satisfactory explanation for the frequency of apical lesions, the predominance of right-sided lesions, of the pathogenesis of tuberculous pleurisy with effusion and other obscure features of this infection.

An Output Study of Users and Non-users of Tobacco in a Strenuous Physical Occupation.—BAUMBERGER, PERRY and MARTIN (*Jour. Indust. Hyg.*, 1921, iii, 1) present their second paper in a series of articles on the significance of the use of tobacco in industry, namely, the relation of the use of tobacco to efficiency in a strenuous physical occupation. They adopted output as the criterion of efficiency, and chose the bottle-making industry for their studies. They conclude that smoking has little effect on output rate in the strenuous physical occupation studied. Chewing markedly lowers output rate. Light smokers have a slightly lower output rate than heavy smokers.

A Survey of Carbon Monoxide Poisoning in American Steel Works, Metal Mines and Coal Mines.—FORBES (*Jour. Indust. Hyg.*, 1921, iii, 11) states that carbon monoxide, as met with in metal and coal mines and about blast furnaces in this country, rarely causes late after-effects following acute severe gassing. When such effects do appear, there is evidence, almost always, of a preëxisting pathological

condition. Frequent exposure to carbon monoxide causes headache and malaise, but no evidence has been found of a cumulative harmful effect. As was to be expected, owing to the compensating increase of hemoglobin and red cells from prolonged oxygen want, it is possible to acquire some tolerance to carbon monoxide. A recent advance in treatment has been made by adding carbon dioxide to the oxygen inhalations administered. Recovery is three times as rapid as when oxygen alone is used. An efficient portable carbon monoxide respirator has been perfected by the U. S. Government.

Superinfection in Experimental Syphilis Following the Administration of Subcurative Doses of Arsphenamine or Neoarsphenamine.— BROWN and PEARCE (*Jour. Exp. Med.*, 1921, xxxiii, 553) conclude that the existence of an infection with Spirocheta pallida does not constitute a bar in itself to the introduction and propagation of a second infection in the same animal; that, just as there is a period following a first inoculation during which a second infection may be implanted with the production of characteristic primary lesions, conditions may again arise in animals which have once become refractory to a second inoculation that will favor the introduction of a new infection with the formation of lesions presenting the characteristics of an original or first infection. Experimentally, such a state may be induced in rabbits with early but well-marked primary lesions of the testicles by treatment with either arsphenamine or neoarsphenamine; hence, treated but uncured animals may be rendered as susceptible to a second cutaneous inoculation as a normal animal, and the manifestations of disease resulting from the second infection may be indistinguishable from those of a first infection. The results obtained showed: (1) That the treatment employed was insufficient to cure any of the therapeutic controls; (2) that the infected controls were highly refractory to a second inoculation; (3) that the treated animals were highly susceptible to a second inoculation, and although not cured of their original infection, reacted to the second inoculation with the formation of lesions indistinguishable from those of a first infection; (4) that in certain instances the treatment given had rendered infected animals more susceptible to infection than the normal controls.

Treatment of Epilepsy.—E. CHRISTIN (*Schweiz. med. Wchnschr.*, February 3, 1921) writes that bromide medication is not wholly satisfactory in the treatment of epilepsy. The sodium salt should be employed to avoid the depressant action of potassium on the heart. Bromides may be given in smaller doses if the amount of chlorides in the diet is reduced as much as possible. The employment of the stimulating ammonium salt is considered irrational. Luminal is considered more favorably. It differs from veronal only in the substitution of a phenyl radical for an ethyl group, whereby it is asserted that the sedative effect is greatly increased. The daily dose consists of 2 grains, in cachets. For hypodermic administration, the soluble sodium derivative should be used. Luminal exerts its sedative action without unpleasant side-effects. A large number of observers recommend its use in rapidly recurring

epileptic attacks; it acts more quickly and surely than bromides but is less useful in petit mal. Potassium boricotartrate, in doses of 45 grains a day, has been successfully used by Pierre Marie. Here also the attacks are prevented without the depression frequently accompanying bromide therapy. The author concludes that luminal and perhaps potassium boricotartrate are the only new agents of value in the treatment of epilepsy. Christin speaks of the new conception of the nature of epilepsy developed by Hortenberg, who believes that inhibition has a large share in the development of the attacks. The main interest of this theory lies in the treatment evolved by Hortenberg. He employed strychnine up to as much as 2 grains by mouth; even these formidable doses never resulted in epileptic attacks but rather improved the condition of the patients.

Study of Oxytoxics.—GUGGISBERG (*Schweiz. med. Wchnschr.*, February 3, 1921) recommends pituitary extracts in the treatment of weak labor pains, but urges the necessity of initial small doses. Intravenous administration is the method of choice. Ergot is the mainstay after labor; if administered before the complete expulsion of fetus and placenta, tetanic contraction of the uterus may occur. Experiments on isolated organs showed that quinine in low concentrations caused more frequent contractions, and this effect lasted longer than that following pituitary extract or ergot. Large doses of quinine caused paralysis after an initial period of marked stimulation. Quinine never caused tetanus of the uterus. The dose of quinine during labor should be 4 grains of the sulphate, repeated after an hour. Quinine is also useful in the treatment of abortion, especially where non-operative treatment is indicated in the presence of active infection. Others have reported favorably on the addition of quinine to the narcotics used in the induction of twilight sleep. Quinine is recommended in the early stages of labor, pituitary extract during the second stage, and ergot at the end of labor. Guggisberg mentions investigations carried out with various combinations of drugs. The most favorable results were obtained from a combination of quinine and pituitary extract, and of ergot with placental extract. The author states that he has proved the existence in the placenta of substances stimulating uterine contractions, the action of which appears to render the uterus more sensitive to normal and therapeutic stimuli.

PEDIATRICS

UNDER THE CHARGE OF

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The Calcium Metabolism of Premature Infants.—HAMILTON (*Am. Jour. Dis. Children*, October, 1920) says that the calcium metabolism of premature infants has never been studied before this, but this study is justified by the fact that these infants are more liable to acquire

rickets than full-term babies. It is also a common experience that bone symptoms appear in the premature at an early age, and that the condition more often takes a grave course than in other infants. It has been assumed that this tendency is caused by the absence of a congenital store of calcium, supposed to be present in full-term babies. About 85 per cent of the body's calcium at birth is stored during the last two or three months of intra-uterine life, so that a premature birth exposes the body to postnatal life with a proportionately small amount of calcium. It is thought that this fact is partly responsible for the prevalence of rickets among the premature. The proportionately small amount of calcium in the body of the premature newborn may possibly lead to a state of calcium starvation in the course of postnatal growth. There are, however, in the postnatal growth of prematures often certain characteristic features which might also unfavorably influence the calcium metabolism. Although the difference in corporal development between the premature and the full-term newborn may be very great, there is in the healthy premature, when properly nourished and cared for, a great tendency to make good this difference. It is not unusual for such an infant to double its weight in three months, and triple it in six months. The question arises whether the tissues formed in the rapid recovery from an acute or chronic nutritional disturbance are of the same composition as in the more slowly growing bodies of normal infants. It is logical to believe that they are rich in water and poor in salts. The author made studies on 4 infants born from four to ten weeks before full-term. The causes of the premature births were advanced pulmonary tuberculosis in the mothers in 3 cases, and nephritis and eclampsia in the other 1. In the cases of tuberculosis the babies were separated from the mothers immediately after delivery. Symptoms of tuberculosis and syphilis were absent in all cases during the period of observation. The Wassermann tests were negative. The infants were nourished from birth exclusively on breast milk given in bottles. They gained rapidly in weight during the months in which the experiments were carried out. The stools at times were both frequent and loose both during the experiments and in the intervals. These were the normal loose and frequent stools that are frequently seen in babies on breast milk. Three of the 4 infants had a very low calcium retention during the first months of life. This might possibly be ascribed to rickets, as in all of the children craniotabes appeared in the second month. This is not in harmony with the fact that although the craniotabes increased in the months that followed, the retention of calcium increased to amounts found in normal infants. It was demonstrated that in those periods where the intakes exceeded 200 mg., the retentions are as large as in normal infants, while in the periods where the intakes were lower than this amount, there was sufficient retention in only 1 case. If sufficient retentions are to be attained, it would seem that the intake must exceed a minimum of 200 mg. The calcium is excreted mainly in the stool. The daily amount of feces excreted by prematures is very large, a fact that may be explained by the low fat absorption found in prematures. The daily values of the total solids are consequently higher than in normal infants, although the quantities of milk taken by prematures are very small. The calcium percentages

of the total solids were found to be lower than in normal infants, but not sufficiently lowered to counterbalance the excess in total solids and the small intakes. To balance these factors exceedingly low calcium percentages would have been necessary. An experiment where a normal infant was alternately fed with ordinary breast milk and breast milk fortified with fat demonstrated that a high fat intake may in the breast-fed infant lead to a temporary loss in calcium. The increased fat ingestion was followed by an increased fat excretion. During the experiment the feces took on the appearance of the feces in prematures. It was due to an excess in fat intake. In the prematures there is suggested an insufficiency of the digestive mechanism.

Butter Fat and the Child Weight.—LARSON (*Arch. Ped.*, October, 1920) presents data from the weight charts of 10 children selected from a number in an orphan's cottage home. The weights were recorded at intervals of six months during two and a half years. The weights of 3 were incomplete for this period, due to the fact they were discharged before the end of this period, or had not been admitted at the beginning of the study. The cottages have a population of about 30 children, but because of the changes those who had not been for some length of time were not considered, and those who had received medical treatment were also not included. It was observed that there was a gain in weight for each six month period except the fourth. During this period the superintendent in compliance with the request of the Federal Government for food conservation, especially of the animal fats, had substituted oleomargerine for butter in the diet of the children. Nine of these 10 children lost weight during this oleomargerine period. The other child was a girl, who was considerably above the weight and height for her age, but her progress was retarded as compared with her gain during the previous and following periods. The 7 children whose records were complete for two and a half years showed a gain of their combined weights for the first three six month periods, but a loss of their combined weights for the fourth period, which was the time in which oleomargerine was used. There was again an increase of their combined weights for the last fifth-sixth month period, during which butter was again added to their dietary.

The Heart in Scarlet Fever.—ROSENBAUM (*Arch. Int. Med.*, October, 1920) studied 1770 cases of scarlet fever. There were 106 patients with recognized cardiac complications, 94 of whom developed these complications during the course of the disease, and 12 were instances of old heart disease. Eighty-eight of these 106 patients or 5 per cent of all the cases had myocarditis. Of these 53 were mild, 31 were moderately severe and 5 were very severe. Myocarditis may occur at any time in the course of the illness, but is most common in the latter days of the acute stage or early in convalescence. Other complications seemed to increase the incidence of myocarditis. It was observed more frequently in the early years of life. Pericarditis was present in 3 cases or 17 per cent. Two of these patients died. Endocarditis was present in 4 cases or 0.22 per cent. Systolic murmurs at the apex were frequently heard, but were usually regarded as functional or relative. The low percentage

of endocarditis as compared with the percentages in several other series may be due to the milder type of scarlet fever in which the case mortality was less than 4 per cent. Unless it was very severe old heart disease does not necessarily indicate a serious prognosis in scarlet fever.

A Note on the Occurrence of Congenital Atrio-ventricular Dissociation.—CARTER and HOWLAND (*Bull. Johns Hopkins Hosp.*, October, 1920) report a case at five years of age. A cardiac lesion had been noted at nine months. At the age of two years an electrocardiographic record showed complete heart block. Two years later the diagnosis was confirmed by a different physician. The patient has never experienced shortness of breath, cyanosis, or given any evidence of an impaired myocardium although she plays around as other children do. An electrocardiographic record made in May, 1919, showed complete atrioventricular dissociation with an auricular rate of 103 and a ventricular rate of 37. The cardiac rate at that time was from 48 to 52 beats per minute. Seven other cases have been reported in the literature. The diagnoses were made at the ages of seven days to fifteen years. Of these 8 cases, including the present, 3 gave no symptoms; 1 had syncopal attacks; 2 had pain around the heart; 1 had dyspnea and palpitation on exertion; the present case had an occasional stitch in the side on exertion. Six cases had complete dissociation. One case had partial 2 : 1 rhythm. Another had alternating 2 : 1 rhythm and complete dissociation. Marked cardiac hypertrophy was present in 5, and slight in 3. All the cases were free from cyanosis except 1.

Hypopituitarism.—LISSNER (*Endocrinology*, July–September, 1920) reports the case of a child of twenty-three months, who was normal until the ninth month. At that time he began to gain rapidly in weight. Symptoms began with convulsions of flexor type, and these continued up to within one month of his death. There was no diabetes or glandular trouble in the family. The eyes showed edema of the retina but the throat was negative. There was a marked muscular dystrophy with profound facial cyanosis, diminutive external genitalis, doubling of weight in the third year, low sugar tolerance and an antemortem temperature of 107.5°. The roentgen-ray of the skull showed a small sella turcica. At autopsy the sella turcica was found to be small with the anterior and posterior clinoid processes underdeveloped. The pituitary body was present but underdeveloped. This showed the line of demarcation between the anterior and posterior lobes lost. Histologically numerous thin walled bloodvessels formed a plexus surrounding strands of polyhedral cells arranged in three or four rows. These cells were of the usual two types found in this gland, and they intermingled without definite arrangement or regularity, the "chief" cells being far more numerous. Here and there were a few follicles lined by low columnar epithelium. There was an abundance of loose connective tissue.

Amyotonia Congenita.—HOLMES (*Am. Jour. Dis. Children*, November, 1920) reports a case which conforms in all the essential details to the condition described by Oppenheim. The condition was present at birth. There was no permanent improvement, and the child died of the

usual pulmonary complications at the age of eighteen weeks. The significant lesions are found in the spinal cord and in the muscles. The spinal cord is relatively large for the age of the child; the anterior roots are diminished in size as compared with the posterior roots. There is no disturbance of the contour of the cord in cross-section. Microscopic examination shows complete absence of any acute or chronic inflammatory process, and no evidence of recent degeneration. Myelinization is normal. The cells of Clark's column are of normal size and well preserved. The large or motor cells of the anterior horns are strikingly few in number, and are in part represented by cells that are much smaller in size but otherwise of the same appearance. A cell of normal size is found only infrequently, but except in size such cells as are found are perfectly normal in appearance. There is no gliosis. In the muscles, areas or bundles of hypertrophied but otherwise normal muscle fibers are intermingled with areas of small apparently healthy muscle fibers. The latter appear to represent less fully developed bundles of muscle fibers. There is no evidence found of past or present degenerative processes. The component muscle cells are embryonic in appearance, resembling most closely muscle cells from a human fetus of the third month. There is no increase in connective tissue and no evidence of replacement of muscle tissue by adipose tissue. The histopathological findings are best explained on the assumption of a delayed or retarded embryological development affecting certain motor cells of the anterior horns and certain groups of developing muscle cells. No anomaly of muscle spindles, peripheral nerves, or bloodvessels is recognized.

The Effect of Diphtheria Antitoxin in Preventing the Lodgment and Growth of the Diphtheria Bacillus in the Nasal Passages of Animals.— GELIEN, Moss and GUTHRIE (*Bull. Johns Hopkins Hospital*, November, 1920) publish the results of their experiments in animals. They say that certain conditions in their experiments with animals were quite different from those present in human beings. This is especially true of the frequency with which the carrier state occurs spontaneously and the ease with which it may be produced experimentally. In a large series of human beings including both children and adults, they found that a single examination revealed an incidence of diphtheria bacillus carriers of about 3.55 per cent. A second examination practically doubled the number of carriers discovered, while a third examination still further increased the original number. Among the 72 animals which formed the basis of these experiments, as well as the 40 additional animals which were also used in other experiments, none showed diphtheria bacilli at the beginning of the study. The investigators were able to induce the carrier state in man experimentally both with virulent and non-virulent diphtheria bacilli. This was not the result in all efforts but occurred in a considerable number of cases. In guinea-pigs, rabbits and cats they found the carrier state difficult to produce, and generally very transient if it occurred at all. In the 70 animals 358 cultures were made. It was found that the production of nasal infection or infestation of cats, rabbits and guinea-pigs was very inconstant even when the organisms were introduced directly into the nose. A somewhat higher percentage of animals showed positive cultures among those directly inoculated than among those merely exposed to a

carrier. Cats and rabbits became infected with about the same frequency, and the incidence of the positive cultures was almost similar. Among the guinea-pigs 66 per cent developed positive cultures, and 26 per cent of the total number of cultures showed Klebs-Loeffler bacilli. The duration of infection was usually quite short. The health of the animals was apparently unaffected by the mere presence of bacilli in the nose. The occurrence and duration of infection were independent of the virulence of the strain of organisms used, and were wholly unaffected by previous administration of antitoxin.

OBSTETRICS

UNDER THE CHARGE OF

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Inevitable Abortion.—VALLIER (*Rev. Argent. de Obst. Y. Gynec.*, 1920, iv, 10) considers these cases with regard to the presence or absence of fever. If rise of temperature has not developed, the indication is favorable, but where fever occurs it is an evidence that infection has reached the uterine cavity and that the lining membrane of the uterus has become involved. The development of symptoms during the third and fourth day results from growth of bacteria which reaches its highest point from the seventh to the ninth day of the puerperal period. Against this process the lochia discharge has some antiseptic power, leukocytosis may aid excessive formation and granulation tissue may limit absorption and prevent the spread of bacteria. If the blood is involved the patient will have rigors and evidence of septic embolism and thrombosis will soon become apparent. Treatment can do no good and the patient's recovery will depend entirely upon the degree of virulence shown by the invading germs. After fever has developed no treatment should be applied within the genital canal and even the finger should be excluded. The best method of emptying the uterus consists in stimulating the uterine muscles to contract which the writer does by the application of cold over the abdomen and the administration of quinin. No interference whatever is practised in the genital tract. If the contents of the uterus are not discharged nothing is done until the fever has subsided, then the uterus should be curetted. If the patient has free bleeding operation is forbidden and if the uterus becomes retroflexed it must first be put in favorable position before it can be emptied. KING (*Jour. Am. Med. Assn.*, 1920, No. 75, p. 147) does not interfere with the genital tract in treating infections after labor or abortion. A very careful bimanual examination is made and if possible a culture obtained from the uterine cavity. If there is reason to believe that a portion of the placenta has not been delivered, this is removed with the least possible disturbance. The patient is placed practically in the Fowler position to secure drainage. High

temperature is modified by the use of water. The patient is given fluids very freely by bowel or the stomach and in some cases beneath the skin or in the vein, and enemata are employed to empty the intestines. If nausea develops it is often relieved by calomel, cold over the abdomen in the acute stage and later copious douches of hot water seems to be of value, such douches can only be given after the acute symptoms have subsided. In choosing the time for operation it is useful to examine cultures from the womb and when they are negative and fever has disappeared, the indications for operation are favorable. Immediate interference may be made necessary by the presence of pieces of placenta in the neck of the womb or by free hemorrhage caused by the retention of a portion of the embryo within the uterus. In 33 patients who had well-marked infection of the blood 8 died, of whom 2 were dying when brought to the hospital. Twenty-three of these cases had pelvic cellulitis develop but in 17 this entirely cleared up, 4 of them had late formation of pus and 2 died after interference which was evidently not indicated. Four patients died from active infection of the peritoneum. There were 266 abortions complete or incomplete in which all the patients made an entire recovery. Of these 86 had some disturbance of temperature. These cases had been followed up and some of them have had healthy pregnancies and natural birth. So far as can be ascertained operations have been performed upon none.

Fatal Cases in Puerperal Period from Sepsis of Other than Puerperal Origin. — From the Clinic of Würzburg, Schmitt (*Monatschr. f. Geb.*, 1920, No. 2, vol. li) reports cases ending fatally from an infection of non-puerperal character, in 20,000 cases of labor in thirty years. There were 5 deaths from puerperal infection following normal labors; 1 of these patients had gonorrhea and had received local treatment up to the time of labor. Two had infection of the blood stream originating in the tonsils and 2 had infection with exogenous germs introduced during digital examination. In these cases the infection was evidently autogenous. Most writers upon the subject had admitted the possibility of autogenous infection by which is meant a general puerperal infection from bacteria present in the genital tract before labor. In these cases bacteria from the lower infected portion of the genital tract make their way upward and enter the uterus. Von Rosthorn first called our attention to puerperal infection from the blood stream. Experiments and clinical observations have shown in 12 carefully studied cases that in 8 the pneumococcus was the infecting germ, in 1 a streptococcus from pneumonia and in another polyarthritis from staphylococcus. In 1 typhoid ulcerations from the intestines and in another the Streptococcus angina. In recent literature there have been reported additional cases of Streptococcus anginosis, 2 of which had origin in the tonsils from which bacteria entered the blood. In the 20,000 labor cases in the Würzburg Clinic 1 of these cases was the only instance of infection developing in the blood stream. The writer describes the case of a primipara, aged twenty-three, who had a normal labor without lacerations. On the fourth day she had chill and fever and on the seventh day had pain in the throat, both tonsils reddened and swollen. The

lochia was normal, the abdomen normal, the uterus not sensitive. On the eighth day the abdomen became distended, on the ninth day peristalsis ceased in the intestines and on the tenth day death ensued. Autopsy showed a purulent pus streptococcus, peritonitis and swollen spleen and apparent parenchymatous degeneration of the liver and intestines. There was no pus in the uterus although the uterine muscle was slightly yellow in color. At the placental site there were small red granulations but no sign of infection. Vessels in the broad ligament were not involved and there was no purulent lymphangitis. The left tonsil was red and greatly swollen, the right was not reddened but swollen and boggy. No bacteria were obtained in the endometrium nor any evidence of infection in the uterus. On microscopic examination pus taken from the peritoneum was swarming with streptococci, from the tonsil streptococci were apparently not present, on making section of the tonsil the characteristic changes produced by infection were found. There could be no question concerning the relation of the process in the tonsil and the fatal result in the patient. We have abundant examples of infection in the other serous membranes of the body for which the focus existed in some comparatively distant organ, but cases of genuine peritonitis following foci in other organs than the abdomen are not common. The second case had also a normal labor but was examined internally three times by students. The first seven days of the puerperal period were normal, but the patient developed high temperature on the eighth day with pain in the upper portion of the left thigh, and in the lower third of the thigh marked swelling and sensitiveness. The patient died on the twelfth day with symptoms of general sepsis. A thorough autopsy failed to reveal evidence of infection in the genital tract nor were the bloodvessels in the genital region involved. On the inner aspect of the left thigh there was a bleb filled with blood, and the connective tissue in this vicinity was infiltrated with bloody fluid. Evidently there had been some lesion in the thigh which had produced the general infection. The third patient had normal labor. On the fourth day she had violent pain in the back and right upper thigh. On the fifth day fever, then chill, with normal lochia and sensitiveness on the right side of the abdomen. On the sixth day distention and on the seventh evidence of acute peritonitis. Operation was performed, the intestines were distended, the fluid in the peritoneal cavity containing streptococci. Drainage was introduced, the intestines became paralyzed and the patient died on the fourteenth day. The vessels in the parametria showed pus, thrombosis of the right femoral veins, the bronchi were greatly reddened, swollen and the right lung adherent to the pericardium. In the lymphatic glands of the region there was dark blackish-red hemorrhage. The uterus, tubes and ovaries were normal. On careful questioning it was found that just before coming to the Clinic for labor the patient had nursed her sister suffering from a severe attack of influenza. The fourth patient came to the Clinic because a child was ill with scarlatina at home. On admission she was isolated and not examined and labor occurred three hours after admission. Chills and fever developed on the fourth day without other symptoms. On the sixth day the lochia became foul and there was tenderness on both sides of the uterus. On the eighth day peri-

tonitis and on the tenth day death without signs of scarlatina. Unfortunately an autopsy could not be obtained. In the reviewer's experience fatal streptococcus infection followed delivery of a patient at which the operator was assisted by a physician who was in constant attendance upon a severe case of scarlet fever. Careful antiseptic precautions were taken during the delivery, the operator not knowing at the time that the assistant was in attendance upon the case of scarlet fever. This fact was concealed as long as possible but the death of the patient and natural questioning as to the possible source of the infection revealed the true circumstances. The reviewer observed a primipara with spontaneous labor, followed on the fourth or fifth day by considerable fever. The genital tract showed no evidence of infection, careful examination of the mouth revealed tenderness at the root of a partly decayed tooth. A dentist incised the gum obtaining about 1 dram of very foul pus, a disinfection of this area was followed by prompt disappearance of the fever and uninterrupted recovery of the patient. In a third case in the experience of the reviewer death followed Cesarean section. At autopsy the genital tract was in an aseptic condition, intestinal mucous membrane was greatly reddened and swollen with areas of ulcerations and lymphangitis in the peritoneum and intestines. The history revealed the fact that before coming to hospital the patient had tried to destroy the child by taking large doses of violent and irritant cathartics. In the absence of other evidence it was concluded that infection had arisen in the intestinal tract and had been the cause of death.

The Moisture and Ash of Maternal and Fetal Blood.—Stander and Tyler (*Surg., Gynec. and Obst.*, September, 1920) published the report of their studies on this subject in the obstetric clinic of the Medical School of Yale University. After stating in detail in tables the results of their work, they find that during pregnancy the water-content of the blood is usually from 77 to 82 per cent of normal. The tendency is toward the larger quantity and this was even exceeded in one-third of the cases. If patients are examined month by month during pregnancy, considerable changes in the water of the blood are found. Until the seventh month, this greatly increases, then remains stationary or slowly decreases. By the time that labor begins it is practically the same as in the early weeks of gestation. Labor itself seems to have no constant influence upon the quantity of water in the blood. The water-content of the blood varies inversely with the corpuscular count. The water in blood plasma, examined month by month, shows the same kind of changes which are found in the whole blood. During pregnancy, so far as quantitative analysis is concerned, the ash of the blood and the ash of the plasma remain normal. So far as blood moisture is concerned, one cannot distinguish eclampsia from nephritis. In both the percentage of water may be sufficient to constitute a true hydremia and this is often seen in patients having marked general edema. When the ash in maternal and fetal plasma indicates that a free exchange of inorganic material is taking place, the proportions of each are identical, and this change is going on through the placenta by the process of osmosis. Moisture of the whole blood is considerably higher in the mother than in the fetus. The moistures

in mother and child approach each other closely, although a difference of 1 per cent in favor of the fetus is generally found. Factors not clearly known keep up osmotic change between the circulation of the mother and child and water passes through the placenta equally well in either direction.

GYNECOLOGY

UNDER THE CHARGE OF

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Vaginal Cysts.—The clinical importance of vaginal cysts is not extensive, neither are they of extreme rarity: their interest lies chiefly in their origin, for which there are several possibilities. In presenting this subject STRONG (*Am. Jour. Obst. and Gynec.*, 1921, i, 357) reminds us that traumatism or operative enclosure may result in a cyst without characteristic features. More interesting are heterotopic vestibular or cervical glands which may give rise to cysts of the lower or upper vagina. Apart from such misplacement of the glands it must be noted that the squamosa of the vagina may, through faulty development, be replaced by columnar epithelium and this may give rise to glandular structures which may become cystic. Vaginal cysts from such an origin are liable to be small, multiple, with a low columnar epithelium which may be in true papillæ. The most interesting form of cysts, is that derived from the Wolffian or Gärtner's duct, and this type may be of considerable size. It is interesting in point of size, in point of complexity of form, and in its predilection site, but apart from these considerations it must be admitted that origin from the Wolffian duct is largely inferential and that there is no determining characteristic. There are three sites of predilection of vaginal cysts, namely, the epoöphoron, the ampulla and the lowest portion of the vagina inclusive of hymen. Abnormalities in form and course of the ducts occur. The epithelium is so variable and individual that one can hardly speak of true abnormalities, and squamous epithelium has been found in adults. Cysts are the commonest variations from the persisting duct and occur in various sites. Finally adenocarcinoma and adenomyoma may be formed from rests.

Gehrung Pessary for Cystocele.—The advantages and method of use of the Gehrung pessary in the relief of cystocele has been emphasized by ILL (*Am. Jour. Obst. and Gynec.*, 1921, i, 338) who reminds us that the pessary consists of the Hodge instrument bent on itself so as to

form a double horseshoe, one lever being a little shorter than the other. Its object is to hold up the anterior wall of the vagina and, with it, the bladder. The position of the pessary is such that the smaller horseshoe or lever will be placed anterior and below the cervix, while the larger one will be just above the neck of the bladder. The junction of the two horseshoes will remain in both lateral fornices. To fit well the pessary should be freely movable and not felt by the patient on walking or sitting down. In fact she should not be conscious of wearing the instrument except that she is comfortable, that she has lost the dragging sensation and the irritable bladder. The introduction of the instrument is rather difficult to describe. The pessary is held between the thumb and the fingers of the right hand by the rounded end of the horseshoe, the smaller one being forward. The connection between the horseshoe to the patient's left is introduced first and then with a rotary motion of 180 degrees the whole pessary is slipped into the vagina where another rotation of 180 degrees will put it in place. Care should be taken that neither horseshoe slips behind the cervix in which case it will have to be removed and reintroduced, for the cervix will form a bar over which the pessary cannot be slipped. It goes without saying that experience and trial can only determine the proper size of the instrument to be used for each case. It is better to start with a small-sized pessary and allow the patient to walk about the office as a test, than to use a large instrument which may produce pain and injury. Ill states that those who will take the trouble and patience to master it will find great satisfaction for themselves and secure immeasurable relief for their patients. The great objection to the pessary is that while the patient can remove it she cannot replace it, Gehrung to the contrary notwithstanding.

Roentgen Treatment of Uterine Hemorrhage.—KINNEY (*Calif. St. Jour. Med.*, 1921, xix, 76) very wisely remarks that uterine hemorrhage is a presenting symptom, never a diagnosis, and the underlying pathology must be ascertained before any intelligent treatment can be instituted. In approaching a case of prolonged atypical hemorrhage one must eliminate, first, the accidents and incidents of pregnancy, second, pelvic infection, and third, malignancy. Having ruled out this triad, practically every case of uterine hemorrhage can be controlled by roentgenotherapy. However, efficient roentgen-ray treatment involves the establishment of the menopause and sterility and, therefore, the roentgen-ray will only be called into use after the general physical and mechanical conditions have been ruled out or properly treated. There are cases on record where the ovaries have been protected during roentgen-ray treatment and normal menstruation and normal pregnancy have followed a clinical cure. However, the danger of the complete arrest of menstruation limits the roentgen-ray treatment of uterine hemorrhage to those conditions where the establishment of the menopause is justifiable. Kinney has found roentgenotherapy efficient and suitable in the following types of cases: (1) In patients that have atypical bleeding from a grossly normal uterus nearing the menopause or as incident of the menopause the hemorrhage can be controlled and the menopause established in practically 100 per cent of cases. (2) In uterine hemorrhage from small fibroids at or near the menopause the

arrest of the bleeding and establishment of the menopause are certain, and the fibroid will disappear or decrease in size and become symptomless. (3) Patients that are poor surgical risks with uterine hemorrhage from any type of fibroid can be relieved from their symptoms of hemorrhage quickly and effectually by roentgen-ray. (4) There are certain cases where uterine hemorrhage and dysmenorrhea are so destroying to the patient's emotional and mental balance or so undermining her physical condition that a menopause is justifiable, and where it is justifiable it can be secured easily and certainly with roentgenotherapy. On the other hand, roentgenotherapy is contra-indicated where the establishment of a menopause is not justifiable, and is contra-indicated in the treatment of uterine hemorrhage where that hemorrhage is a symptom of an urgently surgical condition. Uterine hemorrhage in adolescence can be readily controlled without danger by radium and it is not justifiable to assume the risk of the menopause except where radium is not obtainable or in extreme cases. In the hemorrhage of uterine fibroids in young women the patients should be given a chance of a myomectomy if possible rather than hazard their expectancy of motherhood. Uterine hemorrhage accompanying a submucous of sloughing fibroid is the presenting symptom of a distinctly surgical condition and should only be treated as such. The treatment of large fibroids with symptoms of pressure can be successfully carried out with roentgen-ray and is justifiable in those cases presenting serious surgical contra-indications. But whether the roentgen treatment of large fibroids in patients that are good surgical risks is justifiable is still an open question. Kinney does not believe that it is justifiable and considers that the extirpation should be strongly advised for every patient having a large fibroid or with definite pressure symptoms. Furthermore, uterine hemorrhage with malignancy is an indication for either radium or surgery, and one must be constantly on guard to see that these cases have their radium or their surgery at the earliest possible moment. The foregoing statements and opinions are as fair and unbiassed as any we have ever known to come from a roentgenologist.

Primary Pelvic Lymphadenitis.—Although no little study has been given to the lymphatic glands of the pelvis from both the anatomical and the clinical standpoint, such investigations have been practically limited to the consideration of these glands in malignant disease of the uterus or other pelvic organs. The possibility of non-malignant disease of these glands, as well as that of primary malignant, lymphatic disease seems to have been overlooked. The occurrence of 3 cases of enlargement of the pelvic glands giving rise to striking clinical manifestations during a two months' service had led WILLIAMS (*Boston Med. and Surg. Jour.*, 1921, clxxxiv, 194) to believe that pelvic masses consisting of such glandular enlargement must be of not infrequent occurrence although but seldom recognized. The term primary disease of the pelvic lymphatic glands is, perhaps, somewhat inaccurate inasmuch as, with the sole exception of lymphosarcoma or Hodgkin's disease, involvement of any part of the lymphatic tract must be secondary to a process in some other organ or tissue. He has selected the title, however, to differentiate those cases in which the enlargement of the glands in itself gives rise to important clinical manifestations, from those in

which the enlargement of the glands is solely a measure of the extent of a malignant process in another organ. An analysis of the cases which Williams has observed shows that a mass in the pelvis close to the pelvic brim and definitely not connected with the uterus or its appendages was present in all 3 cases. Pain was present in all 3 cases. In 2 it was localized in the right iliac fossa and in 1 it was localized along the course of the ureter and in the kidney region and was due to occlusion of the ureter by pressure of the glandular mass from without. Psoas spasm was present in 2 of the 3 cases and must be regarded as quite an important symptom. Of course a roentgen-ray of the spine is necessary to rule out the mass and contracture due to psoas abscess from spinal caries. The leukocyte count in all these cases, even the 1 with abscess, ranged between 9000 and 11,600. Further observations may or may not reveal higher white counts in more virulent infections. The white count, obviously, must be influenced in great part by the particular organism concerned as well as the resistance of the patient.

Enormous Ovarian Cyst.—A case of an ovarian cyst which weighed more than the patient who carried it has been reported by HARLEY (*Indian Med. Gaz.*, 1921, lvi, 18) and reminds us of the type of cases that were quite prevalent before the day when Ephraim McDowell showed the way to the medical profession by performing his classic ovariotomy. In the case reported by Harley, the patient had noticed an enlarged abdomen over a period of fifteen years and at the time of operation she weighed 246 pounds, while immediately after operation she only weighed 82 pounds. Thus the tumor and its contents weighed 164 pounds or twice as much as the patient herself. It is unfortunate that the patient did not survive the operation, although it could hardly be expected that she would have much resistance when in such a physical condition.

Results of Radiation in Benign Conditions of Uterus.—As a result of a follow-up investigation in a series of 58 cases of benign pathological conditions of the uterus which were subjected to radium therapy, PAYNE (*Virginia Med. Monthly*, 1921, xlvii, 525) is convinced that radium is the treatment of choice in all cases of small myomata whose only symptom is hemorrhage and in all types of myopathic hemorrhage and in all types of uncomplicated leukorrhea. In his work he noticed that immediate cessation of the periods occurred in about 40 per cent of the cases: two or more periods in about 23 per cent of the cases: a return to normal with regular periods in about 15 per cent of the cases. In about 5 per cent of those cases in which immediate cessation of the bleeding occurred, there has been a return after a period of about one year which has been readily controlled with a second dose of radium. There is usually a profuse leucorrheal discharge following large doses of radium in about 19 per cent of the cases and a slight leucorrheal discharge continuing for about six to eight weeks in about 26 per cent of the cases. Pain coming on after the third day and lasting about a week occurred in about 25 per cent of the cases. In women above forty years of age or in those cases where larger doses have been given, about 50 per cent of them showed symptoms of the menopause following their treatment.

Gynecologic Backache.—In a series of 721 cases of backache studied at the Woman's Hospital in New York by BULLARD (*Am. Jour. Obst. and Gynec.*, 1921, i, 717), 85 per cent were cured by an appropriate operation. About 15 per cent of this series having one or more common gynecologic causes of backache present were not relieved of the backache by anatomically satisfactory operations, but probably much more than 15 per cent of female backache is not gynecologic. This series suggests that 15 or 20 per cent of all women with retroversion, prolapse, pelvic inflammations, obstetric lacerations or pelvic tumors do not have backache. Bullard pleads for closer coöperation with the orthopedist, the internist and the neurologist in order that the gynecologist may better diagnose and treat backache in women.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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Russell's Fuchsin Bodies.—In the course of a study of dental granulomas, McConnell and Lang (*Jour. Med. Research*, 1920–21, xlii, 99), made a careful examination of the fuchsin bodies found in these lesions. The granulomas studied consisted in a chronic or subacute process occurring between the tooth and the surrounding bony tissue, characterized by marked infiltration of plasma cells, with fuchsin bodies occurring in close relation with them. By oil immersion objective, it was apparent that the fuchsin bodies had their origin in the plasma cells, minute droplets being seen in the cells which showed the characteristic staining reactions. The authors consider that they result from degenerative changes taking place within the protoplasm of the cell, in which the nucleus takes no part. No one type of cell can be considered as the sole origin, as no type of nucleated cells can be ruled out. Brown and others believe that fuchsin bodies arise from red blood cells, but the authors think that the evidence is against this, since there was found to be no relationship between fuchsin bodies and capillary channels, no association with hemorrhage, no indication of changes in the red cells and that they show different staining reactions from red cells, being intensely Gram-positive.

Transmission of Specific Immune Bodies from the Mother to the Young.—Howell and Eby (*Jour. Infect. Dis.*, 1920, xxvii, 550), conducted an interesting series of experiments upon six rabbits to demonstrate, (1) the transmission of specific immune substances from the

mother to her offspring; (2) the duration of immune bodies in the serum of off-spring of immune rabbits and (3) the effect of parturition upon the antibody-content of the serum of an immune rabbit. Rabbit 1, was immunized against human red blood cells; rabbit 2, against sheep red blood cells; rabbits 3, 4, 5, and 6 were immunized against streptococcus viridans, Type II pneumococcus, meningococcus and B. typhosus respectively. The results were concisely epitomized in tables. The principles gleaned from the experiments led the workers to conclude that there is considerable variation in the antibody content in the serum of rabbits. The agglutinin and complement-fixation bodies were apparently more stable in the instance of rabbit 6 which was immunized against B. typhosus than in the remainder. The workers demonstrated that complement-fixation antibodies generally were less stable than the hemolysins, agglutinins and opsonins studied in this series. Concerning the original hypothesis, the workers feel that there is a definite transmission of specific immune bodies from mother to offspring, but they are not prepared to state from these experiments the source of these immune bodies, whether from maternal circulation or from mother's milk, and that the duration of the specific immune bodies in the serum of the young is only four to six weeks and ever decreasing in amount. The proof is furnished by the tests that parturition produces a definite decrease in the antibody content of the maternal serum.

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Studies on Measles. I. Susceptibility of Monkeys to the Virus of Measles.—In an attempt to arrive at more conclusive evidence concerning the susceptibility of animals to the virus of measles, BLAKE and TRASK (*Jour. Exper. Med.*, 1921, xxxiii, 385), presented the results of several interesting and fruitful experiments on the transmission of this disease from man to monkeys and the passage of the infection from monkey to monkey. Of 10 monkeys inoculated with both filtered and unfiltered nasopharyngeal washings from seven patients with measles, 8, after an incubation period of six to ten days, developed symptoms closely resembling those of measles in man. The secretions from the human cases of measles were collected by irrigation of the nasopharynx with 20 to 40 c.c. of sterile 0.85 per cent salt solution. Five to 10 c.c. of the nasopharyngeal washings were introduced intratracheally into the monkeys. The symptoms which the animals presented were constant and consisted in listlessness and drowsiness after a definite incubation period (averaging seven days), catarrhal conjunctivitis, a characteristic enanthem usually confined to the labial mucous membrane, a definite exanthem consisting of discrete, red maculopapules constant in character but somewhat variable in extent and duration, and comparable histologically with the lesions of measles, a leukopenia and prompt and complete recovery after an illness of seven to ten days' duration. It was further shown that the characteristic group of symptoms which followed the inoculation of monkeys with the nasopharyngeal washings from patients with measles could be successfully carried through six passages by intratracheal injections of saline emulsions of the skin and buccal mucous membranes of monkeys killed from two to six days after the onset of the symptoms. From the fourth passage monkey the reaction was also successfully induced in 3 monkeys

by means of citrated whole blood injected intravenously. It was found that the blood so introduced was capable of inciting the reaction from at least the seventh to thirteenth days after intratracheal inoculation of the donor monkey but incapable of inducing it from the second to fourth days. Cultures of the blood showed no growth. The incubation period after the intravenous injection of blood was shorter than when intratracheal instillations of the nasopharyngeal secretions were employed, being four instead of seven days. From their experiments the authors conclude that Macacus rhesus monkeys are susceptible to inoculation with the virus of measles.

Hemolytic Streptococci of the Appendix Vermiformis. — KRAFT (*Jour. Infect. Dis.*, 1921, xxviii, 122) comments on the paucity of information at hand on the etiological significance of the hemolytic streptococci in appendicitis. He investigated 48 normal and 77 pathological appendices removed at operation, with the object of determining the frequency with which hemolytic streptococci are found in the normal appendix and in acute and chronic appendicitis, and if possible, the role they play as a primary etiological factor in appendicitis. The organisms were cultured from the appendiceal contents, the mucosa and wall of appendix, being classified according to Holman. Two strains of streptococcus hemolyticus infrequens were isolated from 48 apparently normal appendices where they occurred only in small numbers. Three strains of Streptococcus hemolyticus infrequens and 1 of streptococcus hemolyticus II occurred in 77 pathological appendices in almost pure culture. The acute appendices yielding hemolytic streptococci were either ulcerated or gangrenous. No hemolytic streptococci were isolated from 25 chronic appendices. All strains of hemolytic streptococci isolated were pathogenic for rabbits. A review of other work shows that hemolytic streptococci are frequently encountered in the gastrointestinal tract. In acute appendicitis, however, it appears that hemolytic streptococci when present are the predominant organisms and the principal etiological agent. Thirty-two strains of Streptococcus viridans were isolated from 48 normal appendices. Of 108 strains of nonhemolytic colon bacilli which were encountered 45 were found in the 48 normal appendices and 63 in the 77 pathological appendices; 51 strains of hemolytic colon bacilli were isolated of which 19 were found in 48 normal appendices. Two probably pneumococcus strains were found, also 1 case of pin worm. In addition, many large unidentified bacilli, which, in all probability, were non-pathogenic were found.

Diphtheria Carriers and Wound Diphtheria.— SIMMONS, WEARN and WILLIAMS (*Jour. Infect. Dis.*, 1921, xxviii, 327) report 75 cases of diphtheria and 102 diphtheria carriers occurring at the Walter Reed General Hospital from October, 1918 to August, 1919. All active cases and carriers were isolated. Schick tests were performed on all contacts, and when indicated, these contacts were immunized with diphtheria toxin-antitoxin mixture. All active cases received antitoxin. Throat carriers were treated with various antiseptic solutions and tonsillectomy was performed in selected instances. The average period of isolation was twenty-two days, varying in individual cases from six days to

six months. The character of treatment appeared to play but little part in removal of the diphtheria bacilli, except that in 6 cases tonsillectomy abolished the carrier state in a comparatively short time. Local applications did not effect wound diphtheria carriers to any appreciable extent. Two of the 5 cases of active wound diphtheria died. Of 52 strains tested, 48.1 per cent from contact carriers, 42.8 per cent from wound carriers, 80 per cent from active wound cases and 84.6 per cent from convalescent carriers were virulent for guinea-pigs. Without exception, the organisms conformed to the typical morphological to cultural characteristics of B. diphtheriæ. Neither morphology, fermentation reactions nor other cultural characteristics gave any indication of the degree of virulence of the organisms studied.

Diphtheria Carriers and their Treatment with Mercurochrome.— GRAY AND MEYER (*Jour. Infect. Dis.*, 1921, xxviii, 323) found that in examining 680 individuals, routinely, 23.8 per cent harbored diphtheria bacilli. The majority of positive cultures were secured from the nasal passages. Ninety carriers were treated systemically by dropping, spraying or swabbing with an aqueous solution of mercurochrome— 220, in 0.5 to 2.0 per cent strength. Eighty-eight of the 90 were made carrier-free by an average of 19.1 treatments, the remaining 2 resisting all treatment.

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

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The Heat Resistance of Spores with Special Reference to the Spores of Bacillus Botulinus.—WEISS (*Jour. Infect. Dis.*, 1921, xxviii, 70) states that the free spores of Bacillus botulinus are destroyed within five hours at 100° C., within forty minutes at 105° C., and within six minutes at 120° C. Bath temperatures are indicated. These thermal death points were determined under optimum conditions for survival. The destruction of the spore is a gradual process, not an instantaneous killing and is probably due to a gradual protein coagulation. The spores are evidently injured before they are killed. This is inferred from the fact that the more protracted the period of heating, before killing occurs, the longer the period required for the spore to vegetate. Young moist spores have a higher thermal resistance than old moist spores. Spores that are one month old are found to be three

times as resistant as spores that are five months old. There is a general decrease in thermal resistance as the spore ages. The more resistant individuals change more rapidly than the less resistant ones causing a tendency toward stabilization, the ultimate resistance of the individual more nearly approximating the average resistance. This is shown by the effect of dilution on the thermal resistance of young and old spores, the old spore emulsions being practically unaffected by changes in the number of spores present, while the young spore emulsions show marked decrease in resistance as the dilution increases. The thermal resistance of emulsions of young spores increases as the concentration of the emulsion increases. Sodium chloride considerably lowers the thermal resistance and the rate of this lowering increases rapidly as the concentration of the salt is increased. The hydrogen ion lowers the thermal resistance of the spore and the rate of this reduction decreases as the hydrogen-ion concentration increases. The hydroxyl ion lowers the thermal resistance and the rate of the reduction decreases as the hydroxyl-ion concentration increases. The hydrogen-ion concentration changes considerably in a medium in which Bacillus botulinus is growing and ultimately stabilizes itself at a point near a Ph value of 7.5. In applying these results to the practical problems of processing canned foods, it is necessary to determine the Ph value of the material to be sterilized immediately before the exposure. Any delay between the determination and the processing may cause a sufficient change in the Ph value to require a higher temperature or a longer period of exposure. In all practical processing methods a sufficient safety factor should be allowed. The actual time required in applying such a factor becomes rapidly less as the temperature of processing is increased. Thus, a 50 per cent safety factor applied at a processing temperature of 100° C., the medium to be sterilized having a Ph value of 7, would require an extra heating of sixty minutes or a total of one hundred and eighty minutes. The same safety factor applied at a processing temperature of 120° C., the medium to be sterilized being the same, would require an extra heating of three minutes or a total of nine minutes.

Studies on the Relation of Mineral Dusts to Tuberculosis. I. The Relatively Early Lesions in Experimental Pneumokoniosis Produced by Granite Inhalation and their Influence on Pulmonary Tuberculosis.— Gardner (*Am. Rev. Tuberc.*, 1920, iv, 734) used the R1 strain of tubercle bacillus to infect guinea-pigs by the inhalation method, coincidently and previously exposed to granite dust of a given concentration. He concluded that the occurrence of tubercles is more frequent in the dusted than in the undusted lung. That such lesions tend to run a more prolonged course than those in animals not exposed to dust. That the spread of the tuberculous process to the regional lymph nodes is not prevented.

Experimental Studies of the Nasopharyngeal Secretions from Influenza Patients. I. Transmission Experiments with Nasopharyngeal Washings.— Olitsky and Gates (*Jour. Exp. Med.*, 1921, 2, xxxiii, 125) state that they detected an active substance in 5 patients in early stages of epidemic influenza during 1918–19 and 2 patients in early

stages of epidemic influenza during 1920. It was not detected in 12 cases of the same disease in which the onset of obvious symptoms occurred more than thirty-six hours before washing of the nasopharynx was carried out nor was it found in the secretions of 14 individuals free from the syndrome of influenza either during the epidemics or the interval between them. With this substance a clinical and pathological condition has been induced in rabbits, affecting the blood and pulmonary structures mainly, which could be maintained and carried through at least fifteen successive animals. For this reason, and also because of the dilution between passages, they are led to believe that they were dealing with the actual transmission of a multiplying agent rather than with a passive transference of an original active substance. In some of the experiments secondary infections by ordinary bacteria were encountered. The relation of these microörganisms to this active substance will be dealt with later the authors state. However the essential effects were produced by a substance wholly unrelated to these bacteria. The similarity that exists between the effects produced in rabbits on the blood and the lungs and those occurring in man in epidemic influenza provides a basis for further investigation on the inciting agent of epidemic influenza.

Venereal Statistics of the Army and Navy.— RIGGS (*U. S. Naval Med. Bull.*, No. 1, vol. xv) states that the normal expectancy for venereal disease resulting from illicit sexual intercourse not followed by prophylaxis is about 1 in 20 or 1 in 30. The expectancy for venereal disease when prophylaxis is used depends almost entirely upon the factor of time. The absence of the time factor in a set of prophylactic statistics invalidates any conclusion that may be drawn concerning probable efficiency of prophylaxis. In actual practice the number of infections appears to be reduced by nearly one-half. The questionnaire method of investigation, in which the identity of the individual is concealed, has proved unreliable and the results obtained cannot be accepted with any confidence as to their accuracy.

ORIGINAL ARTICLES.

PYLOROSPASM IN ADULTS: ITS MEDICAL AND SURGICAL TREATMENT.

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Spasmodic contraction of the pylorus, or pylorospasm, while not a common complaint, is observed with such comparative frequency that much interest has been aroused as to its clinical significance. The etiology of this affection is, however, frequently obscure, and in consequence a number of theories have been suggested in explanation of its occurrence. It may therefore not be out of place to consider, briefly, certain factors having an etiological bearing on this condition.

Through the researches of Langley, Meyer, Gaskell and others it has been shown that the involuntary nervous system supplies two sets of nerve fibers to every organ, the one functioning as activator and the other as inhibitor nerves, the two combined exhibiting a regulating mechanism controlling the interactivity of both groups. In the first set we have the autonomic system as exemplified in the vagus group, the stimulation of which results in the production of pylorospasm. In the second set we have the inhibitory fibers as found in the sympathetic system, stimulation of which inhibits spasm. The evidence pointing to the presence of this opposing

nerve influence can be easily demonstrated in rabbits, in which pylorospasm can be experimentally induced by stimulation of the vagus and inhibited by stimulation of the splanchnics. According to Rogers the same phenomenon may be brought about even in a more prolonged and graphic manner by subcutaneous injection of certain extracts of the thyroid, parathyroids or pyloric mucosa into dogs. He was thus able to produce a marked increase both in the flow of the gastric secretion and in gastric motility, which could be inhibited by means of an injection of atropin. Not only will atropin inhibit this reaction but a similar effect can be brought about by the injection of an extract of the adrenal glands. He explains the latter reaction as due to a stimulation of the sympathetic by the extract of this gland. According to Rogers: "If the experimented animal is angered or excited, which is akin to worry in the human being, the gastric juice ceases to flow, due to the inhibitory influences carried to the stomach along the sympathetic. After a prolonged stimulation the sympathetic becomes partially or fully fatigued, allowing the vagus full play, free of inhibition, in consequence of which hyperacidity, hypermotility or pylorospasm is produced, which may be followed, if this condition is much prolonged, even by ulceration." The cause of pylorospasm therefore, according to Rogers, is a continuation of the original failure of the sympathetic, and it is suggested by him that this condition may be best relieved by means of pyloroplasty.

The researches of Cannon are of special interest in this connection. According to this investigator the presence of free hydrochloric acid in the stomach occasions the relaxation of the pyloric sphincter, causing the pylorus to open and thus permit the escape of the acid chyme into the duodenum. The presence of the acid in the duodenum produces a reflex stimulation of the pylorus, which closes and remains so until the contents of the duodenum have again become alkaline. This orderly escape of the gastric contents into the bowel proceeds until the chyme has been entirely emptied into the intestine. According to this theory whenever this orderly relationship between the stomach and intestine is interfered with, whether by nervous or organic conditions, the pylorus ceases to relax and so empty its usual portion of contents into the duodenum, and, in consequence, pylorospasm is produced. The theory of Cannon fails to explain such facts as the emptying of the stomach in achylia gastrica and the rapid exit of water from the stomach. It has been pointed out by means of roentgen-ray examinations that the very first portion of the food ingested in the fasting state may quickly empty itself out of the stomach, at which period the acidity could not have been developed sufficiently to act as a relaxing stimulation. It has been suggested by Lockhart, Phillips and Carson that certain motor activities of the stomach are associated with the relaxation of the pylorus. Marked motor activities either

in the form of changes of tonus or peristalsis may lead to the relaxation of the pyloric sphincter, explaining, according to this theory, the rapid exit of water from the stomach in the neutral state and emptying in achylia gastrica. According to Lockhart, Phillips and Carson, therefore, there is a far more intimate relationship between the muscular activity and the relaxation of the pylorus than between the latter and the chemical reaction of the gastric contents.

McClure and Reynolds have also recently pointed out in an elaborate set of experiments that the acid control of the pylorus is of minor importance, inasmuch as contraction of its sphincter could not be produced by introduction of acid into the duodenum. However, according to their observations, the quiescent pyloric sphincter is found contracted when food is in the stomach and opens regularly at the approach of each antral peristaltic wave.

Pylorospasm may exist in various types: the neurotic, the irritative and the reflex. As a pure neurosis pylorospasm is rather uncommon, occurring, according to our experience, in but a small percentage of all gastric affections. In a large percentage of cases pylorospasm is secondary to some irritation in the stomach itself or appears as a reflex condition due to disease of some other organ. That there are cases of pylorospasm which are purely neurotic in origin, however, there can be but little doubt. Instances of this form have been observed in infants.

In the case of a female, aged twenty-six years, observed by us, in whom all of the symptoms of pylorospasm were manifested and who was finally subjected to operation, no pathological condition was observed, yet entire relief was afforded by means of a pyloroplasty. The purely neurotic form of pylorospasm occurs more frequently in females than in males. In our series three females were affected to one male.

As has already been noted, while pylorospasm does not occur frequently as a pure neurosis it is quite commonly observed secondary to some gastric or abdominal affection, as in gastric or duodenal ulcer, cancer of the pylorus, enteroptosis, gall-bladder disease, appendicitis, renal disorders and diseases of the male and female genito-urinary organs.

The fact that pylorospasm may result reflexly from disease of the organs beyond the stomach is clearly revealed in the gastric upsets which occur so frequently as a result of acute appendicitis or nephritic colic. A graphic demonstration of this fact has been noted by Aaron. By pressure on McBurney's point he was able in some instances of chronic appendicitis to produce gastric pain, and by means of the fluoroscope he was able to note spasm of the pylorus at the same time. In fact, pylorospasm can now be clearly revealed, as will be noted later on, by means of roentgen-ray examinations.

The symptoms of pylorospasm vary in intensity according to the degree of the spasm. With a moderate spasm a mild discomfort

and pressure are experienced in the epigastrium. This occurs about two or three hours after meals and is usually accompanied by acid eructations and regurgitation. The pains are of the hunger types and are due according to the researches of Carlson, Hamburger and others to active contractions of the stomach. When the symptoms become more intense the pylorus suddenly contracts spasmodically, causing severe pain which may be followed by vomiting. The pain usually manifests itself in the epigastrium, radiating from the median line often into the back. At first the spasm appears periodically, but as the disorder progresses it may become continuous and lead to a spastic contraction at the pylorus, with consequent functional obstruction and retention of food. The food is vomited under these conditions and presents all of the characteristics ordinarily observed in cases of dilatation of the stomach. Relief is afforded for a time by vomiting, the period varying from one to four days, when a similar attack again recurs. Relief is also usually obtained by emptying the stomach of its contents by means of lavage.

After a long persistence of the affection other symptoms ordinarily observed in dilatation begin to appear, i. e., emaciation, thirst and constipation. The vomiting in pylorospasm may be persistent, finally terminating in the expulsion of a watery mucus, very acid and containing at times streaks of blood. The vomiting is often explosive in character, the stomach emptying itself suddenly of large quantities of acid contents. As soon as the spasm relaxes the symptoms disappear.

On examination during the attack the pyloric area is found tender to pressure and contraction may take place near the pylorus, producing a firm mass, easily detected on palpation in patients with thin abdominal walls. This gradually disappears as the spasm relaxes. At this time the abdomen is rather contracted and the recti muscles tense. After the spasm disappears the tenderness is less marked and the abdomen again regains its normal appearance. The gastric contents may show a varying degree of acidity, depending largely upon the time when the secretion is removed. During the period of spasm there may be a lowered, normal or hyperacid content, varying according to the intensity of the attack and the time of the onset of the cramps. In the interval between the attacks the gastric contents may be normal. There is usually present, however, a hyperacidity or hypersecretion, the degree of which usually depends largely upon the duration of the affection. It is rather unusual not to be able to demonstrate hyperchlorhydria some time during the digestive period by means of fractional analysis. After long persistence of this disorder, when obstruction with stagnation has occurred, the gastric contents assume the appearance of that ordinarily observed in dilatation of the stomach.

The greatest aid is afforded in the recognition of pylorospasm through roentgenology. It is by this method that both the nervous

as well as the organic forms can usually be readily determined. Aaron has called attention to the value of the fluoroscope in the diagnosis of the reflex forms, and more recently Carman has referred to spasms of the stomach and duodenum from a roentgenological point of view. Spasms of the pylorus may be determined either fluoroscopically or by means of a series of roentgenograms, best by a combination of both methods.

In a study of this character it is important to determine whether the lesion producing the spasm is within the stomach or beyond this organ; or, again, whether or not it is of purely nervous origin.

When spasm of the pylorus is produced by an ulcer a six-hour retention is usually present, together with a definite and persistent filling defect in the stomach, though in a number of instances in our experience the spasm and retention were the only signs pointing to ulcer. It is interesting to note that these signs may occur with ulceration in the stomach even when situated at some distance from the pylorus. The retention so constantly observed has been attributed to various conditions; it has been ascribed to pyloric spasticity due to the hyperchlorhydria, to gastric atony and to interference with the peristalsis due to the ulcer or possibly to a reflex pyloro-spasm.

Pylorospasm is frequently of reflex origin. One finds it not uncommonly associated with cholecystitis or chronic appendicitis. In this condition the bismuth meals are retained at the pylorus for some time; the spasm relaxes to a degree and a part or all of the bismuth is finally expelled. In some instances the spasm is so persistent that it makes one suspect that he is dealing with an ulcer, but in a number of instances of this character under our care the diagnosis of cholelithiasis or appendicitis was eventually confirmed by operation.

Cancer of the stomach is at times, although rarely, accompanied by spasm; especially is this the case in the early stages of the disease or in those instances in which there is obstruction. Ordinarily, however, there is hypermotility with rapid evacuation of contents without spasm. There is usually present, however, a filling defect which is generally surrounded by an invasive area which interferes with motility, producing an apparently dead area. It is highly important to differentiate pylorospasm due to disease in the stomach itself or duodenum from that due to conditions outside of the stomach. Spasm due to ulcer or cancer is usually observed situated near the lesion itself and often in the area opposite to the lesion. Its location is constant and unvarying and the spasm is definitely present throughout the entire examination as well as at subsequent examinations. On the other hand the spasm caused by disease of remote organs is usually short in duration and intermittent in character and not always constant. In some instances the spasm is located at the pylorus, at others some distance from the pylorus

(gastrospasm). Though usually present in the same area it changes its aspect now and then. In these instances a six-hour retention is often found at one examination and not at another. The differential dagnosis is not always certain, and it may be impossible in many instances to differentiate between the two conditions. A well-established test to exclude pyloric spasm of nervous or reflex origin is furnished by means of the administration of atropin or belladonna given in full doses. Spasms produced by lesions of the stomach are not influenced by this drug. Those of nervous or reflex origin usually disappear. In this connection it is interesting to note that pylorospasm, no matter what its origin may be, whether due to disturbance within the stomach itself or without, disappears under narcosis, and it is for this reason that it frequently remains undetected at operation.

As a rule the diagnosis of pylorospasm is not difficult, but to distinguish clinically those forms purely neurotic in character from those due to intrinsic or extrinsic causes is at times a most difficult problem. In order to arrive at a proper diagnosis all organic conditions must be excluded. A correct conclusion may usually be obtained by noting the presence of the attacks of pain occurring two or three hours after meals, which are relieved temporarily by the ingestion of food (hunger pains); in addition a tender area is usually present in the region of the pylorus; there are symptoms of hyperacidity, of intermittent stagnation; and at times a definite resistance is detected on palpation in the region of the pylorus, assuming the character of a small tumor which gradually disappears. Finally the roentgen-ray signs are usually very distinctive and frequently clear up the actual cause of the spasm.

In the treatment of pylorospasm it should be remembered, as has been previously noted, that this condition is frequently secondary to some other affection either located within or without the stomach itself, and that the primary disorder should, as far as possible, be overcome before treatment is directed to the spasm. The treatment of pylorospasm consists primarily in properly overcoming the underlying neurasthenia. On this account, change of scene, massage, rest or even a rest-cure may be found advisable. The diet should be carefully regulated, all irritating food should be avoided and the meals should be small, easily digested and given at regular intervals. In certain instances an ulcer cure with the patient in bed for two or three weeks under a Sippy diet has afforded very satisfactory results. In other instances the administration of olive oil has been of great service. During the attack the best results are obtained by means of hypodermic injections of morphin with atropin; for the pain, codein combined with belladonna is serviceable. Sodium bromide with chloral has been recommended in some instances; hot applications and stupes to the abdomen and a thorough lavage with plain water; permanganate of potash or nitrate of silver solu-

tion has proved serviceable at times. The drug which is most helpful in the treatment of this affection is atropin prescribed in full doses and best administered hypodermically. This drug inhibits the vagotonic irritation and thus relieves the spasm. Stockton has recommended adrenalin hypodermically in some instances and reports remarkable relief by the use of this drug. The administration of adrenalin nucleoprotein, as advised by Rogers, has given relief in a number of instances under our care.

In the intractable forms of pylorospasm which have resisted all medical treatment the operation of pyloroplasty has furnished a means of satisfactory relief. Rogers has reported a case of pylorospasm due to gastric ulcer which was not relieved by gastro-enterostomy, but in which cure was finally effected by means of a pyloroplasty, and he suggests this operation as a relief for this condition on purely theoretical grounds. According to this observation a gastro-enterostomy, whether there be a hyperacidity present or not, does not always cure the pain due to a pyloric spasm.

"The explanation of its persistence or later occurrence, especially when no ulcer is present, must indicate a continuation of the functional failure of the sympathetic, which should be relieved by pyloroplasty."

Our experience is entirely in accord with that of Rogers. We have been greatly impressed with the fact that these cases of pylorospasm which remain unbenefited by medical treatment should be operated on and that pyloroplasty affords the best possible means of cure. Moreover, pain of every character in the upper abdomen should be carefully observed and studied clinically, so that if operation be undertaken for any cause and no explanatory lesion be observed the advisability of performing a pyloroplasty may be considered—provided, of course, that definite evidence of pylorospasm has been previously noted. This fact is of the utmost importance, inasmuch as the spasm is extremely liable to relax under anesthesia, and the actual condition may therefore be entirely overlooked in the course of the operation.

REPORT OF A FEW ILLUSTRATIVE CASES.

CASE I.—Pylorospasm of nervous origin in a female, aged twenty-five years; relieved by means of a rest-cure and lavage of the stomach.

Mrs. G. B. has been affected with nervous indigestion for several years; for the past six months after a series of family worries her nervous symptoms have become intensified; she complains of weakness, is easily exhausted, suffers with insomnia and is extremely hysterical; in addition the gastric symptoms have become aggravated. She suffers with discomfort and pains in the stomach one to two hours after meals, vomits acid gastric contents at times; alkalies and food give temporary relief. During an attack with the appear-

ance of the pain one can definitely palpate the pylorus as a hard mass, which disappears in a few moments. The gastric secretion presents a total acidity of 64, free HCl 50; no retention. A roentgen-ray examination reveals a marked pylorospasm, no evidence of ulcer or any other abnormality. Under a rest cure with frequent lavage and the administration of belladonna the patient made a speedy recovery.

CASE II.—Pylorospasm complicating a case of cholelithiasis in a man, aged fifty-four years; cholecystostomy; recovery.

J. S. had been affected with gall-bladder attacks for five years; a number of these attacks were accompanied with intense colic and jaundice. During the last few months there were severe gastric symptoms present with every attack; the patient would vomit large quantities of undigested food, and at times on the following morning food eaten the day previously; visible peristaltic movements were detected over the region of the stomach during several attacks. No abnormalities could be determined on physical examination. The gastric contents between attacks presented a total acidity of 42, free HCl 31. A roentgen-ray examination revealed the stomach pulled over and held in the gall-bladder region; there was present a six-hour retention and pylorospasm. At operation numerous gall-stones were removed; the pylorus and stomach were found normal. the gall-bladder was drained. The patient made an uneventful recovery and has had no further disturbance.

CASE III. Pylorospasm caused by chronic appendicitis in a female, aged twenty years; appendectomy; recovery.

J. S. sought relief from recurrent attacks of abdominal pain with which she had been afflicted for from six to eight years; the attacks appeared at intervals of from four to eight weeks. The pain would come on suddenly, was accompanied by slight fever and would usually center itself in the right lower abdomen. The pains were usually moderate, and after a few weeks would gradually subside. Soon after the appearance of the pain, gastric symptoms would always manifest themselves, consisting of distress, gastric peristalsis, nausea and finally vomiting; the vomitus frequently contained food eaten six to eight hours previously; as soon as the stomach had completely emptied itself the nausea and vomiting would cease and the abdominal pain subside, although the lower right abdomen remained tender for some days afterward. Knowing the relief afforded by the vomiting the patient has recently been able to abort certain attacks by inducing vomiting artificially by means of emetics. On physical examination there was present every evidence of chronic appendicitis, which was verified by means of a roentgen-ray examination. An appendectomy was performed which afforded permanent relief.

Case IV.   Pylorospasm caused by intestinal stasis in a female, aged twenty-six years.

M. S. had been affected with chronic constipation for at least fifteen years. During the past two years this condition had become more aggravated, so that even with drastic purges relief was not always afforded and the patient was required to resort to enemata frequently. After the constipation had persisted for two or three days the patient would become nauseated, which would be followed in five or six hours by vomiting, and frequently of food eaten the day previously. There were present headaches, great distention in the region of the stomach and much pain, which also would be relieved after the stomach had been thoroughly emptied and after a good bowel movement.

On physical examination of the patient nothing abnormal was revealed between the attacks. The gastric contents presented a total acidity of 72, free HCl 54.   A roentgen-ray examination revealed marked cecal and colonic stasis with a maximum prolapse of the colon. By means of a thorough regulation of the bowel movements the patient was gradually relieved of the attacks.

Case V.—Pylorospasm accompanying renal colic in a man, aged thirty-eight years. Operation; recovery.

F. J. had been having attacks of acute pain in his left lumbar region at varying periods for three or four years. The attacks would appear suddenly, were very intense and were accompanied by severe gastric upsets. At the onset of the attacks there was acute pain in the left kidney region followed shortly by nausea and pain in the region of the stomach. The pain would proceed down the left side into the bladder and penis and within a few hours a rise in the temperature would manifest itself. The stomach would become distended and there was severe gastric pain, nausea and vomiting. The patient frequently vomited food taken five to seven hours previously. The attacks would last six to twelve hours. They would subside under the influence of hypodermic injections of morphin. An examination of the urine following an attack revealed blood. The diagnosis of kidney colic due to stone with reflex pylorospasm was made. A roentgen-ray examination revealed a kidney stone which was removed by operation. Complete relief was afforded.

Case VI. Pylorospasm in a female, aged thirty-nine years, simulating cholelithiasis; pyloroplasty; recovery.

Mrs. W. J. had been affected with acute attacks of indigestion since the birth of her last child, four years ago. The attacks were very acute and could ordinarily be traced to errors in diet, though some occurred without dietary indiscretions. The first attack was definitely noted three days after labor. The attacks were all alike,

though their intensity recently had become extremely severe. These attacks were characterized by intense colicky pains beginning in the epigastriun and radiating toward the right side under the shoulder-blade. This was soon followed by marked nausea and severe vomiting. On two occasions food eaten six and eight hours previous to the attack was noted in the vomitus. Hypodermic injections of morphin were required for relief. At no time were chills or fever observed during the attacks.

On physical examination of the patient the liver was not observed to be enlarged, though there was distinct tenderness under the right costal arch.

The diagnosis of probable cholelithiasis was made, but at operation the gall-bladder appeared perfectly normal; there was present, however, even under the anesthesia a definite spasticity of the pylorus.

A pyloroplasty was done; the patient made an uneventful recovery and has had no further attacks.

CASE VII.—Pylorospasm associated with appendicitis in a female, aged thirty-nine years; appendectomy but no relief; pyloroplasty; recovery.

Mrs. J. M. had been affected with indigestion for the past six years. There was almost constant headache, nausea, marked abdominal distention and severe constipation.

At times the symptoms would become aggravated and there would be severe pain in the region of the stomach, with nausea and vomiting; the vomitus contained food eaten eight to ten hours previously. The acute symptoms would disappear in twenty-four to thirty-six hours, leaving the entire abdomen extremely tender.

On physical examination between the acute attacks the abdomen was found soft; there was a distinct epigastric tenderness and more marked tenderness in the right lower quadrant at McBurney's point, with slight muscle spasm. The gastric analysis at this time revealed a marked hyperacidity; total acidity of 72, free HCl 54. A roentgen-ray examination presented a rather spastic pylorus and evidence of chronic appendicitis. Appendectomy was advised and performed; the patient had moderate relief for a month, when the former symptoms began anew and became more aggravated than before. During the acute attacks the stomach was markedly distended, and on one occasion food eaten the day previously was vomited. A diagnosis of pylorospasm was made and a pyloroplasty performed, after which no further disturbance was noted.

CASE VIII.—Pylorospasm associated with chronic appendicitis and intestinal adhesions with stasis in a man, aged fifty-seven years; pyloroplasty; appendectomy; recovery.

J. C. had been affected with digestive trouble for several years;

recently his symptoms have become aggravated. He complains of nausea and frequently of vomiting, which affords him some relief. There is also present heartburn, acid eructations, anorexia, headache and dizziness. Constipation is marked and persistent. At times these symptoms become acute, forcing the patient to bed for one or two days. During these attacks the patient has vomited food that had been eaten the day previously.

On physical examination one notes a marked tenderness over McBurney's point as well as in the epigastrium; there are no other abnormalities. The gastric analysis presents a total acidity of 63, free HCl 46. A roentgen-ray examination reveals a marked pylorospasm together with a chronic appendicitis and cecal adhesions and stasis; the pylorospasm was so marked that the patient was given large doses of belladonna and another examination made a few days later revealed the identical condition.

At operation the chronically inflamed appendix was removed, adhesions released and a pyloroplasty performed. The patient made an uneventful and perfect recovery.

Case IX.—Pylorospasm of a purely nervous type in a female, aged twenty-five years; no lesions detected at operation; pyloroplasty; recovery.

Miss E. M. consulted us for relief of a nervous indigestion with which she had been troubled for the past six months. There was present loss of flesh, weakness, loss of strength, headache and indigestion. The patient complained of frequent nausea followed by vomiting, and at times of vomiting of very large quantities, with remains of food eaten seven to eight hours previously. The vomitus was exceedingly acid. The discomfort was temporarily relieved by food. On physical examination of the abdomen nothing abnormal was revealed. The gastric secretion presented a total acidity of 68, free HCl 46. An exploratory operation was decided on; no lesion was observed anywhere in the abdomen; the pylorus appeared normal. On account of the persistent pylorospasm a pyloroplasty was performed. The patient made a thorough recovery and has remained well since, without recurrence of any of her former gastrointestinal symptoms.

Case X.—Pylorospasm associated with gastric ulcer in a male, aged forty-seven years; gastro-enterostomy but no relief; pyloroplasty; recovery.

J. K. S. consulted us for a gastro-intestinal disturbance which has persisted for a period of four to six weeks at a time during the past ten years. Four years ago a gastro-enterostomy was performed for a pyloric ulcer; relief was afforded for three months, when all the former symptoms returned. There was present pain appearing two hours after meals, which was relieved by food and alkalies; nausea

and vomiting were frequent and the patient often vomited food eaten a day previously. With the attacks of pain there was often a sensation of movements passing over the abdomen. On physical examination the abdomen was found distended and peristaltic movements were observed on one occasion. A roentgen-ray examination revealed a perfectly patent gastro-enterostomy opening, together with a marked pylorospasm but no filling defect. The diagnosis of pylorospasm with possible ulcer was made. At operation there was no evidence of ulceration. The pylorus was found somewhat spastic, however, and a pyloroplasty was performed; the patient made an uneventful recovery and has had no further return of his former disturbance.

Case XI.—Pylorospasm associated with a chronic gastritis in a man, aged forty-eight years, simulating carcinoma.

E. J. S. had been complaining of nausea and vomiting for the past six months. There was a loss of weight of ten pounds, poor appetite, flatulence and some abdominal pain. On physical examination no masses could be detected and there was no abdominal tenderness. The gastric secretion showed a true achylia and there was blood in the stool. The Wassermann reaction was negative and there was a definite defect at the pylorus revealed by the roentgen ray. The question of malignancy could not be ruled out. An exploratory operation was advised at which a chronic gastritis, together with a marked pylorospasm, was revealed. A pyloroplasty was performed, following which entire relief was afforded.

Summary. 1. Pylorospasm is a complex nervous phenomenon the exact etiology of which has not been satisfactorily established. Experimentally the fact has been definitely demonstrated that pylorospasm may be produced in rabbits by stimulation of the vagus and inhibited by stimulation of the splanchnics. That there is a definite association between this condition and the endocrine system is indicated by the fact that the spasm may be brought about by injection of certain extracts of the thyroids and parathyroids and inhibited by injection of an extract of adrenals. On the other hand there is but little question that changes in tonus or peristalsis are of great importance in the production of this phenomenon.

2. Pylorospasm may exist in one of three types: the neurotic, the irritative and the reflex forms. In the largest percentage of cases this condition is secondary to some irritative lesion in the stomach or is reflex from disease of some other organ. Many of these cases are promptly and completely relieved by removal of the cause, chronic appendix, gall-stones, etc. There exists, however, a purely neurotic form without any demonstrable lesion.

3. The condition can usually be recognized clinically by a careful

study of the case. In the majority of the cases slight if any pathological changes can be demonstrated about the pylorus at operation, as the general anesthetic usually completely relaxes the pyloric spasm. In advanced cases one may observe varying grades of hypertrophy in the pylorus and the pyloric antrum of the stomach.

4. The symptoms of pylorospasm are rather characteristic. These consist of pains of the hunger type appearing two or three hours after meals, which are relieved by emptying the stomach of its contents as well as by the ingestion of food; of contractions of the stomach leading to tumor formation, which disappear as the spasm relaxes; of symptoms of intermittent stagnation and hyperacidity.

5. The greatest aid afforded in the recognition of pylorospasm is by roentgenology, by means of which the nervous as well as the organic forms may usually be differentiated.

6. In the treatment of this affection medical measures should always be given a careful trial; if it be secondary to other abdominal conditions the primary disorder should, as far as possible, be overcome before treatment is directed toward the spasm. The treatment consists of overcoming the primary neurasthenia. This is most satisfactorily accomplished by means of dietetic and hygienic measures. During an attack the best results are obtained by means of hypodermic injections of morphin with atropin following a thorough lavage of the stomach. The drug most useful in the treatment of this affection is atropin given in full doses. When medical measures fail to give the desired relief, pyloroplasty theoretically is the operation of choice and practically gives most satisfactory results.

THE STRIATAL AND THALAMIC TYPES OF ENCEPHALITIS

A CONSIDERATION OF THE SYMPTOMS AND SYNDROMES REFERABLE TO THE BASAL CANGLIA IN EPIDEMIC ENCEPHALITIS.

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EPIDEMIC encephalitis has given rise to a number of rare and interesting symptoms which are largely due to the peculiar nature of the virus and its localization in parts of the nervous system not usually involved. It is not unlikely that the toxic agent possesses a special affinity for certain cellular neurons, thus producing some of the striking clinical results which have been noted.

Of these clinical manifestations those related to the corpora striata have aroused, perhaps, the greatest interest. This is partly due to the recent advances in our knowledge of the function of these structures but also to the extreme rarity of this localization in other types of inflammatory disease. No other acute affection of the central nervous system has yielded so many and such striking evidences of involvement of the great basal ganglia as encephalitis lethargica. This has not only added materially to our knowledge of the symptomatology of these structures but has also enabled us to test the validity of our present theories concerning the functions of this important region of the brain.

While the optic thalamus is frequently involved in encephalitis the thalamic symptoms are milder and less serious than are those of
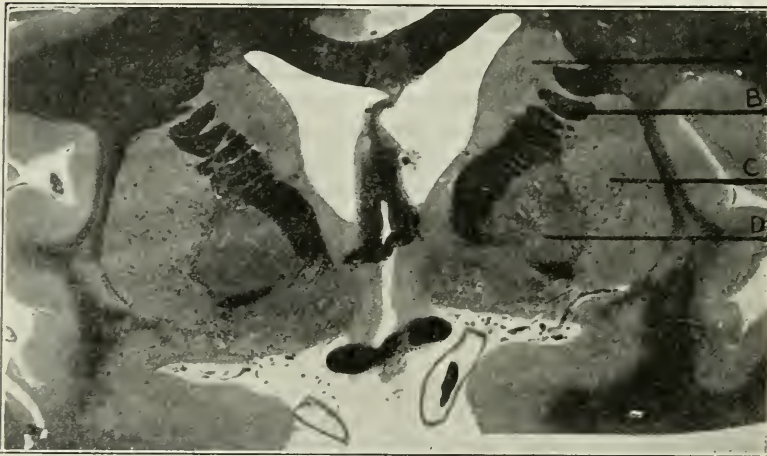
Fig. 1.—Vertical section through corpus striatum in paralysis agitans (primary atrophy of the pallidal system), showing A, caudate nucleus; B, internal capsule; C, putamen; D, globus pallidus. Note diminution of fiber network of globus pallidus. (Weigert-Pal stain.)

the striatum, and the chief emphasis of this study will be placed upon the latter. Before taking up the question of symptomatology I will review briefly the conception of the function of these structures which the writer formulated some years ago, based on clinical and pathological studies of chorea and paralysis agitans.[1]

Anatomical Considerations.—The corpus striatum is a large ganglionic structure which is divided by the anterior limb of the internal capsule into two parts, the nucleus lenticularis and the nucleus caudatus (Fig. 1). The nucleus lenticularis is still further subdivided into an external segment, the putamen and an internal

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[1] Hunt, Ramsay: Progressive Atrophy of the Globus Pallidus, a Contribution, to the Functions of the Corpus Striatum. Brain, 1917, xl, p. 58.

which is termed the globus pallidus. These anatomical divisions are based upon the gross appearance of the ganglion and are purely topographical.

The putamen and caudate nucleus are identical in histological structure and constitute the *neostriatum*, and while described as separate ganglia in man they have the same origin and histological characteristics, the caudate being simply separated from the putamen by the passage of capsular fibers.

The globus pallidus is composed of two segments, an inner and an outer, which is produced by the fusion of nerve fibers in the
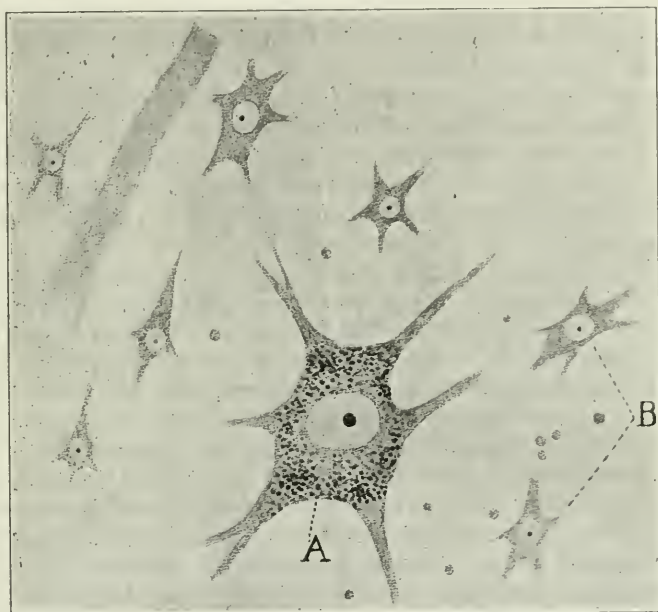
FIG. 2.—Normal cell types of the neostriatum. *A*, large motor cells of pallidal type; *B*, small ganglia cells of neostriatal type. (Nissl stain.)

lateral and mesial medullary laminæ. This portion of the striatum is older phylogenetically and termed the *paleostriatum*. The corpus striatum may therefore be divided into two portions, a neostriatum (caudate nucleus and putamen) and a paleostriatum (globus pallidus), which differ in histological characteristics, phylogeny and, as we shall see later, in their function.

Cell Types of the Corpus Striatum.—In the opinion of the writer a much greater importance is to be attached to the cellular types of this region than to the gross anatomical appearance and subdivisions (Fig. 2).

The paleostriatum (pallidum) contains aggregations of large multipolar cells which are histologically of the motor type (paleo-

striatal or pallidal cells).   In addition to a characteristic arrangement of the Nissl granules many of these cells contain deposits of yellow pigment and resemble the motor cells of the Rolandic area and the multipolar cells of the anterior horns of the spinal cord.

The neostriatum (caudate and putamen) is composed of two cell types.   Of these the more numerous are small, polygonal cells which give the characteristic histological picture of this region (neostriatal cells).   Scattered among these small cells are cells of much larger size.   These are giant multipolar cells, containing Nissl granules and deposits of yellow pigment, and are of the same type as the motor cells of the pallidum (giant pallidal cells of the neostriatum).

The motor or pallidal type of cell is present therefore in both paleostriatum and neostriatum while the small neostriatal cells are peculiar to the neostriatum.

The motor cells (*pallidal cells*) have long axis-cylinder processes and correspond to Type I of Golgi's classification.   These pass by way of the ansa lenticularis and ansa peduncularis to important nuclei in the thalamic and hypothalamic regions and form the efferent motor system of the corpus striatum (*pallidal* or *paleostriatal system*).

The small ganglion cells of the neostriatum have short axis-cylinder processes and correspond to Golgi's Type II.   They terminate in the outer or inner segments of the globus pallidus.   The small neostriatal cells represent a short interstriatal system which unites the caudate nucleus· and putamen with the cells of the pallidal system (*striopallidal* or *neostriatal system*).

It is well to emphasize the fact that the neostriatum also contain giant motor cells which are a part of the pallidal system.   This admixture of cells types, paleostriatal and neostriatal, is responsible for certain variations and peculiarities of the clinical picture arising from lesions in the neostriatum, which will be referred to later.

Pathological Physiology.—Our knowledge of the functions of the corpus striatum has been greatly extended by the pathological study of three chronic disorders of the central nervous system: the double athetôsis, progressive lenticular degeneration and juvenile paralysis agitans.   Madame Vogt,[2] in 1911, showed that the affection called athetôse doublé, and characterized by choreo-athetoid movements, spastic diplegia (without pyramidal tract involvement) and dysarthria, was dependent upon a dystrophic lesion (état Marbré), which was limited to the structures of the neostriatum.   A more recent study by Thomalla[3] has also shown that dystonia musculorum deformans, a clinical type which is closely allied to double athetosis, is also caused by a lesion of the neostriatum (putamen).   It would

[2] Syndrome du Corps Strié, Jour. f. Psych. u. Neur., 1912, xviii, p. 479.

[3] Ein Fall von Torsions Spasmus mit Sektionsbefund und seine Beziehungen zur athetôse doublé, Wilsonschen Krankheit und Pseudo-Sklerose, Ztschr. f. d. g. Neur. and Psych., 1918, Bd. xli, p. 326.

appear from these studies that spontaneous movements of a choreiform and athetoid type associated with muscular rigidity are related to the neostriatum.

In 1912 Kinnier Wilson[4] described the progressive lenticular degeneration, an affection characterized by rigidity and tremor of the paralysis agitans type associated with a tendency to tonic and clonic spasms. This condition was caused by symmetrical bilateral degeneration of the lenticular nuclei, including both the putamen and globus pallidus (neo- and paleostriatum), and was associated with a lobular cirrhosis of the liver. In some cases of this disease spontaneous movements of choreiform and athetoid character were also observed and this feature was emphasized by the earlier writers, and especially by Gowers, who called the affection tetanoid chorea.

Wilson's observation showed that a more massive lesion of the striatum, involving both the neostriatum and paleostriatum, produced symptoms of paralysis agitans (muscular rigidity and tremor) associated with evidences of spontaneous movement (clonic and tonic spasm, choreiform and athetoid movements).

It was therefore clear from the syndromes of Vogt and Wilson that lesions strictly limited to the corpus striatum could be the cause of rigidity and tremor of the paralysis agitans type, tonic and clonic spasms, choreiform and athetoid movements.

In 1917 the writer was able to demonstrate in juvenile paralysis agitans widespread atrophy and loss of the large pallidal cells of the corpus striatum, and referred this disorder to a primary atrophy of this motor projection system of the corpus striatum (*primary atrophy of the pallidal system*). The peculiar and characteristic feature of this lesion was its limitation to a special system of motor neurons.

When the pallidal system is diseased there is produced the motor syndrome which we associate with paralysis agitans. This is characterized by paralysis of automatic associated movements, muscular rigidity and rhythmical tremor (pallidal or paleostriatal syndrome).

The writer also pointed out that the small ganglion cells of the neostriatum which were well preserved in juvenile paralysis agitans (primary atrophy of the pallidal system) showed extensive degeneration and atrophy in Huntington's chorea. The small neostriatal cells were supposed to be coördinating and inhibitory in character. Because of this elective atrophy of special systems of cells the syndrome chorea was referred to a loss of the striopallidal or neostriatal system, and the syndrome paralysis agitans was referred to a loss of the pallidal or paleostriatal system.[5][6]

Two fundamental syndromes of the corpus striatum were there-

[4] Progressive Lenticular Degeneration, Brain, 1911–12, xxxv, p. 296.

[5] Hunt, Ramsay: The Efferent Pallidal System of the Corpus Striatum: A Consideration of its Functions and Symptomatology, Jour. Nerv. and Ment. Dis., 1917, xlvi, p. 22.

[6] Hunt, Ramsay: Primary Atrophy of the Pallidal System: A contribution to the Nature and Pathology of Paralysis Agitans, Arch. Int. Med., 1918, xxii, p. 647.

fore recognized, based upon the differences of function of these two cellular systems.

1. A paleostriatal syndrome (*pallidal syndrome*) characterized by paralysis of automatic associated movements, muscular rigidity and tremor caused by a lesion of the efferent pallidal system of the corpus striatum.

2. A neostriatal syndrome characterized by spontaneous movements of the automatic associated or choreiform type caused by a lesion of the striopallidal system (neostriatal system).

This conception of the functions of the corpus striatum is not at variance with other syndromes which have been ascribed to this region but rather tends to reconcile and explain certain contradictory features. The Vogt syndrome, based upon a destructive lesion of the neostriatum, is characterized by choreic and athetoid movements spastic diplegia (without pyramidal involvement) and dysarthria.

In this syndrome both cell types of the neostriatum, the small neostriatal cells and giant pallidal cells, are the seat of a destructive lesion, the clinical result of which is an admixture of the symptomatology referable to both systems. There is muscular weakness and rigidity associated with choreiform and athetoid movements. The choreo-athetosis I regard as a choreiform manifestation to which has been added a certain degree of muscular rigidity which would ensue from involvement of the motor cells of the neostriatum.

The Wilson syndrome, on the other hand, based on the progressive lenticular degeneration, produces a more extensive lesion of the corpus striatum. Here the paleostriatum and the neostriatum are both involved, the symptoms of which are paralysis, muscular rigidity and tremor of the paralysis agitans type associated with clonic and tonic spasms, and in some cases involuntary movements of a choreiform and athetoid nature.

Here again there are evidences of involvement of the two essential neuronal systems of the striatum. The paralysis, rigidity and tremor are dependent upon involvement of the paleostriatal mechanism (pallidal system) while the involuntary motor disturbances, viz.: the clonic and tonic spasms and choreo-athetoid movements, would be occasioned by a destruction of the striopallidal system (neostriatal mechanism).

Involvement of the pallidal system would cause a paralysis of movements of the automatic associated type, while involvement of the striopallidal system releases this motor center from control, with the development of spontaneous movement of the automatic associated type. The one is a *paralytic lesion* and the other a *discharging lesion* in the sense that these terms were used by Hughlings Jackson.

The great variation in the symptomatology of the corpus striatum would therefore be dependent upon the relative degree of involvement of these two systems.

Functions of the Corpus Striatum.—The corpus striatum may therefore be regarded as a higher coördinating motor center which presides over the realm of automatic and associated movements. It stands in close relationship with the important correlating sensory station, the optic thalamus, and through this structure with the peripheral sensory mechanism, the cerebellum and the cerebral cortex.

In the lower forms of life, before the appearance of the pyramidal tracts and the cerebral cortex, it is the chief coördinating motor mechanism, which by its connection with important nuclei of the hypothalamic region controls and directs the activities of the extrapyramidal motor system. Like the other lower motor centers it is under the control of the cerebral cortex, but also having important independent functions, and when destroyed there is a corresponding disturbance of motor function. This disturbance of motor function may manifest itself in various ways, depending upon the localization and degree of involvement of its two essential fiber systems.

Striatal Types of Epidemic Encephalitis.—During the recent epidemic of encephalitis lethargica all of the symptoms which we commonly associate with affections of the corpus striatum have appeared in one form or another. These manifestations have been slight or severe, transitory or progressive, general or local. In addition many bizarre and fragmentary motor manifestations have been observed which were probably also of striatal origin.

My personal experience is based on the study of twenty-five cases in which evidences of striatal involvement were present at some period of the disease. Many of these were observed in the wards of the Neurological Institute, the New York Hospital and the Montefiore Hospital for chronic invalids. Others I saw through the courtesy of Dr. Tilney, Dr. Casamajor and Dr. Kennedy at the Vanderbilt Clinic or in Bellevue Hospital.

It is not my intention to describe in detail any of these cases but simply to analyze briefly, in a general way, the symptoms of striatal involvement which the epidemic called forth and their relation to our present conception of the function of these ganglia.

Modes of Onset.—Symptoms referable to the corpus striatum occur very frequently in the acute stage of the disease and are evidently associated with an early localization of the inflammatory process in this region. They may also appear at a later period after all acute symptoms of the disease have subsided. Very remarkable is the appearance of striatal symptoms as late sequelæ, weeks or even months after apparent recovery, suggesting a recrudescence of the infectious process.

These special symptoms are accompanied or preceded by the other well-known general or focal symptoms of encephalitis lethargica which serve to give the characteristic stamp to the clinical picture and remove all doubts as to diagnosis.

Symptoms of Striatal Involvement.—Striatal symptoms are of two types corresponding to the two chief syndromes of the corpus striatum, as already defined.

There is a *paleostriatal* or *pallidal type* characterized by paralysis agitans and there is a *neostriatal type* characterized by choreiform movements.

While these two clinical syndromes may appear in pure form there is often an admixture of the two, as a result of which many curious clinical pictures are produced. The *mixed striatal* type is characterized by a combination of the symptomatology of both paralysis agitans and chorea, a *mixed paralysis agitans—choreiform type*.

Of the two the paralysis agitans type is the more frequent and usually the more severe in its manifestations. This is probably due to the course and relations of the pallidal system and the closer proximity of the paleostriatum to the midbrain, which is the chief center of the inflammatory area. Of the 25 cases which came under my personal observation 18 were of the paralysis agitans type, 4 of the choreiform type and 3 were mixed striatal types.

Paleostriatal or Pallidal Type (Paralysis Agitans Type).—The paralysis agitans type is characterized by a fairly acute involvement of the voluntary musculature. Within a brief period of two or three days there develops the typical muscular rigidity, postural deformities, masklike expression of the face and the paralytic disturbances of motility characteristic of paralysis agitans. Generally speaking the tremor is much less constant and when present less conspicuous than in true paralysis agitans. This is probably caused by the sudden development of massive rigidity which masks the tremor, producing the clinical type known as *paralysis agitans, sine tremore*.

When tremor is demonstrable at this stage it is usually slight and localized in the tongue, face or hands. The characteristic pill-rolling movement which we associate with paralysis agitans is quite rare and I have only observed it as a late residual symptom in 2 cases, and never in the acute stage. On the other hand the muscular rigidity, the paralysis of automatic associated movements, the masklike expression of face, the posture of the hands and arms, the gait and attitude appear early and are identical with those observed in true paralysis agitans.

One side is frequently more affected than the other and *hemilateral types* are encountered in a late stage of the disease. Even more limited forms occur (*segmental types*), as, for example, isolated involvement of the face (the Parkinsonian mask). Involvement may also be limited to the upper or lower extremities. The segmental types I have only observed after the subsidence of the acute stage as a late residual manifestation.

The tremor may show a similar limitation and typical rhythmical

tremor may be hemilateral or sometimes segmental, *i. e.*, confined to the head, an arm or a leg. These fragmentary clinical types are usually encountered only as late or residual symptoms.

The rhythmical tremor when present is often coarse and increased by movement. It is then an action tremor and is increased not diminished during the passage of a movement, in this respect differing from the classical tremor of paralysis agitans, but is very similar to what I have observed in the earlier stages of the juvenile paralysis agitans (primary atrophy of the pallidal system). The tremor is not, however, of the intention type and diminishes as the finger tip approaches the tip of the nose. The gait and attitude, the position of the hands and arms and the facial expression differ in no respect from those observed in paralysis agitans. The difference is in the course of the disease and the nature of the pathological lesion.

True paralysis agitans is produced by a progressive lesion of the *pallidal system*, which is atrophic or degenerative in nature while the paralysis agitans of encephalitic origin is merely a symptomatic manifestation due to injury of the pallidal system by inflammatory lesions or toxins. As the acute lesions subside the clinical symptoms disappear, which explains the often rapid improvement in this group of cases. We are not accustomed to this favorable outcome in true paralysis agitans, which is a progressive disorder. Similar recoveries are, however, noted after inflammatory lesions affecting other motor systems, and it is only interesting to note that the pallidal system is no exception in this respect.

A *cataleptic type* of encephalitis has also been described. The association of general muscular rigidity of paralysis agitans type with the peculiar lethargy characteristic of the epidemic encephalitis produces a clinical picture closely resembling catalepsy (flexibilitas cerea). And while true catalepsy has been observed during the course of the epidemic, many cases of so-called *cataleptic type* probably belong to the paralysis agitans group and are of striatal origin.

Hesnard[7] has suggested the existence of a transition form bridging the gulf between the paralysis agitans and cataleptic types, in which the striatum and the cerebral cortex were both affected.

Abortive Types. It is also interesting to note that in the acute stage of the disease mild transitory striatal symptoms are sometimes present. These consist of a certain tightness or tenseness of the musculature, a certain monotony and mild fixity of expression, with slight tremors of the tongue, face or extremities, which disappear as the acute symptoms subside. Cases of this type do not, however, always abort and these initial symptoms may be the forerunners of more serious striatal involvement.

Progressive Type. A tendency to progression in the paralysis

[7] Mental Disturbances with Epidemic Encephalitis, Encephale, Paris, 1920, xv, p. 443.

agitans group is not uncommon. In my experience this tendency has been greater in those cases in which the symptoms make their appearance late in the disease or as relapses after improvement or apparent recovery. It would appear to depend upon a renewal of the inflammatory process or an actual lighting up of old lesions.

A *relapsing* form, unfortunately not uncommon, is a well-recognized type of the disease. Its existence has been emphasized by von Economo,[8] Buzzard and Greenfield.[9] I have also observed two very striking examples of the *mixed striatal type*, in which there was a well-marked tendency to relapses extending over a period of one year. Careful histological study of a relapsing case by von Economo showed the existence of both old and recent lesions, side by side, which explains the peculiar features of the clinical picture.

The *sporadic type* of striatal encephalitis. Mention has already been made of the extreme rarity with which the corpus striatum is involved in other acute inflammatory affections of the nervous system. It is especially noteworthy that epidemic poliomyelitis, which gave rise to so many different clinical types, so far as I am aware, produced no examples of striatal involvement. It is therefore interesting to quote this observation made by Nixon[10] at the Bristol Royal Infirmary a number of years ago.

A boy, aged seven years, was admitted to the infirmary with headache, lethargy and rigidity of the left arm and leg. The teeth were tightly clenched and nasal feeding was resorted to. The cerebrospinal fluid was clear and there was no increase of cells. Later a general hypertonicity and rhythmical tremor developed and the patient left the infirmary with the typical picture of paralysis agitans.

Such a case is interesting as a probable example of sporadic encephalitis localized in the striatum. In a previous paper I have already reported the occurrence of a sporadic type of epidemic myoclonus multiplex[11] (epidemic encephalitis), and it is more than likely that many of the clinical types with which we have become familiar during the epidemic made their appearance occasionally in the sporadic form.

Pallidopyramidal Types of Encephalitis. In my previous studies of the symptomatology of the efferent pallidal system of the corpus striatum[12] attention was directed to the existence of *pallidopyramidal types* of *palsy*. This form is characterized by a combination of the symptoms of both spastic paralysis (pyramidal tract system) and paralysis agitans (pallidal system), and is by no means uncommon

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[8] Encephalitis Lethargica Chronica, München. med. Wchnschr., 1919, lxvi, p. 1311.

[9] Lethargic Encephalitis, its Sequelæ and Morbid Anatomy, Brain, 1919, xlii, p. 314

[10] Paralysis Agitans after Encephalitis: Observed a Number of Years before the Epidemic, 1917–18, Bristol Med. and Chir. Jour., 1920, p. 25.

[11] Hunt, Ramsay: Acute Infectious Myoclonus Multiplex, Jour. Am. Med. Assn., 1920, lxxv, p. 713.

[12] Hunt, Ramsay: Primary Atrophy of the Pallidal System: A contribution to the Nature and Pathology of Paralysis Agitans, Arch. Int. Med., 1918, xxii, p. 647.

because of the close anatomical relationship of the internal capsule and the corpus striatum. In the pallidopyramidal type the paralysis is more complete because both the pyramidal and the extrapyramidal systems are involved, the one controlling isolated synergic movements of cortical origin and the other striatal movements of the automatic associated type. The muscular hypertonicity is also greater and combines the peculiar features of spasticity and paralysis agitans rigidity. Especially characteristic of the pallidopyramidal type are exaggerated tendon reflexes, clonus and the Babinski phenomena of the spastic type in conjunction with a loss of automatic associated movements of striatal type. It is rather remarkable that in my series of 25 cases of striatal encephalitis definite involvement of the pyramidal tracts was only noted in 3 cases.

This is all the more peculiar as we are dealing with a rather diffusely disseminated inflammatory reaction, a type of lesion which one would naturally expect to involve the adjacent pyramidal system of the internal capsule and pes pedunculi. It is possible that certain toxins of encephalitis may possess a special affinity for the cellular system of the striatum which render it particularly susceptible to the infection.

The *neostriatal type (choreiform type)*. The other essential syndrome of the corpus striatum which may develop as a result of epidemic encephalitis is chorea. The choreiform movements of striatal origin are involuntary and irregular in character and are of the automatic associated type. According to the view which I have already expressed they represent a motor discharge of the striatal mechanism in contrast to paralysis agitans which is a paralytic manifestation.

As was indicated in the preliminary sketch, this disorder of motility is ascribed to a loss of the *striopallidal* system or small ganglia cells of the *neostriatal mechanism*, which are supposed to coördinate and control the purely motor functions of the striatum. A degenerative or destructive lesion of this inhibitory system would release the purely motor mechanism from control and allow the development of the involuntary automatic-associated movements of chorea.

The *choreic movements* may be general, hemilateral or segmental (local) in their distribution. They also vary somewhat in character, e. g., mild and severe, large and small amplitude, and occasionally rhythmical. A certain degree of hypertonicity is sometimes present, giving an athetoid character to the movement.

Athetosis or choreo-athetosis I would regard as an admixture of chorea and muscular rigidity due to involvement of both the neostriatal and pallidal systems.

Acute Choreiform Type. Some writers on the subject of encephalitis have described cases characterized by generalized choreiform movements appearing in the acute stage of the disease, associated with delirium and other severe psychotic symptoms. A clinical

picture very similar to the *chorea insaniens* of systematic writers. Archambault[13] has reported cases of this type, as have also Oehmig[14] in Munich and Dimitz[15] in Vienna. Oehmig states that of 14 consecutive cases admitted during one month of the epidemic, 11 were of this choreiform type, which would appear to indicate a form of the virus with a special affinity for the neurones of the neostriatal mechanism. The choreiform movements are, as a rule, generalized, although one side may show greater involvement. Hemichorea has also been observed (Archambault).

This acute choreiform type is apparently rare and I encountered no cases in the New York epidemic. I did observe, however, a number of cases of the "myoclonus multiplex type" which were associated with delirium. This form of movement may resemble but must be sharply distinguished from chorea. Striatal chorea is characterized by the spontaneous discharge of movements of the automatic associated type while "myoclonus multiplex" originates in the spinal and prespinal mechanism and is characterized by contraction of individual muscles or portions of muscles with comparatively slight locomotor effect (myoclonus, myokymia or fibrillary twitching).

Choreo-athetoid Types of Movements. In addition to chorea movements of an athetoid and *choreo-athetoid* type may also occur, both in the early and late stages of the disease. Of special interest is their appearance as late sequelæ months after apparent recovery. The movements of this type like those of chorea may be general, unilateral or segmental (local) in distribution. They differ from chorea in being slower, more stereotyped and associated with hypertonicity of the affected muscles.

In the more localized forms there is a peculiar repetition of slow stereotyped movements occurring at regular intervals. These, except for the limited and rather fragmentary character of the movement, are very similar in their character to other well-known forms of choreo-athetoid movements of striatal origin.

Belonging to this group are other types of movement of somewhat larger amplitude which affect more particularly the trunk and root portions of the extremities, causing curious contortions of attitude and gait. Some of these movements bear a striking resemblance to those observed in the dystonia group of motor disorders, which, since the autopsy report of Thomalla (dystonia lenticularis) must now be definitely allied with the symptomatology of the striate body.

Rhythmical Chorea (Bradykinetic Oscillation). This disorder of motility varies somewhat from the recognized lenticular types.

[13] Choreo-athetoid and Choreopsychotic Syndromes as Sequelæ of Epidemic Encephalitis, Arch. Neur. and Psych., 1920, iv, p. 484.
[14] Encephalitis Epidemic Choreatica, München. med. Wchnschr., 1920, lxvii, p. 660.
[15] Encephalitis Choreaformis Epidemia, Wien. klin. Wchnschr., 1920, xxxiii, 163.

It is characterized by slow rhythmical movements of an extremity, sometimes involving both the arm and leg on the same side, and occurring with great regularity, eighteen to twenty movements to the minute. With the slow rhythmical oscillation of the extremity there is a simultaneous hardening of many of the muscles of the arm or leg, showing the diffuse nature and wide distribution of the muscular contractions. This form of spontaneous movement, in my opinion, is referable to the extrapyramidal system and in all likelihood to the striatal mechanism. It differs, however, in the monotonous regularity of its synchronous rhythm and stereotyped repetition from other forms of striatal movement.

The following case is a striking example of this type: The patient, a young woman, had encephalitis lethargica in January, 1920. During the height of the disease the left side of the body developed a curious spasmodic tendency which persisted after the acute symptoms had subsided. One year later, at the time of my examination, there were present hemichoreatic movements on the whole left side of the body. The movements were rhythmical and synchronous, recurring with great regularity eighteen times to the minute. The spasm was evident in the muscles of the neck, arm scapular group, abdomen and thigh and leg upon the left side. The greatest excursion was of the arm and leg, especially the former, which produced a typical movement of salutation. In the muscles of the trunk there was some tendency for the muscles of the opposite side to participate in the contraction. At times there were slight movements of the face, synchronous with the rhythmical movements elsewhere. There was no paralysis and no evidence of pyramidal tract disease. With the exception of moderate dysarthria and some fixity of the facial expression the only residual of encephalitis was this curious choreo-athetoid disorder probably of neostriatal origin. While the spasm in this case one year after the onset had not diminished, in two other patients it had gradually diminished and finally disappeared.

Marie and Levy,[16] [17] [18] who had a large experience with striatal encephalitis have described cases of this character as Brady kinetic oscillation, and emphasize the peculiar nature of this type of movement and its lack of correspondence with any recognized clinical type. While agreeing with these writers as to the unique character of this curious spasmodic type, of which four occurred in my series, there is a strong resemblance to certain types of movement which I have occasionally observed in the dystonia musculorum deformans. I would therefore regard it as related to the neostriatum.

[16] Syndrome Excito-moteur de l'encephalite Epidemique, Rev. Neur., 1920, xxvi, p. 515.

[17] Nouveau cas de localisation—facio—masticatrice du syndrome excito-moteur tardif de l'encephalite Epidemique, Bull. et Mem. de la Soc. Méd. des Hôp. de Paris, 1920, xxxvi, p. 661.

[18] Quinze cas de mouvements involontaires apparus a la suite d'episodes grippaux ou d'encephalite lethargique, La Méd., 1920, 1, p. 270.

Acute Chorea of Childhood (Chorea of Sydenham). Before leaving the neostriatal type it will be interesting to mention some recent work on the chorea of Sydenham. Attention has already been directed to the fact that certain well-recognized types of epidemic encephalitis have been observed in sporadic form long before the existence of the present epidemic. The question naturally arises: have other clinical types of infection of the central nervous system a similar origin and relationship?

A recent pathological study by Marie and Tretiakoff[19] of the nervous system, from a case of chorea, is very suggestive from this point of view. The case was a typical one of Sydenham's chorea occurring in a child, aged ten years, and which terminated fatally ten days after the onset of the disease. Evidences of inflammatory reaction were found throughout the brain and spinal cord, with the exception of the bulb and cerebellum. The neostriatum and cerebral cortex were particularly affected. These investigators, who have also studied the lesions of epidemic encephalitis, emphasize their great resemblance to those found in the central nervous system of Sydenham's chorea.

This observation would suggest a possible relationship between the acute infectious chorea of childhood and the choreic type of encephalitis lethargica. The occurrence of neostriatal symptoms in such a case, with evidences of diffuse involvement of the nervous system, I would explain by a special affinity of the toxin for the neostriatal system of neurons (striopallidal system).

Mixed Striatal Type (Mixed Choreiform and Paralysis Agitans Types). While the paralysis agitans and choreiform types may occur in pure form it is well to emphasize the fact that these two clinical pictures are not infrequently combined in greater or lesser degree. Indeed, among the most striking features of involvement are the many bizarre combinations which unite both the elements of chorea and paralysis agitans.

In one of my cases there developed during convalescence the typical picture of paralysis agitans which progressed slowly. Four months later there were superadded to the symptoms of paralysis agitans choreiform movements of the right foot and still later typical Brady kinetic oscillations of the whole right lower extremity, which was characterized by a slow flexion of the hip, knee and ankle. This movement was of large amplitude, stereotyped and occurred at regular intervals. It lasted for two months and then gradually disappeared. The symptoms of paralysis agitans, however, continued and grew progressively worse. Two months later there was superadded a tonic spasm and athetoid contractions of the muscles of the neck and of mastication, causing distressing dysarthria and dysphagia. This case is of the progressive type and one year after the onset of the striatal symptoms showed no tendency to abatement.

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[19] Histological Examination of the Central Nervous System in the Acute Chorea of Syndenham, Rev. Neur., 1920, xxvii, p. 428.

The explanation for such clinical combinations, I believe, is to be found in the existence of two striatal systems; a neostriatal and a paleostriatal (pallidal), yielding their respective syndromes of chorea and paralysis agitans. The one a convulsive and the other a paralytic manifestation of the corpus striatum.

Rare Myoclonic Types. Occasionally one observes, after an attack of encephalitis, stereotyped rhythmical movements of the distal portion of the extremities. In one of these cases, which presented typical symptoms of paralysis agitans, there was rhythmical flexion of all the fingers, occurring about twenty times a minute. Movements of this type are so fragmentary that it is rather difficult to localize them with certainty. The association with paralysis agitans and the stereotyped regularity of the movement are in favor of a striatal origin.

Rhythmic twitchings of the face and *jaw*, either alone or in combination, have also been observed. When combined the movements of the jaw and face may be synchronous. Such manifestations may represent disjointed fragments of striatal motility or may indicate a release of kinetic impulses in subsidiary centers of the pons varolii, which contain the motor nuclei governing the facial muscles and mastication.

In one patient of my series who presented a definite sequela of paralysis agitans there was also present a rhythmical clonic movement of the jaw associated with bilateral facial spasm. The movements of the jaw and face were synchronous and occurred with stereotyped regularity about eighteen times to the minute. In another patient the only residuals of the encephalitis were the Parkinsonian mask and a lateral clonic movement of the jaw. Marie[17] has observed similar cases.

Bilateral Synchronous Myoclonia. There is still another type of movement which has been encountered in this disorder, the classification of which is somewhat difficult in the present state of our knowledge. This is a movement of the myoclonic type, involving a large number of muscles and causing bilateral synchronous movements of the trunk and root segments of the extremities occurring in very rapid tempo, fifty or sixty to the minute.

These movements differ from those of the "myoclonus multiplex type of spinal origin" in the large number of muscles which are simulataneously involved and the extent of the locomotor effect. They are also unlike those types of movements which we associate with the striatum.

Hamill[20] has described a group of cases representative of this type, in all of which the movements were increased during sleep in contrast to the ameliorating effects of sleep on the pure striatal types. He suggests their relationship to certain subordinate motor

[20] Encephalitis with Involuntary Movements, Arch. Neur. and Psych., 1920, iv, p. 44.

centers in the pons or medulla which act in conjunction with the respiratory center as auxillary centers of breathing.

I have also observed movements of this type. In my opinion they are neither cortical nor spinal, and if they do not represent lower forms of movement directly under striatal control they are probably referable to some infrastriatal motor mechanism of the paleokinetic system of motility.

The Thalamic Type.—The *optic thalamus* is the sensory counterpart of the corpus striatum. It is the great ganglionic station where the neurons of the secondary sensory paths terminate for their final grouping and distribution.

Many of these neurons terminate in the optic thalamus itself, subserving *affective sensibility*, the greater number pass to the sensory areas of the central cortex to subserve the higher form of discriminative sensibility.

Lesions in this region may produce sensory symptoms of the following character: Spontaneous pain of intolerable intensity and of persistent character; loss of superficial and deep sensibility with anesthesia; ataxia and astereognosis. There may also be present slight hemiplegia as well as choreic and athetoid movements. The sensory loss and pain are alone of thalamic origin; the other symptoms are referable to surrounding parts.

Symptoms of thalamic origin are not infrequent in cases of epidemic encephalitis (Howe[21]). They are often associated with evidences of striatal involvement, but in my experience are neither so severe nor well defined. I have observed no case presenting the complete thalamic syndrome as outlined by Dejerine and Roussy. My experience has been limited to sensory symptoms which it seemed reasonable to assume were of thalamic origin, although one could not deny their possible relationship to the central sensory mechanism of the spinal cord and brain stem.

The most frequent symptom of thalamic involvement in encephalitis in my experience has been pain. This may be of agonizing intensity and is very resistant to all analgesic remedies. It may be generalized or localized and may persist for weeks or months. It is difficult to differentiatiate localized thalamic pains from those referable to the posterior gray matter and posterior root system of the spinal cord. In differentiation I would lay some stress on the coexistence of striatal symptoms which would appear to show inflammatory involvement of both structures at the same level. In no case have I encountered any extensive anesthesia, either superficial or deep. Tactile sensation has shown little or no involvement and the chief sensory disturbances when present have been of pain and temperature sensibility. In no case was the deep sensibility affected.

[21] The Thalamic Syndrome in Epidemic Encephalitis, Neurol. Bull., 1919, ii, 190.

From my personal experience and that of others I am inclined to believe that the thalamic symptomatology is largely limited to intractable and persistent pain associated with mild evidences of sensory loss, especially of pain and temperature sensibility.

As the optic thalamus is the sensory counterpart of the corpus striatum, and as both ganglia are closely connected by short commissural systems, it is interesting to speculate on the possible role which irritative lesions of the thalamus may play in the production of striatal types of movements, such as chorea and athetosis.

While the facts of pathological anatomy point to the neostriatum, and especially the neostriatal system, as the seat of the essential lesion of chorea, it cannot be denied that irritative foci in the thalamus or pallidum might produce spontaneous motor manifestations of the same character as those resulting from loss of its inhibitory mechanism.

Concluding Remarks.—The results of my investigations may be summarized as follows:

The large basal ganglia, and especially the corpora striata, are frequently affected in epidemic encephalitis.

Involvement of the corpus striatum produces three clinical types or syndromes:

1. A *paleostriatal* or *pallidal syndrome—the paralysis agitans type.*
2. A *Neostriatal syndrome—the choreiform type.*
3. *A mixed striatal syndrome—the combined paralysis agitans-choreiform types.*

These three types are believed to be dependent upon the existence of two distinct cellular systems within the corpus striatum.

One, the *pallidal system*, which originates in the motor cells of the corpus striatum and links this structure with important nuclei of the hypothalamic region, and controls the various motor activities of the extrapyramidal tracts. When this system is involved the symptoms of paralysis agitans develop, *i. e.*, paralysis of automatic associated movements with hypertonicity of the muscles and rhythmical tremor.

The other, the striopallidal or *neostriatal system*, which exercises a coördinating and inhibitory influence on the purely motor functions of the corpus striatum. When this system is involved, chorea or spontaneous movements of the automatic associated type develop.

The mixed striatal types result from involvement of both systems with the production of symptoms characteristic of each.

The recognition of these two systems and fundamental syndromes of the striatum serve to explain and reconcile many peculiarities of striatal symptomatology.

The *pallidal* or *paralysis agitans type* of encephalitis lethargica may be general, hemilateral or segmental in distribution. Abortive, relapsing and progressive types are also recognized.

The *neostriatal* or *choreiform type* may also be general, hemilateral or local in distribution. There is an acute choreiform type; a choreo-athetosis and athetoid and rhythmical types.

These types may occur in pure form or in combination. Of my series of 25 cases, 18 were of the paralysis agitans type, 4 of the choreiform and 3 of the mixed striatal type.

Thalamic symptoms also occur in encephalitis lethargica.

When present they consist of severe and persistent pain, with disturbances of superficial sensibility, more especially of the pain and temperature sense. Evidences of the complete thalamic syndrome are rarely if ever encountered.

VEGETABLE PROBLEMS IN DIABETIC DIETS.

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A CERTAIN eminent specialist is quoted as saying that "diabetics must not expect a varied diet." That this is not necessarily true I hope to be able to show. The vegetables in common use are only a fraction of those that mankind has found fit for food in one country or another during the thousands of years that gardening has given pleasure to the rich and the poor. There is a vast store of experience on record in the garden literature of the world which diabetics have a special motive in searching for suggestions as to vegetables of value to them and as to methods of cooking to give added variety. Americans have not begun to know the good dishes of Europe, and India, China and other ancient lands must have accumulated culinary discoveries beyond any that we dream of. I am growing this year 81 species or kinds of plants in 255 varieties, and I have accomplished the aim of having some fresh green vegetables of my own growing every day in the year without a greenhouse. I am sure that others can do the same, and I believe that the achievement will bring them new enthusiasm and contribute to the maintenance of health of body as well as of mind.

Everyone needs a hobby, diabetics particularly, to take their mind from their hunger troubles and give them an interest in life. The culture of rare or uncommon vegetables fills their need admirably. Achievement stimulates renewed effort and it is one of the advantages of gardening that there are always new fields to conquer, new crops to test, new problems of succession cropping, how to get vegetables earlier or prolong their season into the winter by storage.

Only those who have been through it can appreciate the food problems of the diabetic patient, who has to face for probably the rest of his life an altered regimen, with strict limitations of kind and

of quantity of food, old likes and habits broken up, favorite dishes forbidden, temptations to transgress constantly presented, and with the influence of family and friends often misdirected and imperfect.

The difficulties of the diabetic diet center mainly around the supply of vegetables; the provision of variety at all seasons at a reasonable price and cooked and served in a palatable manner. There is nothing lacking in American soil and climate. We can grow everything somewhere or at some season. Our people, however, have not yet become sufficiently herbivorous for their own good. Meat and potatoes are too much the reliance, flanked by corn, peas or tomatoes, to the neglect of health-giving greens or salads. This reacts against the diabetic in a double way. The onset of the disease compels a greater change in his food habits, and the narrow list of vegetables in common use in the community makes it more difficult to obtain supplies in the markets.

We are further handicapped by our primitive methods of cooking. Many cooks seem to know but one way of cooking vegetables; that is, simply boiling and serving *au naturel.* Vegetables that are young and tender and fresh from the garden require little dressing; but, nevertheless, plain boiled spinach gets horribly monotonous if taken twice daily, month in and month out, and our patient is excusable who breaks diet or gets to doubting whether life is worth living.

A wonderful change has been made in the outlook for diabetics by the discoveries of Dr. Frederick M. Allen and his co-workers. To the student of nutrition we have the most interesting disease in the list. Our chances for a useful existence have been multiplied. The treatment is exact. Our diet can be calculated to the gram and checked constantly by simple tests. Old medical traditions are broken, in that the patient is admitted to a full knowledge of the treatment and trained to handle his own case. His chances for long life may be greater than his healthy brothers.

But the problem of food supply stands where it was, and in this field there is great opportunity for progress and improvement. It is not to be solved by proprietary foods or commercial compounds. They may be useful in special cases, but reliance may better be placed upon Nature's original sources.

There is need to spread the information that many unheard-of vegetables are in existence; that they may be grown with ease, and if demanded by a number of consumers would be supplied by the market gardeners.

Diabetics may be divided into two classes: Those who possess gardens and those who do not. The latter, naturally in the majority, constitute a special problem requiring a new line of effort. Many of the vegetables which are recommended below are to be had only in the larger city markets for a very short period of the year. Many are never seen in the market. How can they be had by the non-gardeners? The physician can assist in creating the demand by

interesting the patients in the possibility of enlarging and varying their diet and then putting them in touch with some nearby gardener who will be found willing to produce the vegetables and supply them as needed. A medium of contact between farmer and consumer exists in most communities now in the county agricultural agent or Farm Bureau representative, whose name and address may be had by writing to the State Agricultural College or to the U. S. Department of Agriculture. He is in touch with gardeners and in a position to supply the information needed. If a group of diabetics could be formed to buy together they could make it more worth while to the farmer to take up the new crops and to supply them over a longer season by successive plantings and storage.

In many cases the physicians will be justified in encouraging patients to move to the country or to the suburbs, to do their own gardening, particularly when they have had previous farm or garden experience and are benefited by exercise. With few exceptions regular outdoor activity increases the carbohydrate tolerance and improves the general health to a remarkable degree. It is not always necessary for the city diabetic to change his residence, for the possibilities of nearby vacant lots are often good if the original soil has not been removed or covered and the ground is not shaded by trees or buildings.

The List of Vegetables. The diabetic garden comprises in the main those vegetables which have a low carbohydrate content. We must set in the background many of our standard foods, such as potatoes, sweet potatoes, corn and peas, and Lima, shelled and navy beans, except for the milder cases. Their place is taken by greens and salads, indispensable to every well-balanced dietary through their high contents of salts and vitamines and constipation-controlling bulk.

The reader may be interested in the list of the vegetables I grow and find worth while, though naturally of varying merit:

Asparagus	Dandelion	Parsnip
Basella	Eggplant	Patience
Beans, bush and pole	Endive and escarolle	Pepper
Beets	Finocchio	Purslane
Cabbage	Kale	Radish
Carrot	Kohlrabi	Roquette
Cauliflower	Lettuce	Salsify
Celeriac	Mung bean	Scorzonera
Celery	Mustard	Soy bean
Chard	New Zealand spinach	Spinach
Chenopodium amaranticolor	Okra	Squash and vege-
Chervil	Onion, leek and shallot	table marrow
Collards	Orach	Tomato
Corn salad	Pai-tsai	Turnip
Cress	Parsley	Witloof
Cucumber		

Corn, peas and potatoes, shelled beans, Lima beans and other starchy vegetables are too high in carbohydrate for severe diabetics,

and many of those in the above list can be eaten in moderate quantities only.

Several herbs are useful for flavoring purposes, particularly in connection with thrice-cooked vegetables. Basil, chives, dill, horseradish, mint, sage and many others may be used.

Seeds of most of these can be obtained from the larger seed houses in this country, and all from Vilmorin-Andrieux & Co., Paris.

The Value of Perennials. To maintain a succession throughout the year one needs to give particular attention to bridging the period, of midsummer heat, for which New Zealand spinach basella and chard are valuable, and to have cold-resistant plants to carry production late into the fall and to start it up as early as possible in the spring. The diabetic garden should therefore be well stocked with biennials and perennials. Asparagus comes early, but French sorrel is even earlier. Dandelions are highly prized in the first spring days, especially if brought on early by covering the bed with hotbed sash. The patience dock is another little-known perennial of much merit.

To give the standard methods of culture and cooking of these vegetables would require more space than is available here. There are, however, particular points to be emphasized regarding choice of varieties, succession of supply, storage methods and newer ways of cooking on which the writer's personal experience is contributed.

Blends or Mixtures. I seldom use a single green or salad vegetable alone, but prefer to mix several to add or reduce flavor and substance according to personal taste and the needs of the daily menu. Spinach and chard, for instance, are mainstays in the garden but are rather bland and characterless. The addition of French sorrel, mustard, kale, parsley, pepper or okra remedies this defect. Kale, on the other hand, a much neglected vegetable, has rather too much substance for frequent use by most people and calls for admixture with New Zealand spinach, beet greens and the like. The number of combinations that can be made are almost unlimited and a new interest in the world is provided.

Still more is this true of salads or vegetables served cold, either raw or cooked. Any tender or succulent plant parts may be taken, and on a foundation of lettuce, endive, pai-tsai or witloof one builds a masterpiece or an experiment with asparagus tips, cauliflower, celery, celeriac, chervil, cress, cucumber, mustard, parsley, mung bean sprouts, salsify, sorrel, tomato, apple, orange, grapefruit and so on.

Vegetable Soups. A type of vegetable mixture of very exceptional value to the diabetic is modeled on the Italian vegetable soups. They may be made delicious and different, as rich as a meat soup, though solely of vegetables, and each one a full meal if desired.

The following is a sample. The ingredients may be changed

according to taste and the supply available. The essential points are the preliminary frying in fat, the use of some greens and flavoring herbs in the mixture and the long simmering in broth.

Take several vegetables, including onions, a quantity of greens, such as spinach, kale or cabbage, a moderate quantity of celery, parsley and herbs to suit the taste, carrots, kohlrabi, turnips, etc. Place a measured quantity of oil or fat, such as butter, Crisco or cottonseed oil, in the frying pan. Add the finely chopped onion and fry golden brown, then add the greens, similarly finely minced, and cook until the fat is all absorbed; add the remaining vegetables and enough soup stock or water to cover, and simmer until tender. It is more convenient to run all the vegetables through a meat chopper with the coarsest knife than to dice them separately.

Compute the food value of each ingredient as follows:

Vegetable.	Grams.	Protein.	Fat.	Carbohydrate.
Onion	100	1.7	0.3	9.0
Greens, mixed	500	10.0	5.0	15.0
Carrots	200	2.2	0.8	18.0
Kohl-rabi	200	4.0	0.2	14.0
Stringbeans	300	8.0	1.0	18.0
Celery	100	1.1	0.1	3.0
Fat	100	....	85.0	
Total calories	1247	27.0	92.4	77.0

Canned Travel Dinners and Lunches. The diabetic away from home is at a disadvantage which is well overcome if he has weighed and proportioned meals to take with him. Vegetables are readily canned in seasons of abundant supply and set aside with the calories and grams of proteins, fat and carbohydrate marked on the can. This has been made convenient by the Burpee can sealer, a device for sealing sanitary tin cans at home without solder, a process requiring but a short time, and applicable to a single can of surplus material or to a hundred cans. The best sterilizer is the pressure cooker.

In addition to the various vegetable soup mixtures it is suggested that weighed portions of corned beef and cabbage, sauerkraut and ham, or greens and bacon be put up in tin cans, sterilized and held against the time of need.

Cooking Vegetables. The changes in composition of vegetables due to cooking may be considerable when they are boiled in much water and the water discarded. This element of uncertainty often interferes with the exact calculations of dietary values. For the determination of the exact tolerance of a patient, and for cases in which the carbohydrate tolerance is very low, so-called thrice-boiled vegetables are employed—that is, the water of cooking is drained away, more water is added and the vegetables cooked again and the process repeated. Three cookings remove most of the carbohydrate and, unfortunately, also the greater part of the salts and the flavor.

However desirable thrice-cooked vegetables may be in special cases, protest is made against anything approaching this method when the tolerance of the patient does not demand it. For the use of patients possessing sufficient carbohydrate tolerance, nearly all vegetables, and particularly the green, leafy ones, should be steamed in the pressure cooker at a low pressure or cooked with the addition of an absolute minimum of water, in order that their flavor and food value may be preserved. Their composition can then be reckoned on the basis of their fresh weight and the full benefit secured of their salt and vitamine content.

If vegetables are boiled in water and the water drained away a factor of uncertainty is introduced into the computations of nutritive values. Probably half the carbohydrate in spinach and celery is lost and one-third that in most other vegetables.

Asparagus. That this delicious vegetable requires more space than can be spared in the small home garden is a misfortune only partly counterbalanced by its constant availability in cans from California. The U. S. Department of Agriculture has lately bred rust-resistant strains, the Washington asparagus, which excel the old varieties in size and productivity also. I plant spinach and mustard between the rows in earliest spring and thus get two crops from the asparagus bed.

Beans. String beans are a standby, but they are treacherous in a way, because unless picked very young before seeds are formed in the pods they contain more carbohydrate than analyses usually show. It is best to use only the young and still seedless pods, which may be set down as having 40 calories per 100 grams, protein 2 per cent, fat 1 per cent and carbohydrate 6 per cent; whereas more mature stages with well-grown beans may contain as much as 10 per cent of carbohydrates. Excellent varieties of highest quality are Stringless Green Pod and Maule's Butter Wax for the bush type and Kentucky Wonder pole bean. New and distinct are the soy bean and the mung bean. The soy bean is a protein food, a meat substitute, and only the variety Hahto comes into the diabetic's garden, where it replaces the Lima bean, which may have as much as 22 per cent carbohydrate. Soy beans in general are grown in the southern and central states for oil and forage and may be bought in the market and used as baked beans or ground into meal and cooked as muffins. The seeds and pods of all kinds except the Hahto are too small and difficult to pick and shell for garden culture, but the dry soy beans can be bought from seedsmen.

The diabetic who prefers a vegetable to a meat protein will find these soy beans highly useful. Their dry composition is: Protein 43 per cent, fat 20 per cent, carbohydrate 24 per cent, of which not over 8 per cent is believed to be assimilable, making them quite unique among beans from the diabetic standpoint. To cook dry soy beans, soak overnight, boil a while in the pressure cooker, then

put into the bean pot with a piece of salt pork and a pint of tomatoes and bake rather longer than for navy beans. Soy beans will not, as a rule, cook as soft as common beans. The variety Easy Cook is an exception. The composition of baked soy beans may be roughly estimated as one-half the corresponding weight of dry beans.

Since confectionery is scarce in the diabetic menu it may be mentioned that roasted soy beans are as good as roasted peanuts, and much safer. They are prepared as follows: Take ordinary soy beans and soak them overnight in salted water. Cook an hour, drain and spread thinly on tins and roast in a moderate oven until crisp.

Hahto is a variety with large seeds which I have found of easy culture and worth while in a large garden where space is available. The plant is a vigorous grower, requiring three-foot rows, three or four seeds to the foot and the whole season for development, from the end of May to frost. Gather the pods when the beans are full-grown. Boil in water five minutes to make shelling easier, shell and can the beans as you would Limas—that is, fill the raw beans into cans, cap and process forty minutes in the pressure cooker. Their estimated composition when cooked and canned is: Protein 20 per cent, fat 13 per cent, carbohydrate 4 per cent.

Mung bean sprouts are distinctly a novelty except to those who frequent Chinese restaurants. The bean is a very small oriental type which one buys at Chinese supply stores or grows from seed procured from the Department of Agriculture at Washington. Their special claim to merit is as a winter salad, for mung bean sprouts are one of the links in the all-the-year-round chain of salads. They grow in the kitchen and require only five days from planting time to harvest. No diabetic can afford to be without them. Proceed as follows: First catch your mung beans. Wash 50 grams and soak overnight in water. Place in a covered butter-jar or other crock with only a thin film of water. Twice daily flood with fresh water and drain; this prevents the growth of moulds and bacteria. The green outer skins of the beans float off in the washing, leaving the white sprouts, which are ready to use when they have attained a length of one to two inches. To prepare for the table, wash and dip for two minutes in boiling water, then plunge into cold water and serve on lettuce with French dressing, or the mung beans may be incorporated with a chop-suey mixture of minced chicken and chopped celery or other vegetables, in which case the other ingredients are cooked in a stew pan and the mung beans added just as cooking is completed.

Cabbage. We hurry over this vegetable, merely passing to remind the reader of the possibilities of red cabbage as a desirable change and of the fact that the crumpled-leaved savoy type is of richer flavor than the common kinds and keeps better in the winter. Sauerkraut visits our table regularly only since we began making

it ourselves and discovered the high quality of kraut from home-grown summer cabbage. We plant the variety Copenhagen, which matures in July. Wash and split the heads, slice into a barrel with one pound of fine salt to each forty pounds of cabbage; cover with a board and weight and let stand in a warm room, 70° to 80° F., for three weeks, skimming as necessary; then take the kraut out and can in tin cans with the Burpee sealer or fill into stoneware jars and cover with melted paraffin to exclude all air. Nothing is easier and nothing is better.

Collards. Collards are plants of the cabbage family, much grown in the south on account of their resistance to summer heat and autumn and winter frost. They are worthy of more general trial farther north for eating as cabbage greens. The culture is exactly like cabbage. The collards are tenderer after frost and stand cold to about 12° F. if not too prolonged.

Couve Tronchuda, or Portugal Cabbage. This is a plant grown for its thick leaf stalks. It is at its best in rich, moist soil and a cool climate.

Celeriac, or Turnip Root Celery. This is grown just like common celery as to planting and transplanting, but requires no earthing. The edible part is the enlarged root. Celeriac is used as a cooked vegetable or in soups, but with us mainly in salads. The roots are cleaned, cut in thin slices and these blanched in boiling water five to ten minutes and served with lettuce or other green leaves. The composition is estimated at 6 per cent carbohydrate. Celeriac keeps in a cool cellar better than any other vegetable I have, being still firm and fresh at the beginning of June.

Celery. Celery is of use not only in its raw state but as a cooked vegetable.

Boiled Celery: Cook the outer stalks of celery, cut into small pieces, in boiling salt water for five minutes, then drain and sauté in butter. Add meat stock to cover and simmer until tender. Serve with a sprinkling of grated cheese.

Celery is also an important flavoring ingredient in the vegetable soups, and an early planting is needed in the garden for this purpose in addition to the main crop to be stored for winter.

Chard. Chard is becoming better known. There are really two vegetables here, a summer spinach represented by the Lucullus chard, which produces very large, crumpled leaves, cooked as greens, and a summer asparagus, derived from the much enlarged leaf stalk of the white-ribbed Swiss chard. Try the following method of cooking the latter:

Fried Chard: Take the large leaf stalks, strip off the green leafy part, which may be cooked separately as spinach, and cut the stalks into four-inch sections, boil until tender, drain dry and sauté in bacon fat or oil, turning and frying each piece separately.

Eggplant. Eggplant is very useful to us, not only in season but

canned, to serve as the basis for a baked luncheon dish, as follows: 200 grams of eggplant, 1 egg, ½ cup of washed bran and 10 grams of grated cheese. Boil the eggplant in salted water; wash and mix with the egg, bran and cheese; fill into an individual baking dish and bake in the oven until brown. Serve with butter.

Endive and Escarolle, or Batavian Endive. These are worthy of the highest rank, since they fill in the late fall and early winter period with a salad that is richer, nuttier and crisper than lettuce, and can be kept long in storage. They are plants of the chicory family that form broad, circular rosettes or mats of leaves, and are covered or tied up to blanch the center. They are cool-weather plants and thrive in the autumn months, but do not endure hot weather well. Plant from June to August and transplant the young seedlings to rows eighteen inches apart, twelve to fifteen inches in the row. Give plenty of room, water and fertilize liberally to secure the large plants that will give nicely blanched centers. When grown and about three weeks before using, gather the outer leaves together and tie them over the heart of the plant with twine or raffia. Blanch only as needed, as endive tends to decay if water gets into the tied-up and blanched hearts. Before heavy frosts, take up the plants and set into a cold frame, with all possible earth adhering to the roots; tramp firmly and water the roots, but not the tops. Cover and add protection in the form of hay or straw as cold weather comes on. In this way endive may be carried in good condition past midwinter. The white center leaf stalks only are used for salads, with French dressing or mayonnaise. Try grapefruit in combination with it. Endive and escarolle may also be cooked for greens.

Finocchio. Finocchio is an Italian vegetable related to the carrot, but in appearance reminding one more of celery. The edible parts are the swollen bases of the leaf stalks. The culture is simpler than for celery. Sow in place, thin to 4 inches to 6 inches in 2-foot rows; earth up to bleach when fully grown. Cook in soup mixtures or like celery.

Kale. Kale is a plant that should be in every diabetic's garden. It exists in various types and goes far toward bridging over the cold weather period, both in spring and in fall. The first greens of the season here come from Siberian or dwarf Scotch kale, sown about the end of August, which overwinters and sends up a succulent new growth in March. I plant tall curled kale in early spring for all summer, gathering the lower leaves as formed and later the stem sprouts. The main planting goes in after the spring vegetables are over. The seed is sown June 20 and the plants moved to their permanent rows early in July.

Kohlrabi. Kohlrabi is another indispensable vegetable. This is a cabbage relative with a swollen bulb-like stem, which one eats like cauliflower or turnip. It is as good as the former when gathered

young, 2 inches or 3 inches in diameter, can be grown all summer by making successive plantings and the fall crop keeps well in storage until spring.

Leeks. Leeks have special merit, through their winter hardiness, in extending the onion season. They mature late in the fall and may be stored in pits, packed in earth like celery or left in place and lifted whenever the ground is not frozen. They are especially welcome in early spring.

To have onions the year round is an object on account of the use we make of this vegetable for flavoring greens and salads and soups. There is an Egyptian or top set onion which is planted in the fall, is winter hardy in Washington and ready to use in early spring. Beginning then with leeks as soon as the ground thaws and following closely with the Egyptian or Catawissa onion, the season is maintained by the green onions grown from sets of Danvers or silverskin planted as early as possible in the spring. These are delicious when cooked. They mature in midsummer, and if thoroughly cured by drying will keep into the winter. Shallots keep even better and assist in maintaining the onion succession.

Orache, or Mountain Spinach. Orache is a relative of spinach but a larger plant. If it has a special place in the collection of greens it is in coming later in summer, after spinach has run to seed, and in its flavor, which reminds one of lambs' quarters. Sow orache in May in drills two feet apart. It is not in the market.

Mustard greens are comparatively little grown but are of much merit. There are several varieties of Chinese origin, one type with broad leaves and one much curled, like curly kale. Mustard can be sown in earliest spring and again in the fall, but does not thrive in midsummer heat. The young leaves make an ingredient of salads. I like the Fordhook fancy curled for this purpose and for general spring culture and the broad-leaved or elephant ear for fall planting. Mustard greens go especially well in mixture with spinach.

Pai-tsai is the proper name for a Chinese vegetable sometimes called celery cabbage and Chinese cabbage; an upright cylindrical head, less compact than the common cabbage, with light green outer leaves but white and tender at the heart. This is an autumn crop and of particular value for storing, as it provides a winter salad of exceptional merit.

The cardinal points of success in growing pai-tsai are late sowing, (July 15 in Washington), a rich soil with abundant moisture, and liberal fertilizing to induce a rapid growth. To store for winter, use an empty hot-bed pit; take the plants up with roots and earth adhering, pack tightly in the pit, keep the soil moist, the heads dry and protect from frost, as pai-tsai is more tender than cabbage. The blanching process goes on in storage, and when taken out the heads should be crisp, white and tender, one of the most delicious salads on the list. This vegetable can now be had in our markets at

certain periods.   It thrives wonderfully in winter gardens in southern Florida.

Patience Dock is a relative of the sorrel, possessing a similar pleasant acid flavor and very productive throughout the summer. There is also an African dock, *Rumex abyssinicus*, lately introduced by the U. S. Department of Agriculture, which is adapted to the warmer parts of the country.   Its leaves are strongly acid and the stems and petioles cook up into a rhubarb substitute of merit, because still palatable after thrice cooking, a process that completely ruins rhubarb.

French Sorrel should be in every diabetic garden for two reasons, its distinctive flavor and its early season.   The plant is perennial, of easy culture, commencing growth before spring frosts are over and continuing to yield pickings through the season, except in midsummer.   The broad-leaved, cultivated sorrel has the same oxalic acid flavor we know in the common wild sorrel.   We like it occasionally by itself, but more for mixing with spinach or chard.   The tender leaves are also valuable in mixed salads.   I have never seen sorrel on sale in the market.

All these acid and bitter vegetables possess special merit for saltfree diets, since they are greatly relished by patients from whom common salt is withheld in the treatment of nephritis, arteriosclerosis, etc.

Vegetable Marrow is a type of squash deserving more general culture because it has more substance and a finer flavor than our common summer squash.   The vining varieties are too vigorous growers to be let into the small garden.   They delight in covering rubbish-heaps or manure-piles, but there are bush varieties also, adapted to more limited space.   Try the following of many ways of cooking:

1. Fried Marrow: Gather the fruit while young and tender, cut into slices and fry in the same manner as eggplant.

2. Vegetable Marrow au Gratin: Peel well-grown marrows, remove the seeds and parboil in slightly salted water; cut into pieces and place in layers in a buttered baking dish, sprinkling each layer with salt and pepper and finely minced parsley and a little butter; cover with crumbled bran biscuits and grated cheese and bake thirty minutes.   Serve hot.

Witloof (sometimes in the market as endive or French endive) is particularly to be recommended because it furnishes a superb salad during the winter months and can be forced in the cellar by anyone having a couple of square feet of space near the furnace.

Witloof is a kind of chicory much grown in Belgium.   It is planted and cultivated like parsnips and produces long, white roots, which are taken up, packed in boxes and later brought into a warm cellar and watered.   The heads form in three weeks or so.   When these are cut a crop of slender sprouts follow.   It is relatively easy with

six to eight boxes of witloof to maintain a succession of fresh salad from Christmas until May.

Witloof roots can be purchased and forced by those who have no gardens. To make sure of them it is well to arrange in advance with a gardener to have the crop grown.

Vegetables in the Ornamental Garden. Several of the vegetables suited for diabetic diets are beautiful plants, worthy of a place in the ornamental border, and as they will grow in partial shade if well watered they may be planted in beds along building lines and walls or fences or bordering walks and lawns when no space is available for a kitchen garden. All forms of chard are handsome plants, particularly the red Chilean and yellow Chilean, which have bright red or yellow leaf-stalks. If set a foot apart they will grow two feet or more high.

Chenopodium amaranticolor is a lambs'-quarter from Algeria, with brilliant maroon buds and young leaves, which are eaten as spinach. The special merit of this plant is that it withstands thrice cooking particularly well. In my garden it forms a hedgerow six feet high.

Finocchio is a pretty plant with delicate feathery leaves. Tall curled kale is also handsome. The red orach has red bronze foliage as effective as many ornamental bedding plants.

DEFECTS OF MEMBRANOUS BONES, EXOPHTHALMOS AND POLYURIA IN CHILDHOOD: IS IT DYSPITUITARISM?[1]

By Alfred Hand, M.D.,
PHILADELPHIA.

In the *Transactions of the Pathological Society of Philadelphia,* vol. xvi, 1891–93, under the heading "General Tuberculosis," and also in the *Archives of Pediatrics,* vol. x, 1893, with the caption "Polyuria and Tuberculosis," I made the following report, exhibiting the specimens to the society:

On December 1, 1892, a boy, aged three years, was admitted to the Children's Hospital with a history of great thirst and polyuria which had begun suddenly eight weeks before. He had had enterocolitis at five months of age and croup and measles together at two years. The family history was negative, the parents, three brothers and two sisters being alive and well. One younger sister died of enterocolitis. There had been no miscarriage.

The examination showed the boy to be undersized and puny, with light hair, brown eyes and a bronzed, dry skin. The eyes were

in a condition of exophthalmos, giving him a frog-like appearance, and there was a corneal opacity on each eye, with anterior synechiæ in the right. The thyroid was not enlarged. His chest was very small and narrow and the rachitic rosary could be felt; the lungs and heart were normal. His belly was distended and tympanitic, obscuring for several days the great enlargement of the liver and spleen, which at first were thought to be normal in size; there was an umbilical hernia and the skin of the abdomen was covered with petechiæ and an eruption something like scabies. The feet were edematous.

The urine had the following characteristics: Acid; cloudy; specific gravity, 1.000; quantity in twenty-four hours, 114 ounces; no sugar; albumin distinct.

The boy seemed to suffer so much from thirst that water and milk were not withheld and he was given a drink whenever he asked for it. He was at once put upon 2 minims of the fluidextract of ergot three times daily. This had no effect whatever; at the end of a week the daily amount of food ingested was 180 ounces, of which 150 ounces passed through the kidneys without taking up either albumin or sugar, the specific gravity not rising above 1.000, but the color being like that of a saturated solution of picric acid. During this week the temperature had been rather irregular, but there was no decided fever until the seventh day, when the thermometer registered 102.2°. The ergot was now replaced by laudanum, 2 drops every six hours. Before this the thirst had not allowed more than a few minutes' sleep at a time, but the boy now began to take longer naps, and the amount of fluid taken and excreted fell to 100 ounces. During the next week the urine contained albumin once, but at the end of that time was free from it, had changed to pale yellow in color and had a specific gravity of 1.010. After this the total amount could not be collected, so an idea of the amount voided could only be gained by measuring the quantity of water and milk drunk, which decreased to about 80 ounces. December 20 the urine had its highest specific gravity, 1.012, but the next day it fell to 1.004. On the 22d the temperature rose from 99° in the morning to 105° at 4 p.m. It was normal on the 23d and at 6 a.m. of the 24th, but at noon it was 103°. The opium was then stopped and 1 grain of quinin given three times a day, with a very beneficial result. The temperature for six weeks did not vary 1° from normal, the liver and spleen decreased in size, the petechiæ on the abdomen gradually faded, the boy was able to get up and walk and he ate and drank no more than a child of three years should.

February 12, at 6 p.m., the temperature was 99°; four hours later it had risen 5°. After a few days a bronchopneumonia was discovered and a further diagnosis was made, from a general view of the case, of tuberculosis. For a week the temperature was very irregular and there was a marked systemic depression. On the 19th

the purpuric spots increased in number and an elevated, dull-red, macular rash appeared all over the body and extremities. At 8.30 p.m. he sat up and asked for a drink. Two hours later the body was cold and rigor mortis had set in.

The autopsy was made fifteen hours after death. The rash had faded from the left side but still persisted on the right. As the scalp was stripped off a yellow spot, about the size of a five-cent piece, was noticed near the right parietal eminence. When the skull-cap was removed this spot was seen on the inner side as well and the entire thickness of the bone was soft and movable. Other smaller areas not extending through the vault were seen on the outer surface. In the absence of any history of syphilis these were thought to be tuberculous. The brain was normal to macroscopic examination. The lymphatic glands in the omentum, mesentery, mediastina and, in fact, all through the body, were greatly enlarged. There were a bronchopneumonia of both lungs, a warty endocarditis of the mitral valves and a caseous pleuritic adhesion at the base of the right lung. The liver and spleen were enlarged and firm and the former had minute, gray nodules in its substance. The pancreas was apparently normal and there were no ulcers or scars in the intestines. The kidneys seemed slightly enlarged; the left contained three cysts and in the pelvis of each was a yellow, hard, tubercular mass, almost filling it. Microscopic sections prepared by Dr. W. S. Carter showed nodular masses of small round-celled infiltration in the liver, spleen, kidneys (pelvis), a bronchopneumonia in the lungs and a degeneration of the epithelium of the uriniferous tubules.

Subsequent experience at the autopsy table, with a large percentage of the cases showing tuberculosis, but without duplicating these features, made me begin to doubt whether the tuberculosis in this case had any causal relation to the triad of symptoms described, and this doubt was further strengthened by seeing in 1905 a patient presented to the Medical Society of the State of Pennsylvania by Dr. Thomas W. Kay, and reported by him[2] under the title "Acquired Hydrocephalus with Atrophic Bone Changes, Exophthalmos and Polyuria (with Presentation of the Patient)." Dr. Kay's paper is so interesting that I quote it in full:

"R. S., male, aged seven years, and the only child of healthy parents. Up to four years of age he was healthy and well-grown, as shown by photograph. He was attacked by scarlatina at that age, which was followed by a discharge from the right ear that still persists. Four months after scarlatina he had vertigo and cried occasionally with pain in the head. About this time enlargement of the superior cervical and submaxillary glands took place, which was most marked on the right side. These glands are still enlarged but give no discomfort.

² Penna. Med. Jour., 1905–6, vol. ix.

"Five to six months after the scarlatina the gums began to separate from the teeth, and this was followed by a gradual loss of most of the teeth, beginning with the molars. About the same time the mother noticed a soft spot on the head, which side she does not remember, where there seemed to be no bone.

"Eighteen months ago exophthalmos began to make its appearance and has been getting steadily worse. Now it is so bad that the eyes have to be protected by wearing a handkerchief over them, as they are too prominent for the use of glasses.

"Fourteen months ago polyuria appeared and he would void his urine in small quantities, 200 or more times in twenty-four hours. Now he micturates several times an hour, and as much as 27 ounces at a time is passed. Its reaction is neutral and the specific gravity is 1.000 to 1.001.

"Seven months ago he weighed 32 pounds and he passed 27 quarts of urine daily (54 pounds). Now he weighs 36 pounds and he passes 23 quarts daily (46 pounds).

"The bones of the body, with the exception of the lower jaw bones and of the cranium, are comparatively normal. The lower jaw has lost its bone-salts, and the resultant cartilaginous mass, containing one incisor has been so deformed by the depressor muscles that the chin has disappeared.

"The circumference of the cranium is 53 cm., the right side being slightly larger than the left. The squamous portion of the right temporal bone gives readily to pressure with the finger. The right parietal bone has in large part been absorbed, leaving an irregular 6 x 7 cm. oval opening. The left parietal bone has been nearly entirely absorbed, leaving an irregular 9 cm. x 11 cm. oval opening. The frontal bone has suffered on the left side, resulting in an irregular 4 cm. x 5 cm. triangular opening. The bone at the sites of the fontanelles and sutures is not affected. When I first saw this patient some seven months ago the openings in the bones were not as large by 1 cm. in diameter as now. The patient is irritable but fairly bright, and the organs of special sense and the rest of the body are in as good condition as could be expected. Whether awake or asleep his breathing is somewhat stertorous.. Of course, with polyuria there is a corresponding polydipsia. The causative lesion in this case is situated, most likely, in or near the floor of the fourth ventricle."

Bearing these two cases in mind it was with interest that I saw in the prospectus of the *Osler Memorial Volume* the title of an article by Henry A. Christian, "Defects of Membranous Bones, Exophthalmos and Polyuria, an unusual syndrome of Dyspituitarism," and I hoped that the solution of these two cases had been reached. Dr. Christian's report is very thorough, giving the results of a careful study of his patient during a stay of six months in the hospital. The patient is a girl who was well up to three years of

age, when the teeth began to decay and the gums became sore; exophthalmos began at three and a half years, with increasing thirst and polyuria. When studied at the age of five years the roentgen-ray plate of the skull showed extensive defects in the bones and similar but slight changes were also found in the ilium and ischium. Two similar cases were found by Dr. Christian in a search of the literature, reported by Schueller in the *Fortschritte auf der Gebiete der Roentgenstrahlen*, 1915-16, xxiii, 12, under the title "Ueber eigenartige Schaeldefekte in Jugendalter," one, a boy, aged sixteen years, with dystrophia adiposogenitalis, showing
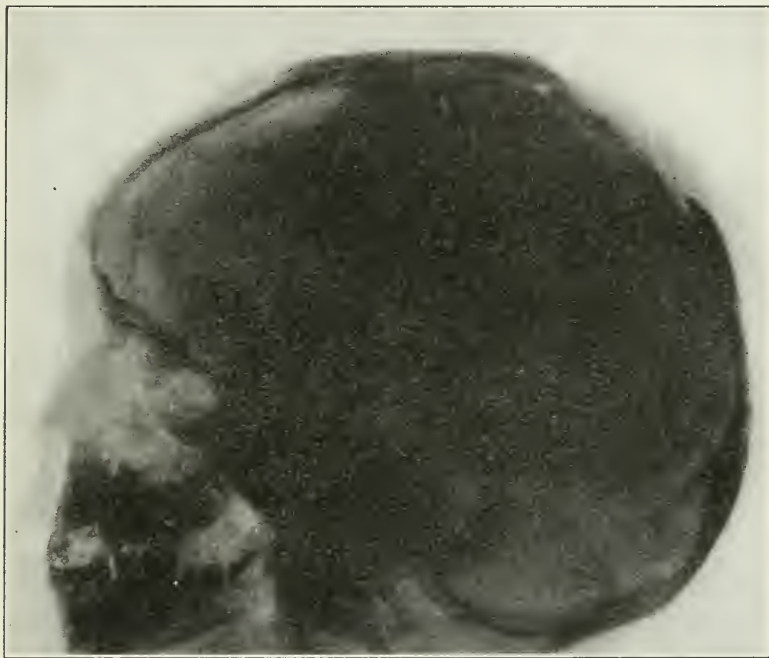
Skiagraph of head showing areas of absorption in calvarium; sella turcica sharply defined.

exophthalmos and defects in the bones of the skull but no polyuria; the other, a four-year-old girl, whose exophthalmos and bony defects began at two years of age, the thirst and polyuria also developing, at what time is not stated. Schueller's report of this case closes with the remark, "We can therefore make a presumptive diagnosis of anomaly of the skeleton as the result of disease of the hypophysis." Dr. Christian treated his patient with pituitary extract, and when this was given under the skin or into a vein a great lessening was seen in the amount of fluid ingested and excreted, but administration by mouth or rectum had no effect. He therefore concludes

that the symptom-complex is probably due to disturbed pituitary function.

Two weeks after I had received the prospectus of the *Osler Memorial Volume*, and while waiting eagerly for the publication, there was brought into my office by Dr. L. F. Luburg, a boy, four years old, from whom there had been removed at two years of age a tumor-like swelling in the left parietal region, absence of the bone beneath it down to the dura being noted; the pathological report on the tissue removed was "No gumma; no sarcoma; slight degree of inflammation; mainly myxomatous change." Since then other swellings have appeared and exophthalmos, greater on the left, has taken place, but as yet no polyuria. The boy was very irritable and objected to being examined, so it was possible to make only a brief examination, which was negative, except for enlargement of the cervical glands. The boy was then taken to the Methodist Hospital, where the blood and urine were examined without showing anything unusual, and a skiagraph of the skull taken which is here presented through the courtesy of Drs. Luburg and Percival. The boy was so restless and irritable that it was a difficult matter to get satisfactory plates, but they all show the large areas in the calvarium without bone, and overlying these the mounding up of the scalp; one of the plates (see illustration) gives a clear-cut view of the base and shows the sella turcica to be uninvolved in the bone-change, differing in this point from the illustration in Dr. Christian's report in which the sella turcica is decidedly affected. The patient was then taken to his home in the interior of Pennsylvania, where he is still (May, 1920) living.

To explain the origin of these cases the theory of dyspituitarism is a very captivating one and receives partial confirmation from the action of pituitrin in Dr. Christian's case. But after a review of the works of Sajous, Gley and Schaeffer on the physiology and known pathology of the endocrine organs, and also after an analysis of these six cases, it seems to me there are several objections to that theory. But let me hasten to state that I agree with Dr. Christian that the polyuria depends on disturbed hypophysis function, as will be explained later. And I also agree with him that the condition does not seem to depend on syphilis. The objections to the theory of dyspituitarism are:

1. Two of the cases have not shown any polyuria.

2. In two of those having polyuria, and probably in all four, the exophthalmos and the bone-changes came first.

3. Injection of pituitrin, although diminishing the polyuria, had no effect on the bone-changes.

4. The exophthalmos is probably not of toxic or endocrine origin, but as Schueller suggests is mechanical, due to involvement of the

orbital plate of the frontal bone, as shown by the four who have been studied by the roentgen rays.

5. The changes in the bones, as suggested by Dr. Percival, are not such as would most likely be produced by a chemical substance, which ought to affect the bones in their entirety; but these changes start in a number of different foci, as though some solid bodies were carried to the bones in the blood supply, and lodging in the medulla or periosteum set up their action there. In confirmation of this is the observation in my first case that in some areas only one table of the bone (the outer) was affected.

6. As mentioned above the polyuria probably depends on disturbed function of the hypophysis, this disturbance being due to pressure from changes in the bone in the immediate neighborhood of the gland. Thus in the two patients who have not had polyuria (Schueller's first and my second case) the roentgen-rays showed the sella turcica to be unaffected, while in the other two who had been skiagraphed (Schueller's second and Christian's, both having polyuria) decided changes were shown in the sella.

Other Theories. Dr. Percival made the remark while examining the plates that the appearance of them is typical of osteosarcoma, but that this can be excluded by the duration of life in most of the patients. This suggests, as one possible explanation, that the primary process may be neoplastic, benign and myxomatous in character, affecting for some unknown reason the membranous bones and producing exophthalmos and polyuria secondarily by pressure.

Another thought, that of a chronic infectious process, is raised by the presence in two of the cases of prolonged suppuration (discharging ear) and in three of enlargement of the lymphatic glands. But these enlarged glands may be only part of a general lymphatic enlargement with an enlarged thymus, which brings us back to the endocrine theory again, but this time referring it to the thymus, about which so little is known. It is known to have some influence on the skeleton, and some disturbance of it is supposed to be associated with achondroplasia, but strangely in that condition the membranous bones are found to be uninvolved, so this theory seems unlikely.

With the possibility of this being an infectious process, and since at least two of the cases seemed to start with decay of the teeth and inflammation of the gums, the thought occurs that the infective agent may gain entrance through these structures and may be animal (ameboid) rather than vegetable in nature. This theory also offers an explanation for the apparent benefit in my first case following the use of quinin.

Further observations are needed before this curious and interesting group of symptoms can be satisfactorily explained.

CLINICAL OBSERVATIONS OF HODGKIN'S DISEASE, WITH SPECIAL REFERENCE TO MEDIASTINAL INVOLVEMENT.

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INTEREST in the affection known as Hodgkin's disease, since its recognition as a clinical entity was established by Wilks [18][19] has been increased and stimulated by extensive study and research. Longcope and Reed have reviewed the development of the history, and little can be added to their reports except the etiologic studies of recent years. Their reports reveal evidence of three great epochs: the age of discovery, the age of uncertainty and the age, of establishing the disease as a pathologic entity.

Wilks defined the disease from the clinical standpoint as it is now known. He pictured it as a gradual and progressive painless glandular enlargement, with anemia and fever, and frequently associated with enlargement of the liver and splenomegaly. He also recognized that it progressed constantly until death, usually from exhaustion, and that this progress might be slow, extending over several years, or rapid, of only a few months' duration.

Within the next few years the disease was described by many writers. The names given the disease were almost as numerous as the papers written. They reflected the point of view, either clinical or pathologic, of the observer. This chaos was finally terminated by the researches of Reed, Longcope and Simmons in 1902 and 1903, who published the description which is now accepted.

A diagnosis of Hodgkin's disease cannot be considered conclusive without the examination of tissue and a microscopic picture in agreement with the clinical description. Twenty-three of the twenty six patients whose records form the basis of this paper submitted to the removal of glands which microscopically were found to be affected by Hodgkin's disease. The conditions of many other patients were considered admissible by clinical or by roentgenographic examination but were not sufficiently well diagnosed to belong to this grouping.

The macroscopic appearance of the glands varied with the duration of involvement, although not necessarily with the chronicity of the disease. A small, soft gland might be removed in a chronic case of long standing or a gland much firmer and more fibrous might be removed in a recent case, depending on the duration of involve-

ment of the individual gland resected. The gland itself, however, in all probability had been involved longer.

The earliest changes were observed in the smaller and more cellular glands and may be divided into four conditions: (1) Hyperplasia of lymphoid cells with active proliferation at the germinal centers; (2) increased vascularity; (3) proliferation of the reticular endothelium, often showing mitotic figures in the rapidly dividing cells; and (4) crowding of the lymph sinuses with large and small lymphocytes, polymorphonuclear leukocytes, of both neutrophilic and eosinophilic types, and epitheloid cells. This is the picture of an inflammatory reaction which in the more advanced stages is altered only by a progressive increase in the reticulum which becomes more and more coarse and extensive until the histologic architecture of the gland is completely lost. Within this reticular network, besides the cells already described as filling the lymph sinuses, are the giant cells described by Reed and believed by her to be a development through the epitheloid, from the endothelium covering the reticulum. They often appear in large numbers and are of two types, the uninuclears and the multinuclears, whose nuclei are grouped in various positions at the periphery or the center of the cell. The cytoplasm is clear and irregular in contour and the individual nucleus is well bounded by a distinct chromatin outline continuous with a well-defined chromatin network within the nucleus itself. The faintly staining nucleus is made conspicuous by one or several well-defined nucleoli which stain deeply. Reed and Longcope are both of the opinion that the uninuclear cell is the parent of the multiniclear; the latter phase is accomplished by repeated division of the single nucleus of the former.

In the chronic cases the entire gland seems to have become fibrous and the cellular elements have become exceedingly few. Adami believes that the formation of lymphomatous nodules in the organs of the body that contain lymphoid tissues is due to this lessening in the number of cells in the glands and is a compensatory reaction. In all of Longcope's cases, even in those in which he believes he saw transformation of preëxisting lymphoid tissue into glands, disease changes comparable with the foregoing description had already taken place.

Simmons agrees that metastasis in the liver, spleen, lungs, and so forth can be explained as an attack on the small amount of lymphoid tissue normally present in those organs.

In Case 1 (134768) of this series such an invasion seems to have occurred and evidence of involvement could be demonstrated in the skin, glands, pleura, lungs, thymus, diaphragm, liver, pancreas, spleen and urinary bladder. The glands themselves were entirely replaced by lymphadenomatous tissue with a great increase of fibroid tissue. The histologic picture shows that the disease is caused by an infective agent, the exact nature of which remains unknown. Levin, in discussing the similarity of the disease to cancer, states

that the infective agent enters from the surface and attacks the gland because it is the first protective barrier. After the invasion and consequent proliferation in the first glands the subsequent development is analogous to cancer, inasmuch as proliferation continues until the death of the patient and the highly specialized function of the original parenchymal cells is lost. He believes that this return to the character of the fetal cell is an evidence of malignancy and places Hodgkin's disease in a borderline position between inflammatory and malignant growths. We believe that the clinical course of the disease (the selection of only one type of tissue in which proliferation occurs) and the almost universal absence of infiltration through the boundaries of the gland indicate an infectious basis. We may add to this the fact that metastasis is a proliferation only of preëxisting lymphoid tissue and does not appear in organs devoid of that tissue.

In recent years Bunting and Yates found a diphtheroid organism which they claim is present in all cases and which may be looked on as the true infective agent. A search for this organism has been made in only a limited number of cases in our series and then only with negative results. Gaarde has made cultures from various glands and has been able to isolate the diphtheroid organism in conditions other than true Hodgkin's disease. So many reports of animal injection have been negative that the method was not resorted to except in one instance, and this with negative results.

Etiology. In our series of 26 patients 16 worked out of doors and 10 worked indoors; their habits of life seemed to be a negligible factor. Seventeen of the patients were males and nine were females; the average age of the former was thirty-five and four-tenths years and of the latter thirty-three and eight-tenths years. The oldest patient was a woman of sixty-four years and the two youngest, one male and one female, were twenty. This is contrary to Reed's observation that children are most often attacked, and possibly may be explained by the fact that relatively few children are registered at the Clinic.

Because of the ancient controversy with regard to the importance of tuberculosis as an etiologic factor in Hodgkin's disease, an inquiry was made into the family history of the patients. One patient reported that a cousin had tuberculous glands in the neck and another patient believed that a maternal aunt had died from pulmonary tuberculosis. Roentgen-ray examination revealed evidence of tuberculosis in only one patient and this could not be confirmed by clinical or microscopic methods. Moreover, at necropsy no evidence of tuberculosis was found in three examinations, and in only 1 case was it discovered during the course of the disease. The history of this patient is not included in the present study because no clinical evidence of mediastinal involvement was found. We do not believe that tuberculosis plays a part in producing the disease,

and no other infectious disease was found that could be considered a cause.

The examination of the histories revealed that four patients had had diphtheria but none less than five years before examination. Six had had influenza or grippe, one of whom had been ill one month and one seven months. All others had been well from actual throat or respiratory disease at least one year. Two had had pleurisy one and three years before respectively. Three had had bronchitis or pneumonia, but none more recently than eight months, and one thirteen years previously. Seven had had tonsillitis, one many times, but none within a year of examination. Six had submitted to tonsillectomy.

From this report it seems extremely unlikely that recent throat infections are of importance in the etiology of the disease. Moreover, in only one instance was a definite disease condition found in the tonsil. We believe that the occurrence of the condition in the cervical glands has not been accounted for. Reed did not find the report of an authentic case in which the condition had not started in the cervical glands. In our series of cases the cervical glands were involved in 100 per cent, but the latter were not always the first to be affected. It is quite probable that other glands may be primarily involved.

Symptoms. In most instances the symptoms were typical of cases in which there was no mediastinal involvement. There were, however, a group with symptoms and signs produced by pressure on the structures that traverse the mediastinum. It seemed remarkable that so few patients made complaints that led to the investigation of the contents of the chest and the absence of symptoms or signs cannot be explained, except on the presumption that the glands retain, more or less, their identity, that they are not so hard as malignant tumors or capable of the pressure of an aneurysm, and that they do not infiltrate the tissues around them.

Many of the patients complained of weakness, anemia, loss of weight, night-sweats, diarrhea and anasarca, but such symptoms could be construed as common to all the patients. Dyspnea, severe enough to be offered as a complaint, was present in six instances. It was found in many other patients who were placed under rigid examination, but this was not considered a fair test, inasmuch as twenty-two of the twenty-six patients were underweight and seventeen were definitely anemic, with a hemoglobin reading under 70 per cent. The patients had been ill from two months to eighty-four months; the average was twenty and two-tenths months.

Orthopnea was complained of in 5 cases.

Pain was complained of in 5 cases, in the abdomen, in the right shoulder, in the right chest, in the neck and arms, and in the back, respectively. One patient complained of soreness only.

Dysphagia due to esophageal pressure occurred in 1 case, an

indefinite sense of pressure occurred in one; and a headache suffi-
ciently severe to constitute a complaint in one.

Dilated veins over the chest were present in 3 cases, and over the
abdomen and the chest in one. Cyanosis and swelling of the face
and the neck was, of course, present in these 3 cases, and could be
easily demonstrated by inverting the patient for a short time. The
return of normal color invariably was much later than that of the
normal person used as a control. The patients often complained
of a sense of fulness in the head during the examination and recalled
that they were unable to stoop with comfort. Only one, however,
was sufficiently affected to offer this symptom as his complaint.

Tachycardia and palpitation was complained of in 2 cases and
dizziness in only one.

Cough was sufficiently urgent to be a complaint in 4 cases, and in
2 the sputum was excessive.

Jaundice, probably from glandular pressure about the common
duct, was noted in 1 case.

Itching skin with variable forms of cutaneous lesions was com-
plained of in 4 cases. This is in keeping with the many examinations
made of uncomplicated Hodgkin's disease. In 20 per cent of our
cases this annoying condition was sufficiently severe to make it a
chief complaint. These data agree with those of Symmers and of
Stokes. We believe that pruritus associated with general adenop-
athy is a symptom of sufficient importance to call attention to the
possibility of Hodgkin's disease as the causative factor.

Fluid was found in the chest, in one thoracic cavity or in both, in
8 cases, an incidence of 30.7 per cent. This can be explained by
the masses of glands exerting pressure on the pulmonary veins and
on the azygos.

It is significant that the recurrent laryngeal, vagus, and sympa-
thetic nerves, and the thoracic duct escaped direct pressure and thus
did not provide signs of help in making a diagnosis, also that few
of our patients made complaints directing attention to the chest,
although in one the right thoracic cavity was found to be filled
with fluid. Chyloid fluid was not observed. It may be present.
Edsall has described a milky albuminous effusion which contained
highly refractile bodies but a low percentage of fat. Williamson
has described a second unusual and interesting finding, pneumo-
thorax preceding hydrothorax. He believed his patient belonged
to the group in which the mediastinum is primarily affected.

Boehme, in discussing symptoms and signs, segregated those of
the posterior and middle mediastinum from the anterior mediastinum.
His observations agree with ours in the infrequency with which
enlargement of the posterior glands causes clinical symptoms or
signs, and in the frequency with which they are found at necropsy.
He, however, calls attention to the finding of dulness over the upper
part of the interscapular region and dorsal vertebræ as low as the

fourth dorsal spine. Our own experience in attempting to detect the presence of glands by physical means, especially by percussion, has been too discouraging to warrant considering the method of any importance. We believe the distance through that area to be too great and the percussion stroke required too heavy to admit of any accuracy of percussion. We have had no success in interpretation of d'Espine's sign. It has been absent even in cases of children in whom we were aware of the presence of glandular masses. Dyspnea from tracheal, bronchial, recurrent laryngeal nerve, or vagus nerve pressure, with cough resembling whooping cough; dysphagia from esophageal pressure; vomiting from pressure on the vagus; and edema of the upper part of the abdomen and serous effusion into the thoracic cavity are to be emphasized. Syncope and cachexia are believed to result more frequently from pressure in the posterior mediastinum than from excitation by a growth in the anterior mediastinum.

We were unable definitely to segregate symptoms and signs and by this means determine the location in the mediastinum; yet by the regular means of physical diagnosis assisted by the roentgen examination, the location of the disease was ascertained. In this group enlarged glands were discovered in the cervical region in 100 per cent of the cases, in the supraclavicular region in 58 per cent of the cases, in the axillary region in 50 per cent of the cases, in the abdominal region in 19 per cent of the cases, and in the inguinal region in 42 per cent of the cases. Splenomegaly was discovered in 23 per cent of the cases and involvement of the liver in 11 per cent of the cases.

Four patients succumbed to the disease and 3 necropsies were performed. In each of these (Cases 185298, 249311, and 134768) a diagnosis of mediastinal involvement had been made by clinical methods and confirmed by roentgen-ray examination. In each case the necropsy revealed widespread and often unsuspected lymphatic involvement. A short *resume* of the necropsy findings in Case 134768 illustrates this observation:*

"On opening the abdomen the stomach and intestines were found moderately distended and the diaphragm at the level of the fifth rib on each side. The liver extended 5 cm. below the ensiform cartilage, 10 cm. below the costal border in the median mammary line on the right, and 4 cm. below the costal margin in the median mammary line on the left. The gall-bladder was free and steel blue. The lymph glands in the area of the lesser curvature of the stomach were markedly enlarged. They measured 3 cm. by 5 cm. by 1 cm., were finely granular to the touch, hard, and deep red. The retroperitoneal lymph glands throughout the abdominal cavity were

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* The description of the widespread and unusual skin lesion will be omitted, since it constitutes a separate report by Stokes, with whom one of us (Lemon) was associated in the treatment of the patient.

markedly enlarged. They were firm and fibrous, and on section presented a coarsely granular and yellowish-white appearance.

"The liver was increased in size and an area below the right dia- phragmatic surface was studded with yellowish-white and dark brown islands; this portion cut with increased resistance and in it only a small amount of liver tissue was discovered.

"The spleen was enlarged and firm and had a thin capsule, but cut with increased resistance. On section many fibrous bands were found and the pulp could not easily be scraped from the surface.

"The pancreas was enlarged, firm, and coarsely granular, and cut with increased resistance.

"The right kidney was smaller than normal, white, and cut with increased resistance. The pelvis was filled with green slimy pus, and the right ureter was much enlarged and was buried and com- pressed by the great chain of retroperitoneal glands that lay along the abdominal vessels and their tributaries. Practically the entire kidney was destroyed; the cortical tissue was very thin and the pyramids were much congested.

"The bladder was filled with fluid similar to that found in the pelvis of the right kidney; around the ureteral openings were granular, dark brown masses.

"The only lymphoid tissue in the abdomen that seemed to have escaped involvement was Peyer's patches

"The right pleural cavity was filled with straw-colored fluid; the lung was moderately contracted and lay near the spinal column. Fluid was also present in the left thoracic cavity. A mediastinal mass, firm and nodular, measuring 6 cm. by 7 cm. by 6 cm. was found. The right parietal and diaphragmatic pleura was studded with small granular masses and the intercostal spaces seemed to be crowded with similar nodes. The aorta could not be seen since it was surrounded on all sides by a continuous chain of yellowish- gray glands of moderate firmness. When this mass of glands was cut through the aorta was exposed. It showed a smooth and shining normal intima."

Sections were taken from the heart, lungs, liver, kidney, spleen, pancreas, suprarenal, thymus, diaphragm and lymph glands, and all except the suprarenal, the kidney, and the heart were found to present the pathologic picture described.

Before the patient's death specimens had been examined from the arm, the wrist, the groin, and the glands; they too presented the typical picture of Hodgkin's disease.

Up to the time when the chest began to fill with fluid and necessi- tated repeated aspirations, the patient had been working regularly. He had been under observation by Dr. Stokes almost continuously for three years.

Despite the extensive disease of the lymphoid structures, there were few symptoms until within a short time of death, and no hint

BLOOD FINDINGS IN CASES OF HODGKIN'S DISEASE*

Case	Date	Hemoglobin	Erythrocytes (millions)	Leukocytes	Polymorphonuclears	Lymphocytes	Large mononuclears	Eosinophils	Basophils	Anisocytosis	Poikilocytosis	Temperature, F.
134768	July 2, 1915	80	4.4	23,900	48.0	23.3	4.3	27.7	0.7	…	…	…
185298	February 19, 1917	50	3.77	12,800	81.7	9.3	7.7	1.0	0.3	…	…	…
185380	February 10, 1917	65	…	5,200	…	…	…	…	…	…	…	99.2
185465	February 12, 1917	85	4.72	5,200	…	…	…	…	…	+	+ +	98.4
185523	February 12, 1917	57	3.25	3,000	59.7	30.7	9.0	0.0	0.7	+	+ +	98.4
195726	May 31, 1917	61	3.72	7,000	86.7	5.7	6.7	0.7	0.3	…	…	98.2
201189	July 12, 1917	88	4.88	13,200	78.7	12.7	5.0	3.7	0.7	…	…	98.6
209445	October 1, 1917	70	5.24	8,600	81.0	10.0	6.3	2.0	1.0	…	…	97.8
211306	October 18, 1917	68	4.04	8,200	50.0	36.3	10.0	2.7	0.0	…	…	99.0
219918	January 23, 1918	64	4.51	23,000	85.5	8.7	3.0	3.3	1.0	…	…	99.8
220896	February 1, 1918	64	4.06	10,000	65.7	18.0	15.3	0.0	0.7	…	…	98.8
232034	May 21, 1918	70	4.4	12,200	85.0	6.7	6.3	2.0	0.0	…	…	100.4
240373	July 31, 1918	55	3.76	8,600	86.3	5.0	4.7	3.3	0.0	+ +	+ + +	98.4
249311	October 21, 1918	47	3.26	16,400	89.0	6.5	4.5	0.0	0.0	+ +	+ +	99.2
252203	November 29, 1918	70	4.88	19,500	83.5	9.5	5.5	1.5	0.0	…	…	…
259761	February 10, 1919	74	4.72	13,800	82.0	12.0	4.0	2.0	0.0	…	…	101.0
263923	March 19, 1919	55	3.76	7,800	…	…	…	…	…	…	…	98.2
265048	March 28, 1919	58	4.4	8,400	…	…	…	…	…	…	…	…
265228†	March 29, 1919	53	4.4	49,000	90.0	5.0	5.0	0.0	0.0	…	…	98.4
268832	April 24, 1919	45	3.46	8,600	84.0	11.5	3.5	1.0	0.0	…	…	…
273780	June 6, 1919	68	4.26	17,400	76.0	19.5	3.5	1.0	0.0	…	…	99.0
274527	June 10, 1919	62	4.8	10,200	87.5	7.5	5.0	0.5	0.0	…	…	99.6
301897	January 7, 1920	50	4.24	15,400	87.5	7.5	5.0	0.5	0.3	…	…	…
Average	………	67	4.23	13,370	77.7	13.2	6.1	2.9 for 18 cases 1.5 for 17 cases				

* Cases 232416, 247052, and 262293 are omitted because blood counts were not obtained.

† Patient was in extremis. Death April 18, 1919.

of the destruction of the kidney, except the presence of pus cells in the urine. Although signs were present, symptoms that might call attention to the widespread disease in the thorax were wanting.

Lyon has reported a case of Hodgkin's disease with perforation of the wall of the chest. He noted the widespread invasion of the lymphoid tissue. We have seen but one similar case; the patient is still alive. It is not known whether the granuloma of the chest wall is continuous with the glands that are so markedly enlarged in the mediastinum (Table).

Blood counts were made in 23 cases; no material changes from the normal were noted. In Case 134768 in which the necropsy findings were given the eosinophils were numerous, but it was thought that the extensive cutaneous lesion may have influenced their proportion. In none of the cases was there indication of an increase in large mononuclear cells, as described by Bunting, nor of an excess of lymphocytes that is so general in late stages of the disease. Levin gives a very interesting explanation for this excess. He believes that the terminal lymphocytosis is due to a crowding full of all the lymphoid tissues and an overflow into the blood stream. He admits, however, that usually the blood picture in Hodgkin's disease is normal. The report of the blood findings would have been more satisfactory if it had been possible to make repeated counts on each patient.

Because the deeper glands may be primarily involved and because their presence may be recognized by clinical examination only with great difficulty, the roentgen ray is used to assist in the diagnosis of mediastinal involvement. Wessler and Greene have reported their results with the roentgen ray and have attempted to form four groups of cases according to the types of shadows: Group 1, the mediastinal tumor type; Group 2, the infiltrative type; Group 3, the isolated nodular type with involvement of the hilus; and Group 4, the nodular type presenting at the root of the lung. Wessler and Greene also call attention to the early involvement of the paratracheal group of glands and regard a shadow in that area as very significant.

This grouping is useful, but in general Hodgkin's disease is suspected when the roentgenogram reveals a bilateral feathery shadow passing outward from each hilus. A pathologic diagnosis hardly should be expected from the roentgenographic findings, but in 8 cases a positive opinion was reached. In 4 cases the picture was complicated by the presence of fluid; in 4 the presence of glands was recognized but their character was undefined. In 3 a suspicious shadow or thickening was seen; in 1 the diagnosis was sarcoma; in 5 the shadow was reported as that of a mediastinal tumor; and in 2 no positive conclusions were reported.

The roentgenogram must be considered a routine method of

examination inasmuch as it is essential to know of mediastinal complications both from the standpoint of prognosis and of treatment.

Besides the usual treatment, which is comparable with that used in chronic tuberculosis, many patients have been treated with radium. The glands respond most satisfactorily. Treatment by the roentgen ray probably offers most in mediastinal complications, and we have used it in a limited number of instances with satisfaction. It results in a replacement by connective tissue and a diminution in the size of the glands. This is particularly true of glands that are still soft and have not passed into the fibrous stage. The improvement in the patient's general health and appearance is out of proportion to the effect of the treatment on the glandular masses. These facts have recently been illustrated strikingly in a patient now under treatment. Treatment should be begun even before the deeper groups of glands can be palpated and should be kept up for a long time in association with radium, which is more useful over the superficial glands.

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CELL-COUNTING TECHNIC: A STUDY OF PRIORITY.

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To the man investigating any particular phase of cell-counting, this paper presents a classified and annotated bibliography which aims to be both up to date and complete, unlike all other articles I have seen, which mainly represent those features favored by each writer. To the practitioner are presented reminders of the methods available, with summaries indicating which seems to be preferable for simplicity and accuracy.

The earliest cell count seems to have been done October 6, 1851, and published in 1852 by K. Vierordt. He made nine erythrocyte counts on himself with the remarkably accurate average of 5,174,400 cells. His method of "microvolumetry" was to make a very fine capillary tube with an internal diameter of about 0.1 mm., but accurately known, and a length of at least 5 mm., though these were not graduated. With this capillary he took a drop of blood, measured its length by comparison with a glass micrometer (divided into $\frac{1}{3}$ mm.) on the microscope stage and thus was able to calculate the size of the drop. He then blew it out into a streak of gummy diluting and preserving fluid on a slide, mixed and smeared it and finally counted the entire spread with the aid of a finely squared micrometer eye-piece. The result was sufficiently accurate but the procedure too tedious, requiring three hours or more.

Since this invention of indubitable importance and originality a multitude of modifications have been put forward whose claims as to both value and priority have been considerably debated.

The best valuation of them and in general of the technic of blood-corpuscle enumeration is the monograph by Bürker, "Zählung und Differenzierung der körperlichen Elemente des Blutes," in Tigerstedt's *Handbuch der physiologischen Methodik*, 1912. The reasons are: (1) Bürker's ingenuity in having "brought the technic of blood-cell counting to a hitherto unattained accuracy," in the words of von Grützner 1912, (2) Bürker's exceptionally extensive experience in actual counting, (3) Bürker's judicial freedom from the critical and anticritical vituperation which obscures some of the issues argued in this field, such as Hohenpolycythemie and the relative value of Potain's pipette in the Thoma-Zeiss modification and in Miescher's modification. The most peppery example is Schauman and Rosenqvist's remark (May, 1900) that Meissen first misquoted them (October, 1899), then in reply to their remonstrance (January, 1900) misquoted them again but differently (February, 1900), and thirdly, begged the question by laying down the law, as he said, "once and for all."

Another sound and careful critical review, which discusses

Bürker's technic and is therefore especially valuable as a complement, is that by Roerdansz in 1913 and 1914. For example, he pointed out that Bürker's complete method uses so much breakable glassware that it involves much loss of time and money, without compensatory gain in value; and this view was sustained by Krotkow in 1913.

Each of these experts, however, like others in this and other fields, shows a bias toward certain methods, not always his own to be sure, but accompanied by a corresponding neglect of other devices or even a summary repudiation of them. Since, however, the experts do not agree on some of the most essential points, even on what to discuss and what to discard, there seems to be room for an article, even "in our days, in which works on the blood shoot up almost like mushrooms from the earth," in the words of Weidenreich in 1909.

This article will accordingly attempt to supplement the existing judicial and somewhat exclusive personal opinions by an inclusive historical review of the men who have contributed to the science of cell-counting. Some students may like to have available a grouped bibliography of the different parts of the method of blood-counting as it is currently used in this country today, and from this to draw their own conclusions. It is true that the technic of this subject is so well established that few are interested in reviewing it, especially as "the counting of the blood corpuscles in counting nets does not exactly belong to the special pleasures of human existence," as remarked by von Grützner in 1912 and cited approvingly by Roerdansz in 1913. In this connection Bürker's experience is interesting: In 1905 he sent questionnaires to all domestic and foreign physiological institutes or departments in seats of learning listed in *Minerva Jahrbuch der gelehrten Welt,* amounting to 202. He received back only 25 (13 German and 12 foreign), *i. e.,* only 12 per cent. Only 11 indicated any special experience with technic.

Furthermore, few men seem to realize the full variety of ingenious devices that have been worked out to relieve this or that small but annoying difficulty. Just now anybody wishing to look up the literature on any particular feature, such as counting-rulings or blood-stickers, in order to select the best for his particular purpose, will, I think, find such a compilation nowhere. This paper then is partly a critical review and partly a historical summary, with the main interest an attempt to discern priority for the various procedures.

Chronological Bibliography. Far the most thorough bibliography extant accompanies Bürker's monograph, already referred to, including 320 titles. It is arranged chronologically, not alphabetically nor in sequence of citation in the text. This order seems worthy of more frequent use, especially to aid in placing workers historically in the development of their subjects and to enable a

writer to cite others simply by name and year when dealing with a subject on which a standard chronological reference list has once been compiled.

The bibliography with this paper, therefore, aims not to recite the three hundred and eighty-six references which I have been able to examine but to dovetail onto Bürker's reference list by:

1. Including certain references overlooked by him.

2. Including certain references incorrectly cited by him.

3. Including certain references subsequent to this work of his (1912).

4. Including certain references to cell counts of other body fluids than blood (namely pleural, peritoneal and spinal punctates), of moulds and of bacteria. These amount to more than two hundred additional titles.

Nomenclature. *Names for this Special Field.* In the development of cell-counting technic a great variety of names are found: microvolumetry (Vierordt in 1852), micrométrie (Malassez in 1872), micrometric numeration (Hart in 1881), Hämocytometrie (Pappenheim in 1912), down to blood-corpuscle enumeration or blood-counting (present-day journals like the *Index Medicus* and the *Journal of the American Medical Association*). The term cell diagnosis of Widal in 1900 is more inclusive, but the broadest and best seems to me cell-counting (cytometry).

Terms for the Counting Chamber. Of the instruments used in cell-counting the chamber has received far the most careful attention and modification. The study of its metamorphoses up to the beautifully made and eminently satisfactory appliance of the present day may appropriately begin with a review of the various names applied to it. First we have the Zahlenmikrometer (Welcker in 1853), then the rectangular capillary or capillary cell (Cramer in 1855), globulimetro (Mantegazza in 1865), compte globules à capillaire artificiel or simply capillaire artificiel, counting capillary or capillary tube (Malassez in 1872), hématimètre or chambre humide (Hayem and Nachet in 1875), Hämatimeter (Hayem-Sahli in 1914).

The term most familiar today, h(a)emacytometer (Gowers in 1877, Durham in 1897, Student in 1907, circulars of Levy in 1916, Leitz in 1919, Bausch & Lomb in 1920) is found in the literature about as frequently as the spelling hæmocytometer (Oliver in 1896, Samut in 1909, Buchanan in 1909, Gulland in 1914, Wells and Sutton in 1915, patent of Levy in 1916, Kennedy in 1916).

Another group of similar names includes the Zähl-Apparat or Zähl-Vorrichtung (Abbe-Thoma in 1879), corpuscle-counter (Hart in 1881), Zählkammer or counting chamber (Thoma in 1882), cytometer or cell-counter (Bizzozero in 1887), Blutkörperchenzähler (Oppenheimer in 1889), blood-counter (Kakowski in 1910), Zählplatte or counting table (Grawitz in 1911), Blutkörperchenzähl-

apparat (von Grützner in 1912), Blutkörper-Zählkammer (Roerdansz in 1913).

Then there was the compte-globules à chambre humide graduée (Malassez in 1880), translated as micrometric graduated corpuscle-counter with wet chamber (Hart in 1881). The term cellule à rigole or moat chamber (Gilbert and Lyon in 1884) was applied to Hayem's hématimètre, and the same instrument has also been called a cellule calibrée (Luzet in 1893).

Another group of titles follows: Schlitzkammer, a circular moat slit chamber (Meissen in 1898), double slit chamber (Starcke in 1898), four-slit chamber (Meissen in 1899), parallel-trench slit-chamber (Bürker in 1905) and H-trench chamber (Bürker in 1907).

In sum, the term most generally used today seems to be hemacytometer.

Type of Slide. *Flat Side.* In the beginning was the flat slide of Vierordt in 1852 and Welcker in 1853 and 1854. It was also used later by Mantegazza in 1865, Loewenberg in 1908, Ellermann and Erlandsen in 1909, Geissler in 1911, Thomson in 1912; and for spinal fluid by Widal and Ravaut in 1900, Laignel-Lavastine in 1901 (?), Joffroy and Mercier in 1902 (?), Nissl in 1904, Niedner and Mamlock in 1904, Fischer in 1906, Kafka in 1910, 1911 and 1915, Geissler in 1911 and Szecsi in 1911 and 1912.

Hollow Slide. The kind of slide or counting chamber in common use in the United States and Europe is of the type generally and deservedly credited to Thoma-Zeiss. It may be remarked, however, that while the instrument made by Zeiss of Jena was preëminent before the World War, now the products of the American manufacturers may be considered equally good, if not in fact the best. It is also of some interest that although Abbe in 1879 announced Thoma's recommendations, Thoma's first publication in 1881 appeared under the joint names of (1) an American, Lyon of Norwich, Conn., and (2) Thoma of Heidelberg. The fame of this so-called Thoma-Zeiss instrument was due mainly to its perfection, for its principal features were not new. These features were three: the slide with the chamber proper, the quadrilled ruling and the site of this ruling. Each of these three will now be detailed:

The earliest chamber may be discerned in the capillary cell or rectangular capillary of Cramer in 1855. This consisted of two parallel glass bands cemented onto a slide close to the long edges, and with another thin slide cemented on top of them. This could apparently be filled by capillarity, though the inventor used a glass tube and an ingenious wooden adapter to permit suction. The capillary of Malassez in 1872-73-74 was very similar. This linear chamber was seen later in Alferow's and in Bürker's devices.

The development of the chamber with a circular pit was begun by the invention of Hayem and Nachet in 1875, who took a plate of glass with an aperture of 1 cm. diameter, ground it with emery

to be exactly 0.2 mm. thick and cemented it tightly to the slide. This style of chamber has been in world-wide use by Gowers in 1877, Thoma in 1879, Henry and Nancrede in 1879, Malassez in 1880, Hart in 1881 (Gower's modification), Laache in 1883, Karcher in 1897, Einhorn and Laporte in 1902, Helber in 1904, Samut in 1909, Sahli in 1909 and Jörgensen in 1913; and all those who have introduced ingenious amplifications of the original Thoma ruling or substituted for it new nets (see under Style of Ruling), besides the mass of the profession who have not published their observations.

Lyon and Thoma in 1881 added a plate in the center of the pit, leaving a circular moat 3 mm. wide.

The principle of two parallel troughs, instead of the circular moat, to limit the counting area, was introduced by Alferow in 1884. By so doing he gained, like Cramer in 1855, the great advantage of having the cover-glass in good position before inserting the drop of blood and also of being able to insert the drop by capillary attraction. These features were made use of by Bürker in 1905 in his parallel trench chamber and in 1907 in his even cleverer double chamber with two counting islands, forming what might be called an H-trench. Parallel lateral trenches were also used by Liebreich in 1916. The H-trench is not only literally the latest word today, but is generally regarded by all who have used it as the last word.

The circular moat chamber gives too high results compared with the parallel trough chamber, by 5 per cent according to Loewenberg in 1908, 10 per cent according to Bloch in 1912 and Adachi in 1912 and by 7 per cent according to Bürker in 1913. Similar conclusions were reported by Marloff in 1919 and Fritsch in 1920.

Another variety of so-called slit chamber which has never apparently won recognition outside a small group of observers was that projected by Meissen in 1898: a Thoma-Zeiss with a narrow and shallow radial furrow 0.5 mm. deep, to make the chamber independent of barometric pressure. A double slit was offered by Starcke in 1898 and a four-slit cavity by Meissen in 1899. Bürker in 1905 noted that whatever advantage under conditions of changing barometric pressure might accrue to a slit chamber, Cramer's, Alferow's and his own afforded this advantage even more completely than those just mentioned. Fuchs in 1908 and von Koranyi in 1908, who used Bürker's chamber, both speak of it as a slit chamber, but since then the term and the dispute are defunct.

Depth of the Chamber. *Depth of Chamber Proper.*—The earliest chamber, Cramer in 1855, was 0.066 mm. deep. Only one shallower has been proposed, that by Liebreich in 1916, which was 0.025 mm. After Cramer, Hayem in 1875 made his newly invented pit measure 0.2 mm., in which he was followed by Gowers in 1877, Malassez in 1880, Alferow in 1884, Helber in 1904, Fuchs and Rosenthal in 1904, Laruelle in 1906 and Glaubermann in 1913. Two greater depths have been used: 0.222 by Friedlaender in 1897 and Cuzzolini-Durati in 1906 and 0.5 by Nageotte in 1907 for spinal fluids.

Thoma in 1879 reduced the depth to 0.1 mm. in order to permit use of a higher power objective with greater magnification, shorter focus and brighter illumination. This depth has been accepted by all since him with the exceptions here noted.

Bürker in 1905 neatly straddled the breach between the two most popular depths by making the depth of the chamber itself 0.1 mm. and then providing twice that depth for use when cells are scanty (eosinophils, erythroblasts or for spinal fluid) by having made what is described below as a double depth cover-glass.

Thickness of Cover-glass. The cover-slips made for counting chambers have varied from 0.15 mm. (van Walsem in 1915), 0.18 (Lyon and Thoma in 1881, Schröder in 1899, Turban in 1900, Gottstein in 1900), 0.35 (Lyon and Thoma in 1881, Schröder in 1899), 0.40 (Bürker in 1912), which is perhaps the commonest, to the extraordinary limit of 3.3 mm. (Turban in 1900). The most ingenious kind is what may be called a two-depth cover-glass, *i. e.*, one of ordinary thickness, to which is cemented a thinner circlet or flat paster of glass pierced in the center with a hole, being in depth 0.18 mm. (Lyon and Thoma in 1881), 0.15 mm. (van Walsem in 1915) or best just 0.1 mm. (Bürker in 1913). The last named makes the chamber 0.1 mm. deep when placed on the slide with the paster side up, 0.2 mm. deep when with the paster faced down.

Occasion may be taken in passing to mention the recommendation by Bürker in 1911 that the two longer edges of the cover-slip instead of being at right angles to the major surfaces and mat in finish should be rounded and smooth-polished, in order to facilitate more rapid introduction of the blood by capillary attraction. This refinement seems plausible, but has not been taken up so far as I am aware.

Site of Ruling. The counting net may be in one of four situations, as summarized by Alferow in 1884: the ocular, the floor of the chamber, the substage whence it is projected on the floor of the chamber and the ground glass of an affixed microphotographic chamber. The last suggestion, by Alferow himself, and the projection principle of Nachet in 1875 have received no attention. The rivalry has run between the first two methods.

The ocular method was the first in use. The eye-piece was either itself cross-ruled or contained a quadrilled glass plate or a diaphragm, and in the beginning no attempt was made to standardize the tube length or graduate the ocular ruling. It was used for orientation only. This was the case with Vierordt in 1852, Mantegazza in 1865, Loewenberg in 1908, Ellermann and Erlandsen in 1909, von Grützner in 1912 and Thomson in 1912.

Then the eye-piece was not only quadrilled but calibrated, an "ocular micrometer" or "micrometric quadrilled ocular." First by Cramer in 1855, who set his tube so that the field coincided with a hole in a tin band lying on the slide like the guide on a slide-rule.

The area exposed by the hole was 0.172 square mm. and the ocular was ruled into 48 oblongs. Malassez in 1872 and 1873 set his tube with the guidance of an objective micrometer and then labelled his tube length. Standardized oculars were also used by Alferow in 1884, Ehrlich in 1898, Hayem-Sahli in 1909, Bürker in 1911, Metz in 1914 and 1915. Kennedy in 1916 patented a hemacytometer comprising a scale arranged in the eye-piece, having a central inner circular area, surrounded by a central larger area and an annular outer area encircling the central areas and divided radially to form bacteria counting chambers.

The floor was ruled but not graduated in the instrument of Welcker in 1854. The base of the chamber was both ruled and calibrated by Gowers in 1877. This was a priceless step in advance and has been followed by Thoma in 1879, Malassez in 1880, Hart in 1881, Alferow in 1884, Bürker in 1905 and all the proponents of new rulings detailed below. Before proceeding to them it may be of interest to quote from Abbe in 1879, in view of the scarcity and inaccessibility of his exhaustive article on the principles involved in cell-counting: "The application of an objective ruling to the bottom of the counting chamber has the great advantage over the ocular micrometer, of dispensing with the determination of the absolute value of the ocular ruling, which naturally varies for every objective and every tube-length." As would be expected from this theory in practice the ruling is in most cases preferred on the slide.

Agasse-Lafont in 1920 suggested rulings both for the island and for the floor of the moat.

Style of Ruling. The kinds of counting nets that seem of possible interest today are those which follow Thoma, in matter of time and more or less in style. The majority were originally ruled in the circular chamber, but are now cut in the parallel trench chamber or might be if so desired.

The classical ruling of Thoma in 1879 and 1881, aptly called the Thoma cross by Breuer 1902, was a gridiron of 1 mm. side, divided into 400 squares which were set off by double lines into sixteen groups of twenty-five squares each. Later the double lines were shifted to make twenty-five groups of sixteen squares each; this accounts for the puzzling difference between some Thoma rulings.

Zappert in 1892 and 1893 drew a line across each of the four ends of the cross which protrude 1 mm. beyond the central square millimeter, enclosing with these four lines 9 sq. mm. instead of 1. For counting white cells in the blood, and particularly in less cellular fluids, this increase of the ruled area was immediately recognized as invaluable and has since been adhered to by the majority of ruling inventors.

Elzholz in 1894 modified Zappert's net by adding three pairs of vertical lines through the left column of 3 sq. mm. and also through the right column. This he illustrated, but incorrectly according to

Türk in 1902, who then gave a figure which he asserted to be correct; not, however, convincingly. Thus the subject is confused by contradictions.

Friedlaender in 1897 depicted an entirely different type without the extra line at the border of every fifth square, which was such a feature of Thoma's grating. This new net for leukocytes measured 4.8 mm. on the side instead of 3 like Zappert's or Elzholz's, and was divided into 16 parts, making 256 squares, with a total counting volume of 5.11 c. mm.

Durham in 1897 modified Zappert's field by dividing each of the four corner square millimeters into four squares.

Türk in 1902 apparently built on the basis of Elzholz's by adding to the verticle double lines horizontal pairs, thus showing in each corner square millimeter sixteen squares, separated by rectangles and tiny squares between the double lines. This net largely displaced Thoma's, and now is being in turn displaced by Neubauer's, which shows also 16 subdivisions of each corner millimeter but more simply separated by single lines.

Breuer in 1902 introduced, and Sahli in 1911 and Morawitz in 1912 commended, a development of Zappert's by the division of each of the eight peripheral square millimeters into 36 rectangles.

Brünings in 1903 used a net something like that of Malassez in 1872. It was cut in a facet in the bore in the center of an elaborate U-shaped pipet, with an ampulla at each end, i. e., a combined chamber and mixing pipet.

Fuchs and Rosenthal in 1904 enlarged the field from 9 to 16 sq. mm., which they lined in new fashion, subdividing each square millimeter into 8 or 16 squares or rectangles. No illustration is seen in the original paper, but may be found in the section on cerebrospinal fluid in Frazier's *Surgery of the Spine*, 1918.

Bürker in 1905 divided each of the 9 sq. mm. into 16 squares by paired lines, just as was done by Türk for the four corner millimeters.

Simon in 1906 followed Bürker's in appearance, but the squares were somewhat larger, and the complete net rather smaller, 4 sq. mm.

Nageotte and Levy-Valensi in 1907 planned for spinal fluid a huge field, 15 mm. on the side, ruled off into 225 sq. mm.

O. Neubauer, date not discovered but first cited by Meyer and Rieder 1907, aimed at simplicity like Durham, 1897, but instead of making only four parts of each corner millimeter made sixteen. This is the same number as proposed by Türk, 1902, but has the advantage of the greater clarity inherent in using single rather than paired dividing lines. The result is the only net which has rivalled the popularity of Türk's and which is now rapidly outstripping it in this country.

Sahli in 1909 and 1914, perhaps earlier, first experimented with

concentric rings around a square, with for calibration an objective micrometer scale of 1 mm. divided into 100 parts.

Kakowski in 1910 for urinary cell counts gave an account of a large round island with a surface area equal to 4 sq. mm., with for calibration a line 3.1 mm. long, finely subdivided.

Dunger in 1910 and 1911 believed that he was simplifying the counting not only of blood but also of exudates, transudates, and especially spinal fluid, by surrounding the Thoma cross by two differently ruled "mantels." He also increased the sides of the field from 3 x 3 mm. to 7 x 7 and $\frac{1}{7}$ mm., the additional seventh being to yield the round figure 50 for easy calculation.

Predtetschenski was credited with a new net design by Goriaew in 1910.

Goriaew in 1910 and 1914 (elsewhere transliterated from the Russian as Goriaeff and Gorjajew) enlarged Predtetschenski's net from 4 to the usual 9 sq. mm., but though the novel design has been taken up by Pappenheim in 1912 and Greene in 1917, its neglect by the rest of the world makes detailed description superfluous.

Howard in 1911 had made by Bausch & Lomb, as a counting chamber for moulds, a Thoma-Zeiss cell with a center disk of $\frac{3}{4}$ inch (18.75 mm) instead of $\frac{1}{4}$ inch (6.25 mm.), as usually furnished.

Morris "some time between 1909 and 1911" (personal communication) was the first to suggest the double Bürker chamber with double Neubauer ruling, which he obtained from Zeiss through A. H. Thomas. This combination he urged again in 1913 and 1916, and today it seems to be the favorite in this country, and increasingly so. It is a great convenience whenever one has occasion to make a count to find the same ruling in general use.

Klyuchareff in 1912 proposed the combination of Bürker's counting camera with Predtetchenski's net.

Pappenheim in 1912 produced a variation which he called the Gorjajew-Pappenheim ruling, based on an interpretation of the former's work, which was erroneous, according to Goriaew in 1914.

Roerdansz in 1913 alternated larger and smaller squares than those of Thoma. The engraving is said to be cut in a new manner so as to show as bright violet.

Schirokauer in 1914 applied Türk's ruling to Bürker's later chamber, what I have called the H-chamber.

Bass in 1915 illustrated a thoroughly novel and beautifully simple ruling. The total field he, however, reduced to 4 sq. mm. The chamber is made in this country by Bausch & Lomb. If it covered 9 sq. mm., like that of Neubauer, it would, I think, prove a rival.

Liebreich in 1916 suggested, instead of squares, oblongs 10 x 0.1 mm. There were 60 of these millimeter areas. Half were further divided by horizontals into four and all 60 were subdivided by verticals into a hundred parts.

Zappert-Ewing, date unknown but first cited by Wood in 1917, consists of a substitution of three single lines for the three pairs of lines used by Elzholz in 1894 to divide each corner square millimeter into four rectangles. This simplification by using single instead of double lines may be compared to Neubauer's simplification of Türk's ruling.

Agasse-Lafont in 1920 proposed a new ruling for the ditch in the circular chamber, in order to give ample space for spinal fluid counts.

Summing up, the style of ruling most popular today is the Neubauer or, as it is sometimes called, the Zappert-Neubauer.

The Best Counting Chamber. From the preceding sections it will be plain that the best cell-counting chamber is generally considered to be the "double Bürker" (slide) "double Neubauer" (ruling).

This combination may be had in this country from the following dealers: Bausch & Lomb, of Rochester, N. Y. (their own make), E. Leitz, of New York City (own make), A. H. Thomas, of Philadelphia (Max Levy's make), and Spencer, of Buffalo (also, as I am given to understand, Levy's make). These names are given in alphabetical order, not in any order of merit. Each manufacturer exhibits modifications, some of distinct value. The underlying principles, and the claims as to results attained, are worth attention, but will not be discussed at present. In the different makes each worker, according to his taste, can secure the standard polished finish (yielding Newton's rings) or the mat (dull) grinding; raised or flush supporting strips; supporting strips of one piece with the slide or cemented onto it; the ruled strip cemented onto the slide or cemented and also recessed into the slide, and additional parallel troughs for convenience of contact.

Any of these makes has seemed satisfactory for practical work. For publishable observations, however, one cannot overlook the reports by Henry and Nancrede in 1879, Hart in 1881, Alferow in 1884, Lyon in 1917, A. H. Thomas in 1920 (personal communication) and the U. S. Treasury, Bureau of Standards (personal communication), as to occasional errors in instruments of the best manufacturers as purchased in the open market. For example, the last-named authority may be quoted: "The need of demanding certified apparatus is understood when we say that the percentage of hemacytometers conforming to the specifications varies from 99 per cent of those sent in from one manufacturer to 68 per cent of those sent in from another manufacturer, the error practically always being in the depth of the chamber." Accordingly a student of finer points in cell-counting would do well to send his chamber, cover-glasses and pipets to the Bureau of Standards for test as to accuracy of compliance with the tolerances adopted by that Bureau, "upon request, in 1918, after considering the accuracy obtainable by the manufacturers by the use of proper methods and reasonable care."

Newton's Rings. Perhaps the most interesting question in connection with this choice of modifications in the slide is whether to use the mat (dull ground glass) finish or whether to adhere to the classical smooth polish which yields Newton's rings. They were first observed by Hooke in 1665 in mica plates, or as it was then called Muscovy glass, and also in soap-bubbles and in other substances. He remarked that "We are able from a colorless body to produce several colored bodies." These he called "fantastical colors." The study was continued by Sir Isaac Newton in 1675 and 1704 with, in the words of Rayleigh in 1911, "his accustomed power, and by him most of the laws regulating these phenomena were discovered. He experimented especially with thin plates of air enclosed by slightly curved glasses, and it should be noted that among slightly curved glasses belong most cover-slips, though supposedly plane, and the colored rings so exhibited are usually called after him 'Newton's rings.'" The name he used was "colors of thin plates." Young in 1802 showed that the formation of these colors was due to the interference of light reflected from the two surfaces of the plates. Hence the name often used, "interference rings."

These rings, often only stripes or bands, have been absolutely required by many of the most careful students of blood-counting technic, notably Abbe in 1879, Thoma in 1881, Schröder in 1889 and Turban in 1900. Brünings in 1903 observed (1) that neglect to produce the stripes was accompanied by an error of 9 to 13 per cent, which was confirmed by Bürker in 1904; and (2) that the depth of the chamber was the same, provided the color bands were present, no matter whether they were broad or narrow, dry or moist; and this too was confirmed by Bürker in 1913. The 386 publications I have read do not all discuss the rings, but among the large number which do, not one fails to insist on their importance. Among the teachers of clinical blood-work whom I have consulted all but one prefer the standard smooth finish. In Guthrie's words: "With the ground-glass type the assumption of good approximation may frequently be correct, but there is no indicator to show that this is so." I agree strongly because I fail to see how the mat finish betrays a tiny foreign body of dust or lint.

On the other hand it must be admitted that the mat finish is heartily favored by one experienced worker whom I consulted as well as used in three of the four American makes of hemacytometer. It is true that in the use of polished chambers care is not always exercised to see that Newton's rings appear, and many workers not familiar with interference phenomena do not understand their significance when they do appear.

Other Counting Methods. The parallel trench chamber of Bürker, without ruling, was used by Bürker in 1907, von Grützner in 1912 and by Metz in 1914.

The hematocrit was used by Hedin in 1891, Daland in 1891, von Jaksch in 1892 and 1893, Lederer in 1895, Schäfer in 1898, Schmincke in 1911, Epstein in 1916, and others whom I have not hunted up, owing to the small part hitherto played by this instrument as a substitute for true cell-counters. It has, however, its uses, and in the judgment of many might well be applied more generally to check red cell counts and to determine the proportion of cells to plasma. A similar volume per cent method was published by Harvey in 1920.

Counting, so called, by an entirely different method is seen in the chromocytometer of Bizzozero in 1887 and the haemocytometer of Oliver in 1896.

Dreyer in 1921 reported a simple procedure for the accurate estimation of blood cells without the use of a counting chamber. He dilutes the blood with a permanent standard suspension of hen's corpuscles, which being elliptical and nucleated are easily counted simultaneously. He claims that this method is cheaper, quicker and less fatiguing than the usual methods.

Total Contents of Chamber. The amount of fluid held in the counting space varies markedly. The smallest volume, as nearly as I can make out, was 0.002 c.mm. (Alferow in 1884). Then 0.008 cmm. (Hayem and Nachet in 1875), 0.011 (Cramer in 1855), 0.02 (Gowers in 1877), 0.04 (Vierordt in 1852, Alferow in 1884) and 0.1 (Thoma in 1879, Meissen in 1898, Starcke in 1898, Turban in 1899, Einhorn in 1902, Samut in 1909, Bloch in 1912 and Roerdansz in 1913). Then 0.2 c.mm. (Brünings in 1903, Helber in 1903), 0.25 (Thomson in 1912), 0.4 (Goriaew in 1910, Pappenheim in 1912, Bass in 1915), 0.6 (Simon in 1906) and 0.9 (Zappert in 1892, Elzholz in 1894, Durham in 1897, Türk in 1902, Breuer in 1902, Bürker in 1905, Neubauer in 1907 and Goriaew in 1914). Then 1.0 c.mm. (Malassez in 1880), 1.5 (Liebreich in 1916), 1.8 (Bürker in 1907, Galambos in 1910, Schirokauer in 1914, Morris in 1916, Levy in 1916), 3.2 (Fuchs and Rosenthal in 1904, Laruelle in 1906), 3.72 (Bürker in 1912), 5.0 (Oliver in 1896, Dunger in 1910), 5.11 (Friedlaender in 1897). Then 10 c.mm. (Loewenberg in 1908, Ellermann and Erlandsen in 1909, Kakowski in 1910, Glaubermann in 1913), 20 (Geissler in 1911, von Grützner in 1912), 40 (Kakowski in 1910, Geissler in 1911). Nageotte's cell was probably the biggest, the contents being variously stated as 10 cmm. (Nageotte and Riche in 1907), 50 or 100 (Bürker in *Tigerstedt* in 1912) or 225 c.mm. (Nageotte and Lévy-Valensi in 1907).

Placing the Cover Glass. The importance of placing the cover glass rapidly, in order to avoid unequal distribution of the cells, was early appreciated. At first the cover was set in a hinged clamp which could be laid on quickly and smoothly, by Malassez in 1880. The later clamps of Gowers in 1877, Alferow in 1884 and Bürker in 1907 were not hinged and merely prevented movement of the slip once it was in place.

Roerdansz in 1913 made a clamp into which the cover-glass was slid after the blood had been dropped in the chamber. A similar but simpler method, the author of which I have lost, was to slip the cover half-way across the circular chamber to deposit the drop, then slip the cover the rest of the way.

To dodge the great difficulty of making the drop neither too big nor too small, many have used the method of placing a good-sized drop, then slipping the cover-glass right *through* the drop, with the result that the "excess will rise on top of the cover and jump across the moat." This seems to have been first published by Eustis in 1913, whereupon rival claims were immediately put forward. Rea in 1913 stated that the method had been used in the Pepper Laboratory of Hygiene since 1899. Barnett in 1913 ascribed the credit to L. D. Zulick, and Kraemer in 1913 reported that the method had been current in the Jefferson Medical College since 1904.

All these methods, however serviceable, seem likely to be superseded by the spread of the Bürker chamber because it allows placement of the cover-glass with the obtaining of Newton's bands prior to the deposition of blood.

Pipets. *Types.*—Of all the pipets for measuring, or measuring and mixing, blood (or other cellular fluids of the body) and diluting (or preserving or staining) solutions the earliest was Vierordt's in 1852. This was calibrated in diameter but not in length, which had to be laboriously determined beside a micrometer laid on the microscope stage. It held about 0.04 cmm.

Welcker in 1854 introduced a pipet holding a fixed volume, 4 c.c., and readable with the naked eye, as have been all pipettes since.

There are two main classes of pipet: (1) Separate capillaries for measuring the sample of body fluid and for the diluting solution, and these incidentally are further complicated by the addition of a mixing vessel in most methods except those in which the mixing is performed directly on the counting slide; (2) a combined pipet for not only measuring but mixing in an ampulla the cellular fluid and the diluting solution.

Separate Pipets. Of this type were Vierordt's and Welcker's, just mentioned, and later those of Mantegazza in 1865, Hayem and Nachet in 1875 (the only widely used design), Mayet in 1888, Ellermann and Erlandsen in 1909, Sahli in 1909, von Grützner in 1912, Ellermann in 1913, Krotkow in 1913 and Sahli in 1914. Of them all Hayem's alone is conspicuous, as one peruses the literature, for wide recognition, mostly in France. But even it has had nowhere nearly the popularity of the combined pipet about to be described.

Single Mixing Pipet, Mélangeur, Mixer. The prototype of this invaluable device was what Roerdansz in 1914, called "the lovely idea of Malassez and Potain." The latter invented his mélangeur in 1867 but no description was published until the paper of Malassez

in 1872. The modern modification is what is known as the erythrocytometer or simply the red pipet.

Sörensen in 1876 pointed out that the upper mark should be close to the ampulla. Thoma in 1879 enlarged the bore slightly to facilitate cleaning; his pipet was about 8 cm. long; the ampulla contained 0.5 to 1.0 c.c., and as a whole his Misch-Vorrichtung was so reliably calibrated by Zeiss that it promptly earned the preeminent popularity which after forty years still persists. Hart in 1881, noting that Gower's counting chamber was 10 per cent inaccurate as to depth (which had already been reported by Henry and Nancrede in 1879), recommended recalibrating Potain's mélangeur to compensate. This procedure was obviously rendered unnecessary by the precision of several manufacturers since Zeiss set the pace at Thoma's request.

Thoma made a still further contribution in 1882 by having for white cells a similar Mischgefäss, diluting 1 to 10. This has been frequently called a leukocytometer or simply a white pipet.

Stierlin in 1889 credited to O. Wyss a modification of Potain's mélangeur with two ampullæ, but this has received no further recognition.

Rieder in 1892 gave an account of his shortening, for convenience sake, of the pipet to two-thirds the Thoma-Zeiss, and of his new graduation 1 and 21, i. e., a dilution of 1 to 40.

Miescher in 1893 among other inventions defined two which, though not in general use, have been highly commended by such practised observers as Lederer in 1895, Kündig in 1897, J. Karcher in 1897, S. Karcher in 1897, Veillon in 1897, Suter in 1897, Schauman and Rosenqvist in 1898, Müller in 1910, Bürker in 1911, Roerdansz in 1912, Krotkow in 1913, Emerson in 1913 and Wood in 1917. These improvements seem unfortunately unknown in this country except to those few who have had an opportunity to use the Fleischl-Miescher hemoglobin pipets, which show the same features. These are:

1. Ring graduations instead of the usual short horizontal lines. Krotkow in 1913 thought these ring marks even more legible when cut as incomplete circles, in the gap of which the meniscus should be read.

2. Accessory graduations, "Hilfstriche," just 1 per cent above and below each mark.

Brünings in 1903 proposed an entirely strange pipet with two ampullæ and between them a counting field engraved on a flat facet in the lumen.

Roerdansz in 1912 elaborated the Thoma-Zeiss pipet with a second ampulla, using the first for diluting only and the second for mixing. This device he further developed in 1914. It goes sometimes by the name of the Fleischauer-Zeiss pipet, after the two firms who manufactured it for him.

Liot and Poussin in 1918 and Harvey in 1920 used ordinary Pasteur capillary pipets.

In conclusion of this section it may be said that by far the most popular pipet today is the single mélangeur of Potain-Malassez in the more accurately made model of Thoma-Zeiss. Further, that the Miescher modifications of the latter deserve wider use.

Automatic Pipets. The next attempt at improvement, both in point of novelty and of time, was this attempt to dispense with judgment by the eye as to when the meniscus touched the mark, and therefore with the invariable anxiety and the frequent error associated. The three-way cock in the gas analysis pipet of Geppert in 1885 had already been adopted for an automatic urine pipet by M. Cremer (nature unknown despite search of the *Index Medicus* back to the first volume in 1879) and was modified by Voit in 1895 for blood-work. May in 1903, in turn, altered Voit's instrument by the addition of a second three-way cock. Hirschfeld in 1909 added a mixing ampulla and had a pipet each for red and white cells. Roerdansz in 1914 reported an "automatic mixing pipet" which followed closely that of May.

The overflow principle as a rival of the three-way cock was first set forward by Hirschfeld in 1911, who took the idea from the Ueberlaufpipette "Mikra" devised by Weichardt in 1910 for his epiphanin reaction for syphilis. Hirschfeld's device seems to have got no notice except condemnation from Roerdansz in 1913. Thomas in 1910 made a simpler automatic pipet by applying to a delivery milk pipet a T-tube, an appliance which might perhaps be as advantageously used with a blood pipet. Wright in 1914 illustrated an overflow pipet, also Harvey in 1920.

Summarizing this section it may be remarked that these refinements have won no place in practice, however valuable they may be to occasional research workers.

Aspirators for Pipets. To govern suction more accurately than is easy for many with the usual mouth method, many contrivances have been described.

The throttle is the simplest. A. E. Wright in 1897, 1912 and 1914 effected resistance to too rapid suction by drawing out a capillary tube to a fine point. An analogous construction was inserted by Boggs in 1907 and by Bürker in 1912 into the blood pipet suction tube. Hirschfeld in 1909 indicated the even easier way of inserting a bit of cotton.

A rubber bulb or teat or camera bulb was introduced for bacteriological pipets by Robert Koch in 1890, who also was the first to use a hole (in the rubber) in order to control the vacuum. The same idea was recommended by Benmosche in 1906 (without the hole) and with the control hole by Beck in 1896, Boggs in 1907, Münzer and Bloch in 1909, Portmann in 1909, Klemensiewicz in 1910, Permin in 1911 and A. E. Wright in 1912 and 1914.

Suction by means of a screw clamp passed around a rubber teat or around a bit of tubing plugged at one end was applied by Gabrit-schewsky in 1891 to a pipet much like Potain's mélangeur; and also by Gaertner in 1892, Grijns in 1894, Eijkman in 1894 and 1898 and by Levy in 1897.

The same principle was applied somewhat differently when Wieck in 1909 made a frame with a metal wheel and roller which squeezed the rubber tube, filling or emptying the pipet according to the direction in which the roller was moved. This Präzisions-sauger was noticed by Grawitz in 1911 and Bloch in 1912. A similar device was independently put forward by Maddox in 1913.

Syringes were initiated by Ebstein in 1903, who fastened the syringe to the blood pipet by means of a set-screw. Galli in 1904 also employed a syringe, with the plunger further elaborated by a screw which permitted slighter movements as well, what we might call a fine adjustment. Küster in 1906 arranged for delicate suction by putting on the plunger a knob which moved in a spiral groove on the metal stub of the barrel and attached his aspirator by a rubber washer and perforated closing screw which turned down on the washer to make it fit pipets of different sizes. Hirt in 1908, inde-pendently of Galli, used two plungers, one inside the other, each with a micrometer screw, one for coarse and one for fine adjustment. Weichardt in 1908 used a micrometer screw like Galli and also made another syringe which he attached to the pipet by a short piece of thick rubber tubing. Küster in 1909 modified his previous syringe so that it could be either pulled for coarse adjustment or turned in a slot for fine adjustment. Lautenschläger was credited by Koch in 1910 with having made some kind of sucker; probably this was the Mikropipette regulated with a micrometer screw manu-factured by F. & M. Lautenschläger, of Berlin, for Weichardt in 1910. Stroschein was also credited by Koch in 1910 with having melted a Luer glass syringe on to a Thoma pipet. Koch's own device in 1910 looked like a movable lead-pencil holder slipped over the upper end of the pipet and held there by an internal rubber grip, and was in fact a metal syringe, the suction piston of which was moved by a button sliding along the side of the barrel. Engel-mann was credited by Bloch in 1912 with a microsyringe, but how this too differed from earlier devices is also not clear from his article nor have I been able to find the original report despite a search of the volumes of the *Index Medicus* for the years 1913 back through 1908. Van Walsem in 1914 put foward a syringe working with a terminal thumb-screw, in principle like the fine adjustment part of the design by Galli in 1904. Saxon and Drummond in 1915 illus-trated an apparently practical "aspirator:" a metal syringe with incidentally a flat flange projecting at right angles from each end in order to cap the pipet for carrying.

Cheaper than a syringe was the durable and so-called automatic

suction pipet or syringe credited to Voigt and illustrated by Keim
in 1906. This seems to be a development of Voigt's (1900) Lym-
phebläser for smallpox vaccine work, but embodies all the features
independently urged by the writers below for blood-work, namely,
an external test-tube sliding up and down outside the top end of
the pipet for suction, made snug by a surrounding bit of rubber
tubing 1 cm. wide and 2 mm. thick, and internal prolongation of
the pipet which allowed use of the overflow principle. For sero-
logical use the idea was expatiated on by Wolff in 1908. The device
was applied to blood pipets by Pappenheim in 1909, who recom-
mended it also for the automatic pipet of Hirschfeld in 1908. Inde-
pendently shortly afterward Portmann in 1909 used the same kind
of sliding barrel made snug by a ring of rubber tubing over the
upper end of the Thoma pipet, which he had prolonged to receive
it; and he also applied to this a lateral control hole similar to that
used by Koch in 1890 in his rubber bulb and first applied to a glass
suction instrument in the blood viscosimeter of Hess in 1907.
Stroschein was credited by Fuhrmann in 1910 with practically the
same scheme. The next step of progress, in accuracy though not
in simplicity or cheapness, was made by Pappenheim in 1911 and
1912, who ground the glass like the barrel and plunger of a "Lühr-
schen" (Luer?) syringe. In 1912 he further recommended, in order
to make the vacuum incomplete so as not to aspirate too rapidly
and forcibly, that the grinding be not perfectly snug; and later still,
in 1912, he substituted for this loose grinding the control hole as used
by Portmann.

Other automatic pipets or Sicherheitspipetten, the original de-
scriptions of which I have not been able to see, are those of Kapeller
in 1907, Meyer (quoted by Keim in 1906), of Gaffky and of Was-
sermann (quoted by Kempff in 1910); of Dafert, of Kühn and of
Wollny (illustrated in catalogue of Vereinigte Fabriken für Labora-
toriumsbedarf, Berlin, n. d.).

In summary of this section it may be observed that none of these
ingenious inventions has in practice displaced the classical bit of
rubber tubing 0.5 cm. in diameter by about 15 to 30 cm. long.

Pipet Carriers. Devices for carrying pipets fall into two groups,
cases and caps. Cases have been described (*a*) for pipets and
chamber, by the various manufacturers and (*b*) (which is ordinarily
more useful) for pipets and diluting fluids by Malassez in 1872,
Sutton in 1911 and Haden in 1920.

Caps began apparently in the shape of ordinary elastic bands,
as noted by Seymour in 1910; or the mouth end of the suction tubing
drawn over the point, as mentioned by Hartz in 1915; or a rubber
band cut from a $3\frac{1}{2}$ inch automobile inner tube, as specified by
Putnam in 1919. In the case of each of these the frequency of punct-
ure by the sharp end of the pipet led to the introduction of hard
objects, such as caps. Seymour in 1910 took gray rubber tubing,

such as the thinner-walled variety often used for suction, and cut it to a length slightly less than that of the pipet; occluded the ends by hard rubber plugs and sliced out half the tube lengthwise to within about 1 cm. of each end; then by stretching what remained he slipped it easily over the pipet. This has served me, and many another, well; and seems *a priori* as effective, durable, simple and cheap as any subsequent scheme.

Bunnell later in 1910 used two BB cartridge shells fastened together with a piece of wire and a rubber band. Roerdansz in 1912 had caps of glass ground to fit and relied on the snugness of grinding to keep them in place. Van Walsem in 1914 similarly pushed a small cork stopper onto each end of the pipet, following the familiar trick of guarding the ends of needles or hatpins. Croy in 1914 followed Seymour and Bunnell in employing a rubber connection between the caps, which in his case were two disks of any thin metal. Saxon and Drummond in 1915 also used metal caps but joined them by a spring, superimposed on their aspirator for filling the pipet. McJunkin in 1919 recommended, much like Van Walsem, small soft-rubber stoppers pushed on to each end of the pipet.

Actual stoppers, rather than caps, were introduced by Katzenstein in 1911 by simply inserting the small rubber plugs from serum vials.

Summarizing, the best capping device seems to me Seymour's plugged tubing.

Pipet Shakers. Little in 1917 illustrated a complex electrical motor driven machine for shaking two blood-mixing pipets. Putnam in 1919 much more simply attached the pipet to an ordinary electric buzzer bell and Haden in 1920 showed another electrical machine simpler than Little's and holding four times as many pipets.

Methods of Cleaning Pipets. The technic of removing clotted blood and even of the deposit that occurs periodically with the best of care has been discussed by Türk in 1902, Benmosche in 1906, Bürker in 1911, Thomson in 1912 and Morris in 1913.

Quick Method of Drying Pipets. When a mechanical air draft is not available, a rubber bulb has been reported as useful by Gray in 1921.

Miscellaneous Modifications of Pipets. Galli in 1904 enclosed his instrument in a glass mantle to prevent dilation from the warmth of the hand. The same idea, with the addition of circulating water, recurs in the "Mantelspritze" of Determann in 1905 and of Münzer and Bloch in 1909.

Bürker in 1907 emphasized that the tip of the pipet when angular, as is usual, should be rounded off with emery in order to yield a neater drop.

Thomson in 1911 and 1912 offered a suggestion which seems sensible but has not yet been taken up, namely, that blood pipets

be made, like clinical thermometers, with a white opal background of milk glass, and with the front edge bevelled as a magnifier.

Schroeder in 1914 showed a figure of a tiny metal mirror made to slide on a ring along the pipet in order to facilitate reading the calibrations.

Blood Needles. The history of blood-stickers, needles, lances or lancets is confusing owing to (1) the scanty descriptions and indistinct illustrations given in the literature, and to (2) the loose use of some terms. Blood lancet, for example, seems to have indicated sometimes an instrument with a true lanceolate or spear point, sometimes a narrow surgical knife or lancet and sometimes categorically any sticker. Blood needle also may mean an ordinary sewing taper-point needle, a surgical two- or three-edge cutting needle, a glover's three-edge cutting needle (usually shorter cutting edges than a surgical needle), a Hagedorn or Boldt flat needle with a single bevelled cutting edge.

The earliest pricker I have found may serve as an instance of this vagueness, for the nature of its point is not clear from either the text or the cut in the paper by Gowers in 1877.

A sheath or guard with a screw to fix it at varying distances from the tip, and so regulate the amount of blade exposed, was introduced by Malassez in 1880. This fundamental idea is seen in most of the instruments since proposed, namely, in those of Alferow in 1884, Reichert in 1889, Francke in 1889, Daland in 1891, Bensaude in 1893, Oliver in 1896, Ries in 1904, Bürker in 1912, Zapf in 1913, Van Walsem in 1914, Sahli in 1914 and Boldt, date unknown.

A spring lancet was arranged by a spiral wire inserted within the handle, in order to make the stab sudden yet smooth, by Alferow in 1884, then used by Reichert about 1889 and improved by Francke in 1889. The latter, "Francke's nadel," has generally received the credit from those who have written on stickers, and it has been subjected to a number of changes. Ries in 1904 made the point removable and had a space for spares within the distal end of the handle. Boldt and Moore, like Ries, had both the regulable sheath and removable point, but introduced a different spring release. Müller in 1910 recommended that the "Lanzette" of the Francke "Schnäpper" should be semicircular instead of pointed in order to render bleeding freer; and for the same purpose Bürker in 1912 altered the tip from lance shape to that of a broad chisel. Zapf in 1913 made the tip of Francke's needle of platinum-iridium so that it could be disinfected in the actual flame. Van Walsem in 1914 changed the tip to a rather large sewing needle, English No. 4; he is the only author I have discovered who is satisfied with the small amount of blood secured with a taper point. Greene in 1917 substituted for the lance tip a trocar point; the three edges of this, being short and stubby, have seemed to me much less satisfactory than those of a glover's or a surgical needle.

A signet ring, concealing a pricker which looks in the illustration like a true spear point, was projected by Schottelius in 1907.

For the tip of the instrument, leaving out of consideration the handle, more than a dozen kinds of point have been recommended, as follows:

Point with One Edge. 1. Hagedorn in 1881, 1882 and 1885, straight surgical needle. This has a single bevelled cutting edge, which is more easily kept sharp than most other types of edge. The shaft is flat, unlike all other needles suggested; and is long (varying from 4.5 cm. up to 9.5 cm.); both these features make the needle stiffer, stronger, easier to hold and to sharpen. It has been commended by Sutton in 1911, Hastings in 1912, Morris in 1913, Webster in 1914 and McJunkin in 1919.

2. Clean steel pen with one nib broken off. Wright in 1897, von Domarus in 1912, Morris in 1913, Webster in 1914, Williams in 1915.

3. Semicircular end. Müller in 1910.

4. Chisel end. Bürker in 1912.

5. Piece of broken cover-glass. Greene in 1917.

6. Small "lance," one-edge like a narrow scalpel or knife-blade. Gowers in 1877 (?), Malassez in 1880, Bensaude in 1893, Champy in 1913, Webster in 1914, Stein in 1917.

Point with Two Edges. 7. True lance or spear point with two edges. Gowers in 1877 (?), Alferow in 1884, Reichert in 1889, Francke in 1889, Daland in 1891, Oliver in 1896, Ries in 1904, Schottelius in 1907, Zapf in 1913, Sahli in 1914, Swan, date unknown, Webster in 1914 and 1920.

8. Regular surgical straight needle. This title is illustrated in Kny-Scheerer's catalogue as two-edged but *non*-cutting. Favored by Bass in 1910.

Point with Three Edges. 9. Trocar point. This has the shortest cutting edges of any triangular needle, as they extend only about a quarter of the total length of the needle. Katzenstein in 1911, Greene in 1917.

10. A glover's needle or a surgical straight shaft triangular cutting needle or a Keith's abdominal No. 6, are all practically the same. The cutting edge extends about a third of the total length. Probably the most widely used blood needle at present.

11. Bonney's straight needle has three still longer cutting edges, extending about half the total length. It has not hitherto been recommended for use as a blood sticker.

Hollow Tip. 12. Paracentesis needle. Wieck in 1909.

Taper Point. 13. Ordinary cambric or larger sewing needle. Van Walsem in 1914.

Summing up: As the object in view is free flow of blood without the necessity of squeezing the ear the best sticker is that handiest for each worker. I like a large Hagedorn needle.

Methods of Recording. *Record Blanks.* Schemata or blank forms for noting the count of individual fields, with spaces for totalling and for computing percentage differential counts, were outlined by Bürker in 1907 and 1911; his form has been commended by several, especially favorably by Müller in 1910.

Osmond in 1910 had a slate, or a ground-glass plate ruled and labelled permanently in ink, and noted the counts in pencil.

Watters in 1913 pictured graphic charts for leukocytes, showing total counts, differentials and daily variations.

Schilling in 1913 designed an elaborate blank with the headings not only printed but concisely defined by cuts of the corpuscles meant to be included under each title.

Sahli in 1914 printed tables for calculating percentages.

Simon in 1918 illustrated some charts.

Recording Machines. A mechanical instrument for "noting and automatic calculation of blood and other cells" was claimed by Tojbin in 1909 and 1912 to be "the first counting and calculating machine." This "Cytax" bristled with knobs and cost 140 marks. It seems to have been noticed only by Schall in 1912, who proceeded to devise an instrument which he thought simpler, and by von Putkowski in 1913, who used the original.

Schilling in 1911 and 1912 illustrated and wrote at length on his differential leukocytometer. This consisted of 100 steel balls and several metal slots, with graduations at the back of the slots for direct reading off of the number of balls in each slot. This, though rather bulky, would seem, especially if equipped with 200 shot, worthy of trial as a time-saver by those who have occasion to count cells frequently. In 1913 Schilling described his "neue Differential-Zähltafel."

Van Walsem in 1914 recommended (1) an ordinary typewriter, using each of the lower row of keys for a particular variety of white cell, recording blindly without taking the eye off the microscope and afterward counting the different letters; and (2) his Zähllineal, which was a ruler with slits to guide one's pencil, so that here too the eye need not leave the microscope.

Cummer and Dexter in 1915 illustrated a small wooden box to hold upright four "counting machines" which look like the watch-like tally machine in use at admission gates.

Number of Digits to Use. In recording counts more figures are generally used than necessary, and that without signifying any greater accuracy, as pointed out by Bürker in 1911 but since neglected. Three numerals are ample, the rest should be ciphers.

Leukocyte Count. *Total White Count.*—This procedure seems to have been initiated by Malassez in 1874 and since him studied by the following: Gowers in 1877, Thoma in 1882 (modified for leukocytes the dilution of the red pipet, giving the instrument so universally used ever since), Alferow in 1884 (distinguished white cells by

raising the tube to lengthen focal distance), Toison in 1885 (first to make fluid permitting counting of white cells in the same pipet with reds; an ideal pursued by Schüffner in 1911 and Türk in 1912), Reinert in 1891 (counted visual fields with a known setting of tube length), Zappert in 1892 (first satisfactory ruling), Rieder in 1892, Elzholz in 1894, Friedlaender in 1897, Durham in 1897, Einhorn and Laporte in 1902 (white count directly from smear, by noting the ratio of whites to reds and counting only the reds in chamber), Türk in 1902, Breuer in 1902, Joffroy and Mercier in 1902, Engel in 1902 (differentiation of whites by refraction of light, much like Alferow), Bürker in 1905 and in 1907, Ellermann and Erlandsen in 1909, Dunger in 1910, Galambos in 1910, Hill in 1912 and Roerdansz in 1913.

Differential White Count. This seems to have been first been done in the smear by Einhorn in 1884 followed by Krönig in 1899 (on spinal fluid), Widal and Ravaut in 1900 (also on spinal fluid), Simpson in 1906, Sheaff in 1912, Schilling in 1913, Nieuwenhuijse in 1914 and Johns in 1914. These writers, it may be mentioned, discussed technic rather than interpretation.

The use of a stain in the mixing pipet with subsequent differential counting of the whites in the chamber was introduced by Zappert in 1892. The idea was worked over by Elzholz in 1894, Zollikofer in 1900 (Kämmerfarbung), Türk in 1902, Riebes in 1905, Dunger in 1910, Schüffner in 1911, Hill in 1912, Zapf in 1913, Lenzmann in 1913 and Gifford in 1920.

White Count Simultaneously with Red Count. The attempt to perform both counts in the red pipet was made by Toison in 1885, Zappert in 1892, Türk in 1912, Zapf in 1913 and Lenzmann in 1913. The latter pointed out that "The attempt to differentiate the white blood cells in the counting chamber, and in this way to make an exact count of the different forms . . . failed always, owing to the difficulty of staining the white blood cells differentially and simultaneously rendering the red blood cells invisible." Zapf had tried to stain the whites and afterward to destroy the reds. Lenzmann experimented with a reagent to be used with the differential stain to harden the white cells, after which he destroyed the reds with acetic acid. His choice ended with 0.3 per cent corrosive sublimate and 5 per cent formalin in water.

Platelet Count. This subject is of interest mainly to special workers, involves little apparatus notably different from that already covered, and has been recently reviewed both as to methods and results by Zeller in 1919, Degwitz in 1920, Gram in 1920 and Thomsen in 1920.

Cell Distribution on Counting Fields. *Red Cells.* In the examination of this important topic we may refer to Malassez in 1880, Reinert in 1891, Brünings in 1903, Student in 1907 and Bürker in 1904, 1907 and 1913. The latter found by his own counts "Colossal

errors . . . through the unequal distribution of cells on the bottom of the counting chamber," and also found these errors easy to avoid by laying on the cover glass first and afterward inserting the drop of blood by capillary attraction. Later the subject was touched on further by Roerdansz and Jörgensen in 1914.

White Cells. The distribution of the leukocytes in the counting chamber is a matter of significance, though less so than with the red cells, owing to the smaller number of them; their distribution in the stained smear is of more import. Zollikofer in 1900 noticed the tendency of certain kinds of white cells to be collected in the thicker parts of the smear, namely, at the two sides and at the end of the slide, and also the further inequality due to the destruction of cells in the thinner part of the spread. Türk in 1902 and Zapf in 1913 described the inequalities somewhat differently. Schilling in 1913 suggested that these two tendencies be counteracted by counting in a "meandering line," zigzagging to and fro from edge to center, in a manner resembling crenelated battlements or a mattress suture. Nieuwenhuijse in 1914 discussed this suggestion. Johns in 1914 also has something to say about the distribution of leukocytes. Obviously consideration must be given to the way in which the smear was made, whether with cover-slips (Ehrlich), slides (Jansco-Rosenberger) or "thick drop" (Ross and Thomson). The cover glass method has been most recently urged by Meulengracht in 1920, as yielding an evener distribution of leucocytes.

Mechanical Stage. Accessory stages to permit moving the counting slide evenly and systematically past the nosepiece have been reported by Welcker in 1853, Hayem in 1889, Canon in 1892, Klein in 1893, Friedlaender in 1897, Bezançon and Labbe in 1904, Detto in 1906, Sahli in 1909 and Geissler in 1911. Today the perfected movable stage may be obtained from the various manufacturers under their names, not those of the inventors.

Counting Diaphragm. Diaphragms to set limits, fixed or adjustable, to the counting field have been recommended by Cramer in 1855 (perforated piece of tinfoil lying on the slide; contrast this with later diaphragms inserted in the eyepiece), Koch in 1878, Alferow in 1884 (metal or paper), Ehrlich in 1898 (Blenden-ocular, a Huyghenian eyepiece with a square stop which is capable of being varied in size by means of an external knob), Einhorn and Laporte in 1902 (metal with a square hole subdivided by two crossed threads), Bürker in 1905, Larrabee in 1906 (simple but practical, cardboard with a hole cut out), Samut in 1909 (the aperture cut to coincide with the "four squares of the central platform of the counting chamber"), von Grützner in 1912 (three square openings lying in one radius of the eyepiece, which is meant to be rotated to cover the field), Sheaff in 1912 (piece of end of a slide cut off, a small square ruled in its center to afford a sufficiently restricted field for counting leukemic bloods, and this glass diaphragm placed in ocular),

Metz in 1914 (a small square in center, subdivided by crossed lines, much like the device of Einhorn and Laporte), Schirokauer in 1914 (used the so-called Thoma-Metz counting ocular just described), Van Walsem in 1915 (tin square cut to correspond to the medium-size square of the Thoma ruling, *i. e.*, one of the sixteen squares separated by the double lines).

Dark Field. The proper illumination of the counting chamber is important, owing to the fact that the cells are in most cases unstained. The dark field has been discussed by Raehlmann in 1905, Neumann in 1907 and 1908, Posner in 1908, Dietrich in 1908, Wiener in 1908, Leva in 1909, Bürker in 1913. The last named has emphasized the value of Abbe's substage condenser and diaphragm in accentuating the colorless ruling of the chamber.

Binocular Microscope. This instrument is beginning to be seen in medical laboratories. Its most striking advantage seems to be the greater comfort of using both eyes. Its history and characteristics have been extensively discussed by von Rohr in 1920.

Theoretical Mathematics. The higher mathematical side of cell counting has been taken up by Abbe in 1879, Lyon and Thoma in 1881, Lyon in 1881, Gram in 1884, Reinert in 1891, Miescher in 1893, Liebreich in 1905, Zuntz in 1905, Student in 1907, Bürker in 1912, Ellermann in 1913, Aebly in 1919, Alder in 1919, Rohrer in 1919 and Kilgore in 1920. Under this heading are considered both the empirical error in the handling and observation on the part of the worker and also the so-called probable error in any given series of observations.

The empirical error should be no larger than 4 per cent; that is, according to Emerson's simple rule, a student should begin by counting blood from the same normal person daily at the same hour until successive results differ by less than 200,000. Experienced men report better figures: Cramer in 1855 claimed 1.6 per cent, Abbe in 1879 felt that 3 per cent was assured if one counted 5000 cells, Reinert in 1891 got 4.6 per cent, Türk in 1902 got 3 per cent, Bürker in 1912 got 1.8 per cent and Ellermann in 1913 got 3 per cent. A different "error" is attained in part, owing to usage of the word by different men for a different mathematical constant. For example, two counts satisfying Emerson's rule would be 5,000,000 and 5,200,000. The second varies from the first by 2 in 50, giving a 4 per cent error; or under another interpretation one might say each count varies from their mean, which is 5,100,000, by 1 in 50 or 2 per cent. Any of these results is obviously excellent compared with the 5 to 10 per cent error put up with, according to Rohrer in 1919, in most clinical methods.

In practice the most important use of the mathematical calculation of the probable error is to decide whether a variation in two consecutive counts is truly significant or whether it must be discarded as falling within the limits of the known likelihood of varia-

tion: three times the "probable error." For the actual method of calculation, reference must be made to one of the articles cited or to a modern text-book such as Yule's *Statistics*.

Diluting Solutions. This subject is so large that the following list, unlike the rest I have compiled, makes no attempt to be complete. Of the many writers included in the bibliography mention may be made of: Hayem in 1875, Gowers in 1877, Toison in 1885, Mayet in 1887 (eosin for staining reds brilliantly; osmic acid), Muir in 1891, Zollikofer in 1900, Simon and Spilmann in 1904 (further study in eosin for red cells), Riebes in 1905, Rous in 1907, Dunger in 1910, Pitfield in 1911, Hill in 1912, Gelbart in 1912, Zapf in 1913, Callison in 1914, Jörgensen in 1914, Van Walsem in 1915, Diner in 1917 and McJunkin and Charlton in 1918 (new stain for differential count).

The consensus of opinion favors Hayem's solution for red cell counting, *e. g.*, Bürker in 1905 and 1911, Sternberg in 1905, Boston in 1905, von Domarus in 1912, Türk in 1912, Champy in 1913, Morris in 1913, Sahli in 1914, Williams in 1915, Webster in 1916, Wood in 1917, McJunkin in 1919 and Naegeli in 1919. In the community where I live Gower's fluid is the one generally used, apparently owing to the influence of Cabot's monograph in 1904. Toison's solution is recommended by Greene in 1917 and Simon in 1918.

For white cells the favorite remains the simplest—acetic acid, 0.5 per cent.

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CHRONOLOGICAL BIBLIOGRAPHY OF CELL-COUNTING TECHNIC.

This list is supplementary to Bürker's, discussed on page 527, and with that covers the literature completely, I believe. For the reader of this paper it would be more convenient to have the two lists consolidated, but space forbids.

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MALIGNANT TRICUSPID ENDOCARDITIS: WITH A REPORT OF FIVE CASES.

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RIGHT-SIDED endocarditis (fetal endocarditis) is familiar to all. Vegetations on the tricuspid or pulmonary valves in association with similar lesions on the valves of the left side of the heart are not rare, as autopsy statistics certify. But primary acute endocarditis confined to one or another of the valves of the right heart is infrequent.

Osler, in his Gulstonian Lectures, analyzed 209 cases of endocarditis and found the right heart alone involved nine times only. He mentions it as a rare finding and still more rarely diagnosed. Among 21,000 autopsies at Guy's Hospital, endocarditis confined to the tricuspid valve was encountered twelve times. At Bellevue Hospital among a series of 6800 autopsies primary tricuspid endocarditis was met with four times.

References to the lesion in text-books of medicine and even in monographs are scant indeed. Mackenzie dismisses it by simply mentioning its rarity. Herz does likewise. Hirschfelder calls attention to the rarity of organic tricuspid insufficiency in contrast to the frequent finding of relative insufficiency. The latter, he asserts, is probably present in every dying or failing heart. He calls attention to the fact that primary tricuspid endocarditis is usually a malignant endocarditis, a statement which is confirmed by other statistics. An unfavorable prognosis, therefore, usually follows its diagnosis. According to Broadbent the relative tricuspid insufficiency is usually not accompanied by a murmur unless the insufficiency is extremely marked. Strümpell refers to the lesion as follows: "Endocarditis on the tricuspid valve is seldom seen except as a secondary affection in old cases of heart disease. In a case of acute ulceration in a grown man seen by us the process was confined exclusively to the tricuspid valve and there were very many embolic abscesses in the lungs. This may be considered a great rarity."

The diagnostic problem which the condition presents is not without interest. Its rarity and obscure symptomatology on the one hand and the differentiation from the often present relative tricuspid insufficiency on the other make diagnosis oftentimes impossible. It is the intention of this paper to consider certain points in the diagnosis of this lesion. A more extended discussion on the diagnostic problem of tricuspid insufficiency is given in Young and Cotter's paper.

The percussion of the right heart and auscultatory symptoms of the tricuspid area do not aid us, chiefly because of the signs given by mitral disease and relative tricuspid insufficiency. However, the associated phenomena in other structures are of sufficient importance, at least to the extent that if found we shall be placed on our guard and suggest the possibility of this lesion. Of these the jugular pulse is most often present; less frequently a liver pulse, though in Young and Cotter's paper the order was reversed. But to distinguish between a jugular pulse of organic origin and one due to relative tricuspid insufficiency is impossible except occasionally during therapy. Relative tricuspid insufficiency is due to poorly contracting heart muscle. If upon the administration of digitalis the heart muscle improves the physical signs of relative tricuspid insufficiency (loss of pulsations, loss of congestion, loss of murmurs and diminution in area of cardiac dulness) become less marked or disappear entirely. The danger of mistaking such improvement for healed valve disease must not be overlooked. The reverse obtains in organic disease. With improvement in the muscular contractions the physical signs become more marked (due to a larger volume of blood being thrown back). The jugular pulse, due to tricuspid insufficiency, is a systolic pulse, and while not absolutely diagnostic is usually present only in tricuspid incompetency. Like all venous pulses it is produced by a slowly distending vessel. During the systole of the right auricle when the latter is emptying, systolic emptying of the jugular does not occur because of the back flow of the blood, and hence the vein remains distended in systole, in contradistinction to the normal jugular pulse and that due to congestion, as in mitral disease, for example, in which circumstance the jugular vein does empty itself, producing a negative pulse during systole. The sign, therefore, in tricuspid insufficiency— either relative or organic—is a jugular systolic (positive) pulse.

The hepatic venous pulse must not be confounded with aortic impulse transmitted to the liver. The latter is a short, very quickly appearing and disappearing impulse. The venous pulse in the liver is slow, markedly retarded and always in two phases, the time relationship being presystolic-systolic. It can usually be felt best when the abdominal muscles are relaxed and deep palpation is possible.

Manges described an interesting case of double mitral disease accompanied by tricuspid regurgitation, in which both the liver and the spleen pulsated. He could not account for the mechanism producing this phenomenon.

Lung infarction, with or without abscess formation, is almost constantly present and generally leads to a diagnosis of bronchopneumonia.

Long-continued physical signs in the lung which are evanescent or rapidly changing, together with the heart signs and associated

jugular and hepatic pulse, should make us fairly certain of tricuspid endocarditis.

The following five cases of primary acute tricuspid endocarditis presented several interesting points clinically and at autopsy. The first four cases represent the Bellevue Hospital series; the fifth case was encountered among 429 autopsies in the American Army.

CASE I.—F. W., aged thirty-six years, admitted to Bellevue Hospital complaining of chills and fever for three weeks previous. On admission the temperature was 104° F., respiration 28, pulse 120. There was dulness and diminished breathing at the right base posteriorly. Tentative diagnosis: Pneumonia. The patient remained in the hospital for twenty-five days, during which time he ran a septic temperature, with rapid breathing and pulse averaging 120. The sputum was at times profuse and blood-tinged. Physical signs of the heart showed a systolic murmur about 2.5 cm. to the right of the apex, which was in the fifth space. No venous or hepatic pulsations noted.

At autopsy each pleural cavity contained about 400 c.c. of serofibrinous fluid. The pleural surfaces of both lungs were covered with a fine fibrin deposit, underneath which there were many large and small petechiæ. The left lung on section presented a glazed surface in the upper lobe, with slight increase in fibrous tissue. At the apex there were several calcareous tubercles. The lower lobe presented a dark reddish surface from which considerable blood exuded. The right lung presented a similar picture to the left except that there was a large wedge-shaped, dark reddish, sharply circumscribed area in the lower lobe. The bronchi on both sides were congested and contained about 30 c.c. of blood-stained serum.

The heart was of normal size and its surface showed a few petechiæ. The tricuspid ring admitted four fingers. The middle leaflet of the valve was the location of a large, cauliflower-like vegetation which extended down the chordæ tendineæ to the papillary muscles. The remaining valve segment showed old thickenings and scarrings. The remaining valves of the heart were entirely normal. The foramen ovale was patent, the right ventricular cavity somewhat dilated and the heart muscle pale brown in color. The coronary vessels are normal. The aorta showed a few small atheromata at its commencement.

The surface of the liver was smooth. On section it showed marked fatty infiltration.

The spleen was large, soft and grumous in appearance.

The remaining organs showed no changes worthy of note.

Anatomical diagnosis: Acute tricuspid endocarditis; patent foramen ovale; double serofibrinous pleurisy; hemorrhagic infarction of right lung; purulent bronchitis; healed apical tuberculosis; fatty infiltration of liver; acute splenic tumor; septicemia.

Case II.—S. F., aged twelve years, admitted to Bellevue Hospital January 28, 1906, died February 12, 1906. Patient had had high fever and was delirious for one week previous to admission. General examination on admission showed a poorly nourished body; the skin and mucous membranes were pale; a few petechiæ were seen in the conjunctivæ and over the chest. The temperature was 104.2° F., respiration 36, pulse 124. Scattered bronchial breathing was noted over both lungs. This continued with occasional areas of dulness to flatness until death. The heart was slightly enlarged to the left by percussion and a loud, blowing systolic murmur was heard at the apex. Distinct pulsation was noted in both jugulars. There was little or no sputum. The temperature remained high, the pulse continued rapid and respirations became more labored. The patient developed a swelling over the right shoulder and right hip-joint, which was painful and tender, but showed no pus on aspiration. Blood culture showed the Staphylococcus pyogenes aureus. The white blood count was 18,200; polymorphonuclears 86 per cent.; the urine was full of albumin and casts. Diagnosis: Malignant endocarditis-septicemia.

At autopsy the pericardium was covered with a thick, shaggy film and contained about 100 c.c. of thin, purulent fluid. The heart was somewhat large and the muscle was pale and flabby. The endocardium was smooth. The right leaf of the tricuspid valve showed an area of thickening about 5 mm. in diameter, beneath which the valve was adherent to the right ventricle. Along the margin of this leaf there were many small verrucous vegetations and one large pendulous, reddish-gray, thrombotic mass which projected into the ventricular cavity. The remaining leaves of this valve were normal. The remaining heart valves were normal. The coronaries showed no lesions. The aorta was normal.

The lungs on the surface showed a number of sharply circumscribed, depressed and purplish areas which, on section, corresponded to hemorrhagic infarcts. In the center of several of these there were one or more minute yellowish foci. The parenchyma of the lung in the lower lobes showed considerable congestion and edema. The bronchi were slightly injected.

The spleen was markedly enlarged. On section it was dull reddish in color and fleshy in appearance.

Both kidneys on section showed numerous miliary abscesses on the cortex and in the substance, each surrounded by a prominent hemorrhagic zone.

The right tonsil on section showed a yellowish, purulent focus about 5 to 10 mm. in diameter.

Anatomical diagnosis: Purulent pericarditis; acute tricuspid endocarditis; miliary abscesses of lungs and kidneys; hemorrhagic infarction of lung.

Bacteriology: Staphylococcus pyogenes aureus obtained from the spleen.

CASE III.—E. M., white, aged sixty-eight years, was admitted to Bellevue Hospital on July 14, 1910, with a history of swelling of the abdomen and extremities, chills and fever of several weeks' duration. Examination revealed an elderly, emaciated female, with moderate edema of the lower extremities. The heart was not enlarged by percussion, the sounds being faint but clear. The lungs showed bronchovesicular breathing in both upper lobes, with many fine rales scattered through both organs. The temperature was 102° F., pulse 120, respiration 24. The abdomen was prominent and there was an umbilical hernia which was ulcerated and through which a hard mass could be felt. There was no tenderness or rigidity. The abdomen was flaccid; no fluid was found. During her stay in the hospital the patient became progressively worse, the signs in the lungs spread, the heart became irregular and a systolic murmur developed over the tricuspid area. Urine: Acid; sp. g., 1.012; trace of albumin and granular casts. Patient died on July 30, 1910. Diagnosis: Ovarian tumor; nephritis; pneumonia.

Autopsy. The body was that of a very much emaciated white female. The skin was pale and there was no edema of the subcutaneous tissues. There was a large umbilical hernia, the mass protruding for a distance of from 8 to 10 cm., the apex being ulcerated and exuding fluid on pressure. The abdominal wall was considerably thickened by dense connective tissue to which a large tumor mass was adherent, occupying the entire anterior and lateral portions of the abdominal cavity. On dissection this mass was found to be a large multilocular cystadenoma attached to the right broad ligament. A diffuse serofibrinous exudate was present.

Both lungs showed cicatrices and areas of interstitial pneumonia at their apices. The left lower lobe was reddish in color, firm and smooth on section. The branches of the pulmonary artery of the left lung were the seat of reddish, soft thrombi which were firmly adherent in places. The right lung was likewise the seat of thrombi and small areas of lobular pneumonia. The bronchi were extremely congested and partially filled with mucopurulent exudate. The longitudinal striations were prominent. The upper lobes were pale and inelastic, the lower lobes dark, congested and edematous.

The pericardial sac contained about 100 c.c. of clear fluid. The heart was small and the vessels tortuous. The tricuspid valve showed a vegetative growth about 8 mm. in length, with small ulcerative areas surrounding it. The remaining heart valves were normal. The heart muscle was pale and very flabby, with some prominent whitish delineations.

The kidneys were small and contracted, the cortex normal, pyramids indistinct and the surface granular.

The remainder of the autopsy was irrelevant.

Anatomical diagnosis: Multilocular cystadenoma of the right ovary; acute tricuspid endocarditis; chronic interstitial pneumo-

nitis; lobular pneumonia; emphysema; chronic bronchitis; chronic interstitial nephritis.

CASE IV.—W. S., aged fifty years, laborer, was admitted to Bellevue Hospital on October 14, 1914. The wife of the patient stated that he had caught cold five days previous to admission and that fever and cough steadily increased. Physical examination revealed a moderately developed and poorly nourished adult male, acutely ill. The right eye was entirely destroyed; the left pupil was regular and reacted to light and accommodation; no ptosis. The pulse was regular and of good force and volume. The vessel walls felt thickened and tortuous. Blood-pressure, 135. The apex-beat was heard in the sixth left interspace, four inches from the midsternal line. Pulsation was also felt in the fifth space in palpable thrills. The heart sounds were clear and of fair muscular quality; no murmurs heard; pulmonic second sound accentuated; right border of heart not obtained. Respirations were labored and expansion of the right chest diminished. In the left chest the percussion note was resonant. The breath sounds were bronchovesicular. Numerous coarse bubbling rales were heard laterally and over the lower lobe, chiefly at the base. Fremitus was increased at about the angle of the capsula. Right chest: Down to the sixth rib there was flatness; bronchial breathing with increased fremitus; many fine and coarse rales were present. Below this the note was resonant and the breath sounds bronchovesicular. Posteriorly, from apex to base, there was flatness, increased fremitus and bronchial breathing, with many fine and coarse rales. No pleural friction heard.

The abdomen was markedly distended and tympanitic; there were no palpable masses and no rigidity or tenderness. The liver was palpable two fingers' breadth below the free border of the ribs in the nipple line.

The patient perspired freely. There was a scar on the left side of the face and scalp and numerous petechiæ over the body. There was no edema or swelling. The face, ears and extremities had a cyanotic tinge.

Bones and Muscles. Limitation of extension at both elbows; slight irregularity in bone at right ankle.

Head. Rachitic; furrow between frontal bases.

Provisional Diagnosis. Lobar pneumonia (right).

On October 15 the patient was considerably worse. Cyanosis and dyspneic respirations more marked; perspiration very profuse. Died at 4.40 P.M. on October 15, 1914.

Urine. Acid reaction; albumin; granular casts; sp. g., 1.018.

Temperature, 102.8° F. on admission; remained at 102° until death. Respiration, 36 to 48. Pulse, 120 to 144.

Blood culture was positive for pneumococcus. Wassermann reaction four plus.

Autopsy. The body was that of an elderly white male, 160 cm.

in length, of fair nutrition and well-developed musculature. The right eye was absent. There were numbers of petechiæ distributed over the body.

The lungs were firmly adherent by dense fibrous adhesions. The right lung was the seat of a massive pneumonia—the upper portion in the stage of gray hepatization, the lower in the red hepatized stage. The left lung was very edematous and showed a small area of consolidation (about 4 cm. in diameter), which was somewhat soft and necrotic. The bronchi were intensely congested.

The heart was large. The right auricle was markedly distended by a blood-clot. The tricuspid valve was considerably thickened and showed a few minute verrucous vegetations on its auricular surface, averaging about 1 mm. in diameter. The pectinate muscles in the right ventricle were prominent and the papillary muscles were hypertrophied. The wall of the right ventricle was about 5 mm. in width. The remaining valves were normal, as were also the coronaries and aorta. The left ventricle was hypertrophied.

The spleen was small, friable and grayish-red in color. The kidneys were grayish red in color, the cortex swollen and the markings indistinct.

Anatomical diagnosis: Lobar pneumonia (right); bronchopneumonia (left); pulmonary edema; acute bronchitis; acute tricuspid endocarditis; chronic valvulitis (tricuspid); chronic adhesive pleuritis; septicemia.

This case in all probability represents vegetations developing on a weakened valve, the seat of a former rheumatic process.

Case V.—O. C., male, mulatto, aged twenty-five years, was admitted to Bellevue Hospital on November 28, 1918, complaining of fever and pains in the chest. His temperature was 104°, pulse 120, respiration 30. There was scattered dulness and bronchial breathing over the right lower and middle lobes and over the left lower lobe. A diagnosis of bilateral lobar pneumonia was made. The patient stated that he had had a "cold" for two weeks previous to admission, with chills and fever, and had suffered from rheumatism and tonsillitis frequently for six or seven years past.

The signs in the chest continued until December 10, when they became less marked, though an area of bronchial breathing was noted in the right axilla. During this time the patient expectorated profusely, at first blood-tinged, later purulent. Toward the middle of the month the chest was almost clear, but on December 30 there were small areas of dulness and bronchial breathing throughout both lungs. The heart was negative. These signs continued, with varying intensity, until January 28, when 300 c.c. of thin, yellowish, purulent fluid were aspirated from the right chest. On February 1 the patient was operated on for empyema. He did not improve after the operation and died on February 4.

During the entire illness the patient had a typically septic tem-

perature, ranging from 100° to 105.4° F. His pulse was rapid, averaging 120 to 130; respirations were likewise always rapid. He was very restless, often irritable, and lost a good deal of weight. His sputum was profuse and frequent attacks of coughing annoyed him very much. He was delirious at times. Of the laboratory examinations, unfortunately, it was possible to find only a urine report which showed albumin, casts, pus and epithelium. No blood cultures were taken, neither was the empyema fluid cultured. The clinical diagnosis was lobular pneumonia and empyema.

Autopsy. The body was that of a slender adult mulatto, 179.5 cm. in length, poorly nourished. The external configuration and development of the body and its appendages were normal. Rigor mortis was marked. There was an incised wound 1.5 cm. long in the right posterior axillary line, in the seventh interspace and a larger but similar wound in the tenth interspace in the back. The distribution of hair was abundant, coarse, black, short and kinky. There were a few superficial scars over both tibiæ. The conjunctivæ were pale; the scleræ clear; the pupils equal, regular and contracted; no petechiæ. The ears and nose externally were normal. The lips were excoriated, the teeth in fair condition, the tongue dry, furrowed and covered with a brownish coating on the surface. There were old operative scars over both inguinal regions.

The thymus was replaced by fat. The ribs were normal. Many firm and several loose fibrous adhesions on the right side formed numerous encapsulated sacs which contained yellowish purulent fluid. In the left chest there were about 200 c.c. of cloudy fluid which contained fibrin flakes. A few easily destroyed adhesions were present at the apex, but the base was firmly adherent to the diaphragm.

The precordial area measured 12 cm. across. The pericardial sac contained 5 to 10 c.c. of clear, straw-colored fluid. The heart was large, especially the right side, weighing about 450 gm. A few petechiæ were present in the posterior epicardium. The muscle was soft and flabby and pale, yellowish brown in color, measuring 18 mm. in width at the base of the right ventricle. The tricuspid valve was covered almost everywhere by numerous verrucous vegetations, especially on the posterior cusp where the vegetations had pyramided with its apex directed downward, hanging free in the cavity of the ventricle. There were a few minute verrucæ on several of the chordæ tendineæ. The remaining valves were perfectly normal. The fossa ovalis was without a foramen. The coronary vessels were not opened but their commencement was normal.

The left lung was covered with a thin purulent fibrin, and there were many subpleural hemorrhages. The organ was rather firmly adherent at the base. The right lung was covered with a shaggy fibrinous exudate. On section both lungs presented an irregularly firm, reddish-gray, mottled surface, exuding frothy fluid in many places. In about a dozen places in each lung there were firm, sharply

circumscribed, dark hemorrhagic areas, many of them pyramidal in shape and varying in size from 1 or 2 cm. to 4 or 5 cm. At the base of the right lung posteriorly and near the surface there was an area about 3 cm. in diameter, soft and necrotic, presenting multiple miliary abscesses which contained yellowish purulent fluid. The bronchi were intensely congested. The lymph nodes were anthracotic, large and succulent.

The spleen was large, weighing 600 gm. It was soft and, on section, presented a dull red, fleshy and grumous surface in which the lymphoid structures were not recognizable.

The right kidney on section presented near its lower pole an encapsulated area, about 2.5 cm. in diameter, containing some opalescent fluid. In the pelvis of this kidney there was a large irregular, tri-branched brownstone and several smaller stony granules. The pelvis and upper part of the right ureter were moderately injected. On both kidneys the capsule bulged but stripped off readily. The cortex was red and swollen, the pyramids prominently delineated. The ureter on the left side was normal.

The remainder of the autopsy was irrelevant.

Anatomical diagnosis: Acute tricuspid endocarditis; cardiac hypertrophy; fatty infiltration of myocardium; multiple pulmonary infarcts; lobular pneumonia; pulmonary edema and congestion; acute bronchitis; empyema; adhesive pleuritis (left base); hyperplastic splenitis; renal calculus; pyonephrosis; acute parenchymatous degeneration of kidneys; septicemia; operative wounds of thorax.

Bacteriology. Cultures were made from the heart valve and from a lung infarct, and both showed Streptococcus hemolyticus in pure culture.

Summary. 1. Five cases of tricuspid endocarditis are herewith reported.

2. The lesion is rare.

3. Bacteriologically, the lesion is associated with different varieties of actively pathogenic microörganisms.

4. Lung emboli or abscesses are practically invariably present.

5. The prognosis is extremely unfavorable, the average duration of life from onset of symptoms being two to three months.

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THE TREATMENT OF SYPHILIS.

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In 1919 there was published an article by Newcomer, Richardson and Ashbrook[1] in which the present writer gave certain tables covering the status of some patients in the salvarsan clinic of the Pennsylvania Hospital. These patients were divided into what essentially were two groups: patients who had had considerable salvarsan and others who with less salvarsan had, however, started treatment in the primary or secondary stage. The net result of these tables was to leave the impression which the writer then expressed that the securing of a permanently negative Wassermann reaction was a relatively infrequent occurrence. Of 46 patients with 10 to 42 doses of salvarsan only one could be considered as permanently negative and he started treatment with a primary infection. Of 18 patients with primary and secondary lesions hardly a third were beginning to appear in a favorable light.

It has been possible to follow for a further appreciable period the story of 30 of these patients. The tables as published in 1919 ended August, 1918. The present study ends September, 1920. Table I contains in full an account of the salvarsan they have received and the Wassermann reactions which they have shown. Lateral dots in the column of each patient denote where the report ended as given in 1918. From this table the reader can judge for himself as to the results of the treatment. The table also gives a summary of the condition of these patients, a judgment as to their probable present sustained serologic reaction, the total salvarsan they have had and the number of weeks which they have been under treatment. As reported in 1918, 24, or 80 per cent of these patients, were still positive. They had been under treatment for an average of forty-two weeks (primary and secondary thirty-five weeks, tertiary forty-six weeks) and had received an average of 109 decigrams of salvarsan (primary and secondary 104, tertiary 112).

During the subsequent period which is being reported these patients received 51 per cent more treatment (primary and secondary 28 per cent, tertiary 72 per cent) over a period of time 139 per cent greater (primary and secondary 120 per cent, tertiary 150 per cent) than the period first reported. Their Wassermann reactions have been followed for a somewhat longer time, 173 per cent. of the first period (primary and secondary 215 per cent, tertiary 146 per cent). Table II gives these data in another form.

During this subsequent period of time the number of patients with apparently permanently negative Wassermann reactions has increased from 6 to 19 (primary and secondary 6 to 11, tertiary 0 to

[1] Am. Jour. Med. Sc., 1919, clviii, 141.

TABLE I.

Number .
Old number .
History number .
Final condition .
Stage .

39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75 76 77 78 79 80 81 82 83 84 85 86

TABLE I—CONTINUED

	Number
First period, wks.	First period, deg.

First period, wks.	Total weeks	First period, deg.	Total decigrams	Final condition	Number
8	64	43	155	0	30
22	101	94	227	+	29
17	32	53	64	0	28
50	50	158	158	+	27
15	50	85	115	0	26
20	20	59	59	+	25
23	102	95	140	0	24
14	14	55	55	0	23
21	110	85	121	0	22
35	35	80	80	0	21
22	132	54	153	0	20
18	70	79	146	0	19
21	110	96	131	△	18
22	44	88	148	+	17
25	87	61	65	0	16
88	175	108	188	0	15
36	116	167	179	0	14
27	95	147	283	0	13
85	142	102	141	+	12
56	88	100	131	△	11
31	138	140	265	△	10
66	135	97	172	0	9
83	139	130	155	0	8
89	196	142	319	0	7
50	129	118	191	+	6
38	75	203	274	+	5
42	58	146	170	0	4
81	215	114	174	+	3
61	96	171	227	0	2
83	113	200	230	0	1

The figures of the table indicate decigrams of salvarsan. A (°) indicates a negative Wassermann, a single dot (.) a one or two plus and a double dot (:) a three or four plus Wassermann. The figures in the left outside column show the time in weeks. At the head of the table is the serial number and the old number, a composite number referring to the tables of the previous article, the first digit being the table number and the succeeding digits the serial number of that table. The line final condition is a judgment as to the probable sustained serological reaction.

8) and of the tertiary patients four have become doubtfully nega-
tive. Of the 30 patients 63 per cent have an established negative
Wassermann (primary and secondary 85 per cent, tertiary 47 per
cent), 13 per cent (primary and secondary 0, tertiary 23 per cent)
are doubtfully negative and 27 per cent are still positive (primary
and secondary 15 per cent, tertiary 30 per cent).

TABLE II.—SUMMARY OF TREATMENT.

	All patients.	Primary and secondary.	Tertiary.
Average salvarsan, first period . .	109	104	112
Average salvarsan, to date . . .	164	134	193
Average weeks, first period . . .	42	35	46
Average weeks, to date	99	77	117

The figures give the average per patient of decigrams of salvarsan during the
respective periods and the number of weeks during which it was administered.

In this very decided change for the better the lapse of time seems
to be a very important factor. The increase in time under observa-
tion far overshadows the additional treatment received.

But first one should compare the situation of these 30 patients
with that of the patients reported by Anderson[2] in his Table II.
We will omit from his table those patients who are among my 30
(those marked with an asterisk). The remaining 28 patients form
a group as to amount and length of treatment and care of observa-
tion quite similar to the 30 patients of this paper. Of the 28 patients,
10 are cases of primary and secondary syphilis. The 28 patients
have been under treatment for an average of 109 weeks (primary
and secondary 74, tertiary 129) receiving an average of 124 deci-
grams of salvarsan (primary and secondary 120, tertiary 127).
Probably 16 out of the 28 patients, or 57 per cent, have an estab-
lished negative Wassermann (primary and secondary 40 per cent,
tertiary 66 per cent). For the primary and secondary cases this is
a relatively poor showing. It can perhaps be partly accounted for
in that some late secondaries are included. For the tertiary cases the
situation is relatively a little better than with the tertiary patients
of Table I. If the 4 doubtful patients of Table I are negative then
the two groups of tertiary patients are quite alike, one having had
more treatment in less time.

Broadly considered the present conditions of the two groups are
really remarkably alike. If we combine them we get 23 patients
with primary and secondary syphilis having had an average of 125
decigrams of salvarsan over a period of seventy-five weeks with
66 per cent having an established negative Wassermann. There
are 35 cases of tertiary syphilis having had an average of 161 deci-
grams of salvarsan over a period of one hundred and twenty-four

[2] AM. JOUR. MED. SC., 1921, clxii, 80.

weeks with about 65 per cent having an established negative Wassermann.

As Anderson[3] has pointed out, the patients of his Tables VI and VII make a very good therapeutic showing, but it is the experience of the clinic that patients under observation for such lengths of time not infrequently become positive again for a longer or shorter period. In addition they were somewhat peculiarly selected. The patients so far discussed were chosen from the records of the clinic because they had considerable salvarsan. After removing them the patients of Tables VI and VII were chosen as residual patients with clearly negative Wassermanns. These latter patients therefore of necessity have had less treatment than the patients already discussed. It is nevertheless striking that so many of them have had repeatedly negative Wassermann reactions.

There are 28 patients in these two tables. They have had an average of 76 decigrams of salvarsan (secondary 74, tertiary 79) over a period of sixty-four weeks (secondary 46, tertiary 87). By referring to Table II it will be seen that this is somewhat less salvarsan than that received by the 30 patients of this table during the first period but the time is appreciably longer.

It seems that the most striking information to be derived from a study of these statistics is that time plays a very important factor in the treatment of syphilis. The patients must have a certain amount of salvarsan, from 120 to 180 decigrams and its administration in appropriate doses must be spread over a considerable period of time. That factor in treatment which varies with the stage of the disease is not so much the amount of salvarsan as the length of time over which it is to be administered. In primary and secondary syphilis the salvarsan should be administered within a period of about a year and results may be expected within the next half year. In tertiary syphilis the treatment is to be spread over a greater period of time, two to three years before results may be expected. These statements can only be considered as generalities. Individual patients vary greatly and furthermore no one would suppose that, having arrived at this point, the treatment should be stopped. Further treatment is advisable for all of these patients. How much and for how long future judgment must decide.

[3] Loc. cit.

A MEMORANDUM ON THE OCCUPATIONAL STUDY OF SYPHILIS, WITH SPECIAL REFERENCE TO FARMERS.

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In January, 1919, the authors published[1] an account of a clinical investigation of syphilis in 100 railroad men examined in the Section of Dermatology and Syphilology of the Mayo Clinic. At this time it was planned to extend the work to similar clinical studies of syphilis made on the personnel of other occupations with a view to determine whether occupation as such could serve as a factor of predisposing or modifying influence in the course of the disease. With a view to securing a type of person whose mode of life was as different as possible from that of the railroad man, farmers were selected for the present group. A survey of 100 patients whose present and past occupation had been that of farmer or farm laborer has disclosed a very striking similarity between the two groups. In the table the two groups of fifty railroad men each who comprise the first survey are compared with 100 farmers. The slightly lower incidence of frank neurosyphilis in the farmers and other minor variations among the various details of the statistical compilation are the only differences apparent. None of these differences is sufficiently marked to justify the conclusion that syphilis among farmers as seen at the Mayo Clinic differs in any essential particular from syphilis as seen in railroad men.

Two questions at once arise in the interpretation of such a result: (1) Were we in examining 100 farmers with syphilis really examining an occupational type of the disease? (2) Did we not merely examine a medically selected type of the disease in persons who because of the character of their symptoms and the relation of the medical profession to the general problem of syphilis inevitably gravitated to a diagnostic group for the final interpretation of symptoms whose anomalous character prevented a diagnosis by the general practitioner? On careful consideration of these questions we have reached the conclusion that we were in all probability dealing with the general problem of the diagnosis of syphilis, and especially of late syphilis, and not with the peculiarities of syphilis in any special occupational type. In order to reach a correct interpretation of the possible modifications in the course of syphilis

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[1] Stokes, J. H., and Brehmer, Helen E.: Syphilis in railroad men. Jour. Indust. Hygiene, 1920, i, 419-427.

induced by occupational factors the investigation must evidently be carried to the group and not be based on a study of that portion of the group which for one or another reason may be attracted to a center for medical examination.

The reaching of this conclusion does not for a moment invalidate the significance of our findings in those members of a given group whom we have examined. It is fully as important as ever for us to realize that railroad men with active neurosyphilis and with grave cardiac lesions are engaged in the operation of trains and in other work involving responsibility for the safety of the travelling public and the property of their employers. The farmer at his plow may fall a victim to cerebral hemorrhage with perhaps less serious consequences to the immediate physical safety of the public.

In the parallel columns presented in the table we have, therefore, a cross-section of syphilis as it is observed in a general diagnostic clinic such as that from which this material is taken. A number of the conclusions drawn from our previous papers may be drawn with equal reason from our study of farmers. The limited value of the history of infection and the blood Wassermann test in the diagnosis of the medical manifestations of the disease is again apparent. The masked onset of syphilis and gonorrhea falls to an average of 18 per cent. The slightly lower percentage of positive spinal fluids and of neurosyphilis in the farmers is possibly due to the fact that taking the cases at random led to the inclusion of several more cases of primary and secondary syphilis among the farmers than among the railroad men. The conspicuous absence of a history of secondary manifestations in both groups seems to confirm the aphorism that the patient with severe secondary manifestations is fortunate rather than otherwise, since he is the only one who receives enough treatment to protect him against late complications. The very striking correspondence of pupillary and neurological findings in the two groups again points to the fact that the profession at large is not as yet utilizing to their full value the clinical earmarks of the disease produced by its encroachment on the nervous system.

Conclusions.

1. A survey of syphilis in 100 farmers whose records were taken at random from the files of the section of dermatology and syphilology in the Clinic reveals no distinctive difference between the clinical picture of the disease in farmers and that in railroad men.

2. This result is not to be interpreted as precluding the possibility of special occupational types in the disease. For the determination of such types the investigation must be taken to the groups instead of subjecting the group to a species of unconscious medical selection involved in resort to a diagnostic clinic.

3. The figures given in the table therefore present essentially the diagnostic problem of late syphilis in general medicine. They sug-

gest further that physicians at large could profitably give less attention to the history of infection and the serum Wassermann test and more attention to the spinal fluid test and to the physical and especially the neurological and ophthalmic findings in their effort to recognize late syphilis and to interpret the medical picture presented by a given patient.

COMPARISON OF DUPLICATE SURVEYS OF TWO GROUPS OF FIFTY RAILROAD MEN EACH, AND ONE GROUP OF ONE HUNDRED FARMERS.

| | Railroad men. | | |
	First series. Per cent	Second series. Per cent	Farmers. Per cent
Cerebrospinal fluid positive	64.0	79.0	51.7
Lues, central nervous system	79.5	83.0	68.5
Lues III, cardiovascular	18.7	20.0	12.0
Blood Wassermann negative	57.0	58.0	43.0
Blood Wassermann positive	43.0	42.0	50.0
Wassermann weak positive	4.0	2.0	7.0
Use of alcohol	75.0	61.0	55.0
Heavy drinkers	36.0	33.0	32.0
History of lues II unobtainable	62.5	60.0	60.0
Lues recognized at some time	55.0	57.0	
Age of onset late symptoms—over thirty	78.0	75.0	70.7
Gonorrheal history positive	80.0	73.0	52.0
Gonorrhea only	24.0	19.0	12.0
Symptoms appearing from six to twenty after infection	71.0	67.0	46.0
Percentage infected by the age of thirty-two years	91.0	81.0	77.0
Wassermann on men under twenty-five years will reach	70.0	60.0	61.0
Sterile or pathologic marriages	44.0	50.0	32.0 (of 59)
Age on entry—patients between thirty-five and forty years	32.0	36.0	19.0
Concerned in operation of trains	76.0	70.0	
Concerned in operation of engines	36.0	36.0	

SYMPTOMATOLOGY.

	First series. Per cent	Second series. Per cent	Farmers. Per cent
Gastric	28.0	22.0	25.0
Not suggestive of lues	18.0	24.0	8.0
Headaches and head pains	16.0	16.0	13.0
Cardiac	14.0	16.0	4.0
Diplopia and poor vision	14.0	10.0	16.0
Malaise, weakness	12.0	8.0	10.0
Shooting pains	10.0	20.0	19.0
Bladder (subjective)	10.0	4.0	13.0
Nervousness	8.0	4.0	
"Do I have syphilis?"	8.0	6.0	4.0
Laryngeal	8.0	6.0	4.0
Rheumatism	4.0	18.0	7.0
Ataxia (subjective)	4.0	6.0	13.0
Girdle pain	4.0	4.0	16.0 (paresthesia)
Dizziness	2.0	8.0	13.0
Loss of consciousness	....	7.1	10.4

OBJECTIVE EXAMINATION.

Abnormal knee reflexes	65.1	79.0	73.7
Abnormal Achilles reflex	78.1	62.0	61.9
Romberg positive	38.0	42.0	50.7
Speech defect	15.7	17.0	11.0
Mental symptoms	38.4	38.0	41.6
Paresthesias	55.8	51.3	41.0
Ataxia (objective)	36.8	36.3	41.0
Bladder (objective)	47.5	20.5	31.0

EYE FINDINGS.

"Slow" reflexes	25.0 per cent. of 48 cases	21.7 of 78 cases.
Argyll-Robertson pupils .	37.0 " " 48 "	32.0 of 78 "
Unequal pupils	14.5 " " 48 "	23.8 of 67 "
Irregular pupils	14.5 " " 48 "	26.8 of 67 "
Muscular paralyses . . .	12.5 " " 48 "	10.5 of 67 "
Fundus changes	26.5 " " 34 "	4.4 of 67 "

THE HEART IRREGULARITY CALLED "SINO–AURICULAR BLOCK."

By S. CALVIN SMITH, M.S., M.D.,

PHILADELPHIA.

Introduction.   While examining recruits to determine their cardio-vascular fitness for military service, my attention was attracted by a
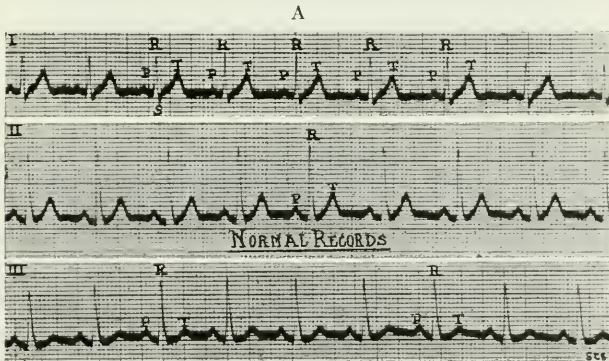
EXHIBIT A.   A Normal Electrocardiogram.   (Presented for comparison with the illustrations which follow.)   The *P* wave, which is the representative of auricular activity, is followed by the ventricular complex *Q–R–S–T*.   The *R* wave represents initial activity at the base of the ventricles; the *T* wave is believed to represent final activity at the base of the ventricles.   From the ending of the *T* wave to the beginning of the *P* wave is the rest period of the heart.   Normally, each *T–P* or diastolic period is equal in length or nearly so.   In the condition called "sino-auricular block" the *T–P* interval suddenly becomes of a length much greater than the usual rest-period between heart-beats.

form of heart irregularity which frequently appeared following exercise in healthy youths of the athletic type.   The exercise test which was prescribed for cardiovascular examinations consisted in hopping

100 times on one foot; such effort could be expected to raise the pulse-rate approximately forty beats, and the healthy heart returned to its preëxercise-rate well within the time-limit of two minutes. The majority of the pulse-rates returned to the preëxercise status by a gradual decline in rate. There were some instances, however,

B
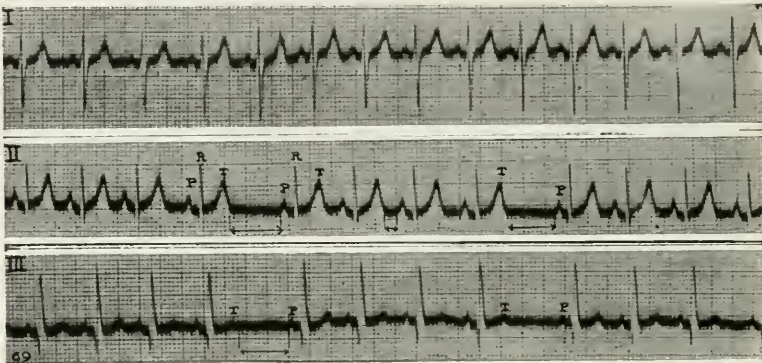
EXHIBIT B. The Heart Irregularity Called "Sino-auricular Block." Five-year-old Child; Record Taken Three Months After Illness from Diphtheria. "A peculiar disturbance of the heart's action, . . . consisting of dropped beats, . . . in which the auricular beat is lost as well as the ventricular. The rhythmic action of both auricle and ventricle is disturbed by a cycle of unusual length, the long cycle being approximately the length of—usually somewhat shorter than—two normal cycles. It is ushered in by slight quickening of the whole heart and is succeeded by cycles which, while at first a little long, shorten up until the usual length of the cycle is reëstablished. . . . The P–R interval is usually prolonged but shortens again after each long diastole."*

C
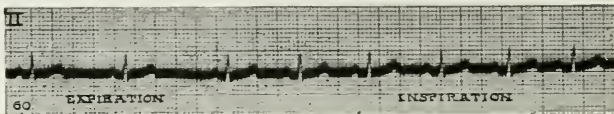
EXHIBIT C. Sinus Arrhythmia. Sinus arrhythmia, which is physiological in childhood, may be confused with "sino-auricular block" unless one remembers that in sinus arrhythmia the rate gradually decreases on expiration and increases on inspiration (as noted in the above figure). Also in sinus arrhythmia the irregularity disappears when the breath is held; but in "sino-auricular block" holding the breath causes no change in the "dropping" of beats.

in which this gradual decline in rate did not occur; the pulse would fall precipitately from a rate of 132 in the first ten seconds following exercise to a rate of perhaps 98 twenty seconds afterward; ten seconds later the pulse might mount to 120; such oscillations in rate-return would continue until the preëxercise-rate was reached and maintained. It was customary for some of the army examiners

* Quoted from Lewis's Mechanism and Graphic Registration of the Heart-beat, 1920.

to refer to the pulse which gradually declined as "a pulse that slid down;" the other variety was described as "a pulse that skipped
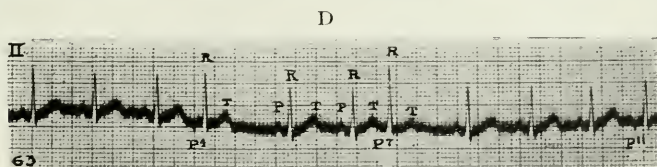
EXHIBIT D.   Auricular Premature Contractions.   Premature contractions originating in the auricles produce an irregularity which on casual glance may simulate that of "sino-auricular block."   On closer inspection, however, it will be observed that the P (auricular) wave is either changed in direction (P^4–P^{11}) or buried in the T wave of the preceding ventricular complex (P^7).   It is also usual to find that the *period of disturbance plus the distance of the subsequent compensatory pause* is not equal in length to the distance of two uninterrupted cardiac cycles.
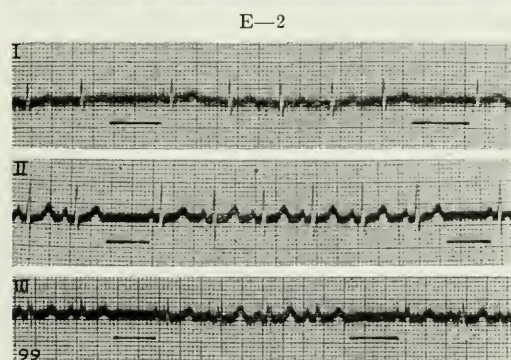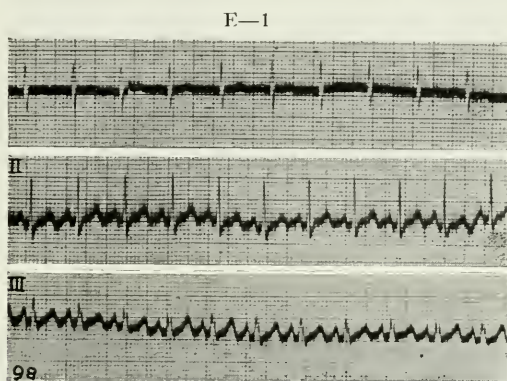
EXHIBIT E.   "Sino-auricular Block" Probably Due to Atropin.   Four-year-old child acutely ill with diphtheria.   The irregularity was not present on admission to the hospital (Fig. E-1), but was manifest twenty minutes after the hypodermic administration of strychnin 0.01 gr. and atropin 0.0067 gr. (Fig. E-2).   Rate of Fig. 1, 130.   Rate of Fig. 2 approximately, 105.   Within an hour the irregularity had disappeared.

down" to the preëxercise-rate.   This "skipping" form of arrhythmia during   the   rate-return   from   exercise   was   rather   frequently

encountered and a line was given to it in our printed cardiovascular blank records in order that the irregularity might be properly appraised. Inquiry developed the facts that this type of arrhythmia was not present before exercise, not present during sustained physical effort, not present in the quiet hours of physical rest, not noticeable

F
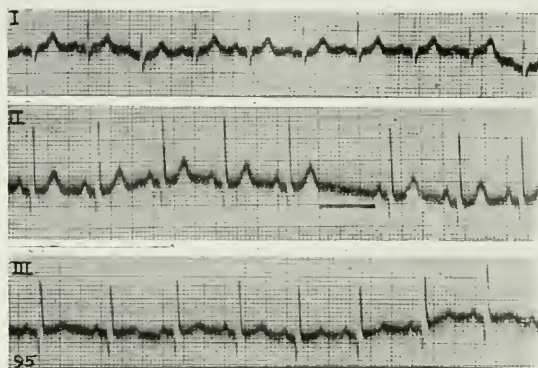
EXHIBIT F-1. "Sino-auricular Block," Eighth Day of Convalescence. The pulse irregularity which the resident physician had discovered in a diphtheria convalescent eight years of age all but disappeared at the time of the electrocardiographic study: Lead II, however, shows an isolated instance of sino-auricular block. Heart-rate, 112.

F—2
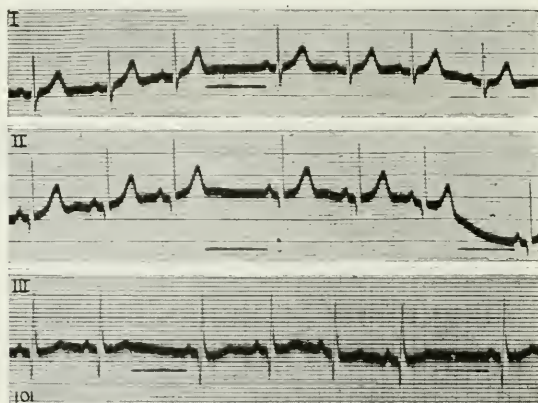
EXHIBIT F-2. Same Patient as Exhibit F-1; Patient Dozing. "Sino-auricular block" appeared every third or fourth beat, in all three leads. Heart-rate averages 75.

when the patient was dozing off to sleep—the arrhythmia was evidently not present at any other time than following the return of rate from forced and sudden exercise. Needless to say, in such recruits there was no evidence of cardiocirculatory damage or they would not have been accepted for service.

The Irregularity in Convalescence.   Upon return to civil practice and during a series of studies at a hospital for contagious diseases I noted the same type of pulse irregularity in children—present, however, under conditions other than exercise. This irregularity could be identified electrocardiographically as "sino-auricular block." (See Exhibit B.) Being noticed for the most part in children who were in the diphtheria ward the irregularity was naturally
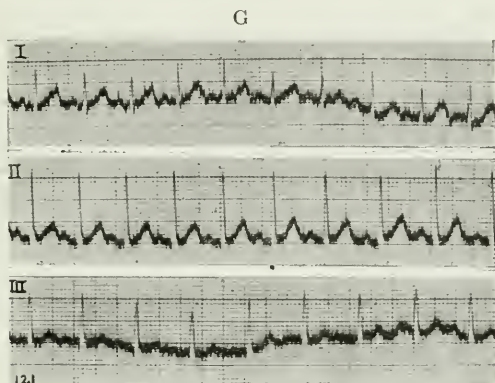
Exhibit G-1. Same Patient as Exhibit F; Child Mentally Stimulated. The irregularity was made to disappear by exercising the patient. Rate, 128.
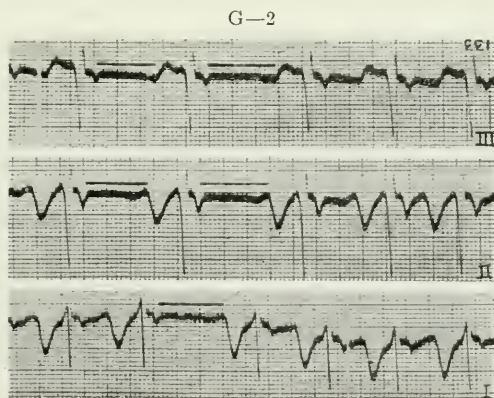
Exhibit G-2. Same Patient as Exhibit F; Day before Discharge. The throat cultures were finally negative and the child was told that he would be sent home. He was not inclined to go and was pensive when these records were taken. "Sino-auricular block" is most apparent in all leads. Heart-rate averages 75.

believed to be of pathological significance and perhaps premonitory of higher grades of heart-block. However, as the electrocardiographic records began to accumulate (see Exhibits E, F, G, H) it was noticed that "sino-auricular block" almost invariably occurred (with the sole exception of Exhibit E) in children who were convalescent from diphtheria, the duration of convalescence ranging from the second week to the third month of hospitalization. The children

were free from any evidence of cardiocirculatory fault other than this evanescent form of arrhythmia—they were convalescents kept in the hospital either in order that the arrhythmia could be watched or else because the throat cultures were not yet negative following the attack of diphtheria.

H
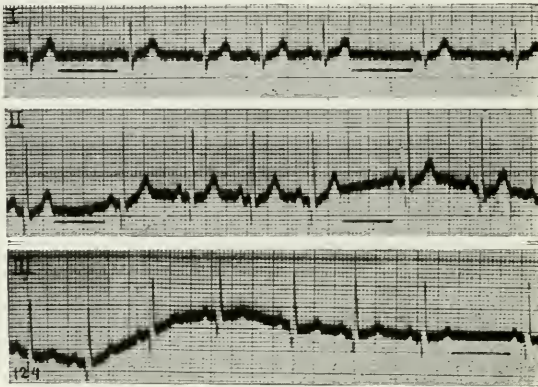
EXHIBIT H-1. "Sino-auricular Block." The six-year-old girl was contentedly resting when the records were taken. Sino-auricular block is marked through all the leads. Rate averages 75.

H—2
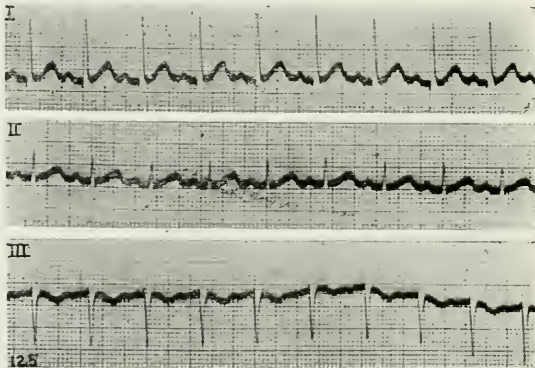
EXHIBIT H-2. Same Child as H-1; patient fretting. "Sino-auricular block" disappeared from the record. Rate 105.

In the patient from whom Exhibits F and G were taken it was noticed that the arrhythmia could be made to appear or made to disappear in the manner stated in the legends below these records. Exhibit H shows the occurrence of "sino-auricular block" due to emotional disturbance alone. It is to be remembered that the convalescent children from whom these records were taken were not receiving any cardiac drugs. Exhibit E, however, shows "sinoauricular block" twenty minutes after the hypodermic administra-

tion of strychnin and atropin, thus suggesting that the latter drug is, in all probability, capable of producing a slowing in heart-rate (from 130 to 105) by the production of "sino-auricular block"— perhaps by its action on the vagus center.

The observations so far made might lead one to conclude that "sino-auricular block" is an irregularity which in children is the result of or in some way associated with the toxins of diphtheria. That such is not the case is shown in Exhibit I, which record was taken from a child convalescing from an attack of mumps. Another

I
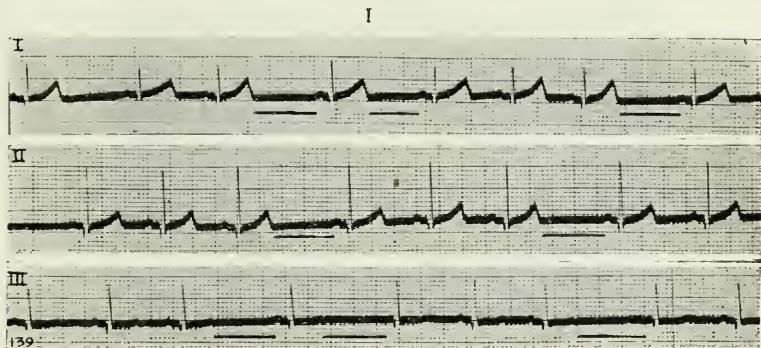
Exhibit I. Mumps: Fourteenth Day After Parotid Swelling was Noticed. A six-year-old child, apparently well, yielded the above record of "sino-auricular block."

J
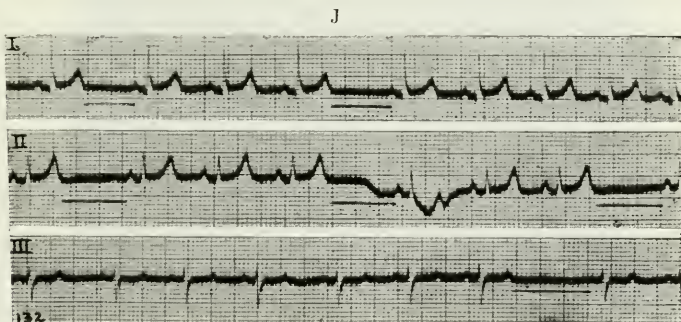
Exhibit J. Whooping-cough: Thirteenth Day. A four-year-old child, between paroxysms of coughing, presented "sino-auricular block" in the electrocardiogram.

youngster, suffering from whooping-cough, yielded Exhibit J between infrequent paroxysms of coughing, indicating that "sino-auricular block" may be one of nature's methods of slowing the heart-rate when the heart-rate is for any reason accelerated—as it was accelerated, in this instance, by violent paroxysms of coughing.

The Irregularity in Health.—In further support of the observation that "sino-auricular block" is probably natural to certain hearts, much as that other irregularity, sinus arrhythmia, is physiological in childhood, Exhibit K is offered in evidence. The records were

taken from a buoyant, active child of eight years. After hopping 100 times on one foot there was noted the same type of arrhythmia as had been so frequently observed in military practice following the return of the heart-rate from exercise.

This particular record, K-2, is not so characteristic of sino-auricular block as are other of the illustrations; it may be contended that K-2 is an exaggerated sinus arrhythmia. If it proves to be so it illustrates that the border-line between the two conditions is not closely drawn and that one may merge into the other, thus placing

K—1

K—2
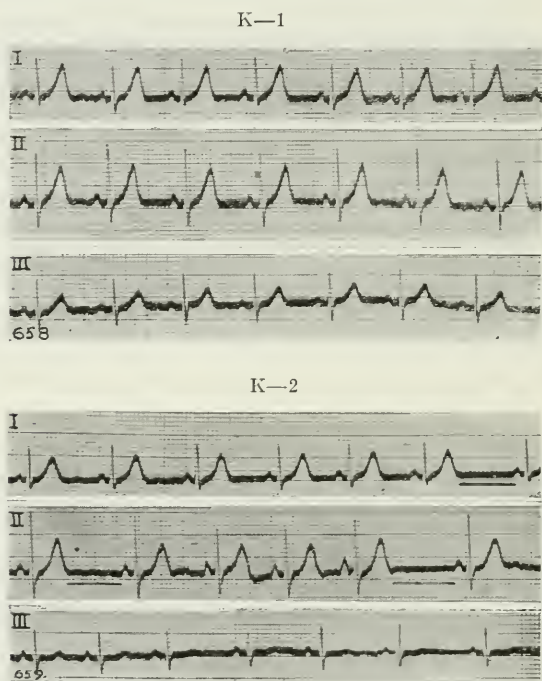
EXHIBIT K. Healthy Child of Eight Years Before and After Exercise. After hopping 100 times on one foot an irregularity resembling "sino-auricular block" appeared in the record.

both "sino-auricular block" and sinus arrhythmia on the same physiological plane. The record (K-2) seems capable of sino-auricular interpretation under the analysis given by Lewis, which follows:

"A peculiar disturbance of the heart's action, . . . consisting of dropped beats, ; . . . in which the auricular beat is lost as well as the ventricular. The rhythmic action of both auricle and ventricle is disturbed by a cycle of unusual length, the long cycle be ng approximately the length of—usually somewhat shorter than —two normal cycles. It is ushered in by slight quickening of the

whole heart and is succeeded by cycles which, while at first a little long, shorten up until the usual length of the cycle is reëstablished. . . . The *P-R* interval is usually prolonged but shortens again after each long diastole."[1]

Another record from an apparently normal youth of nineteen years is shown in Exhibit L. His previous history was negative, but he had accidentally discovered that a pulse irregularity was
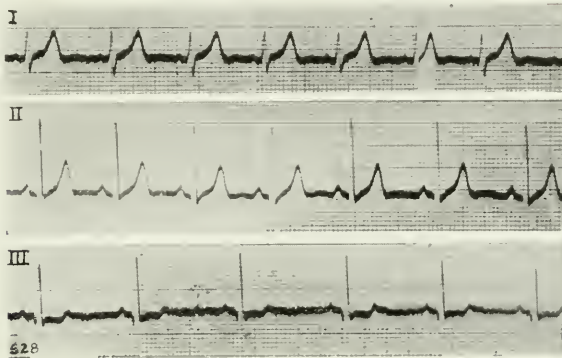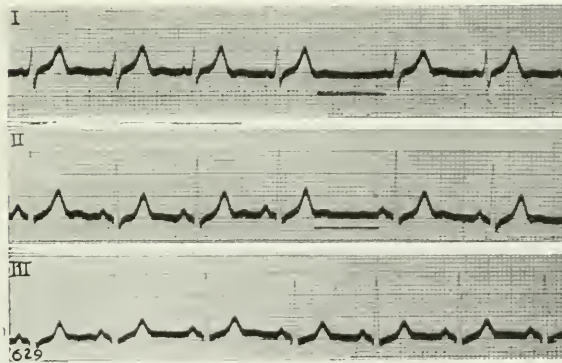
EXHIBIT L. Healthy Youth of Nineteen Years; Before and After Exercise. After 100 hops on one foot an irregularity resembling "sino-auricular block" appeared in the record.

fleetingly present at times when he was resting from a dance. After hopping 100 times on one foot the irregularity was recorded in Exhibit L-2. Weighed in the balance of judgment, Exhibit L-2 tips the scales to sinus arrhythmia, again illustrating the resemblance between sinus arrhythmia and "sino-auricular block." Exercise did not produce any cardiocirculatory distress in the child of eight years nor in the youth of nineteen years. Neither one at any time

[1] Lewis, Thomas: Mechanism and Graphic Registration of the Heart-beat, 1920.

had symptoms or physical signs of cardiocirculatory fault, nor was there any history of circulatory embarrassment; yet both exhibited an irregularity following the exercise test of hopping 100 times on one foot. Evidently "sino-auricular block" is a phenomenon natural to certain hearts as the pulse-rate returns to normal from the stimulation of exercise. I have also recorded the irregularity in the mother heart, in records taken during the tranquil period which follows the birth of the child.

Literature. It is generally understood that "sino-auricular block" is a low grade heart-block, as capable of eventuating in block of higher grade as is any other low-grade interference with the passage of the impulse for contraction in its course along the conduction system from the pacemaker to the fibers of Purkinje. The literature on the subject is not extensive. Paul White, [2] in reporting one of seven cases seen at the Massachusetts General Hosp'tal in the past five years, presents records of a healthy athlete who exhibited "sino-auricular block" after exercise, and quotes Levine[3] as having noted the condition in four patients, three of whom had been taking digitalis. Levine collected fourteen cases from the literature, in seven of which there was the history of digitalis administration. Brown[4] reported a patient, eleven years of age and suffering from acute arthritis, in which atropin abolished "sino-auricular block."

Conclusions. 1. "Sino-auricular block" is not as rare as the paucity of literature on the subject would lead one to believe. It was clinically suspected, with some degree of certainty, in scores of healthy young men in military examinations; it has been cardiographically proved to be present fourteen times in the last ten months of the writer's experience.

2. "Sino-auricular block" can be clinically suspected in a person whose pulse is irregular as the rate returns to normal after exercise and who is free from symptoms and signs of circulatory fault. The condition is to be differentiated from sinus arrhythmia and from premature contractions; in sinus arrhythmia the rate increases on inspiration and decreases on expiration, the irregularity disappearing when the breath is held. Respiration has no effect on the irregularity called "sino-auricular block." Premature contractions may be associated with other evidence of cardiocirculatory fault; they disappear on exercise and do not usually recur for several minutes following increased physical effort; they are especially noticeable when the patient is at physical rest or falling asleep. A person whose heart exhibits premature contractions (particularly if they be of ventricular origin) is usually conscious of the irregularity; the intermittency of "sino-auricular block" produces no such subjective symptoms.

[2] Arch. Int. Med., 1920, xxv, 420.
[3] Ibid., 1916, xvii, 153.
[4] Ibid., 1919, xxiv, 458.

3. "Sino-auricular block" is not associated with nor is it the sequel of any one definite type of infective process.

4. It is not necessarily dependent upon nor secondary to an infective process, as it occurs in individuals who are well.

5. In a rapid heart it was recorded within twenty minutes following the hypodermic administration of strychnin and atropin.

6. It has been observed in persons who had no other clinical evidence or physical signs of cardiocirculatory disturbance.

7. "Sino-auricular block," in certain persons, can be made to appear following physical exertion, mental excitement or emotional strain; it may also follow the administration of drugs; it is therefore likely due to a change in nerve control of the heart.

8. In seven of the eight patients whose electrocardiographic records are here shown there was no other evidence of cardiac disturbance in the graphic records (the exception being Exhibit H-2, which shows inversion of lead III).

9. The premises above enumerated lead to the deduction that "sino-auricular block" is not a pathological condition, but is, in all likelihood, a physiological manifestation in certain hearts. As such its detection does not require drug interference nor does it furnish an indication for modifying the individual's accustomed manner of living.

BACTERIA ON SUBSIDIARY COINS AND CURRENCY.

By Charlotte B. Ward, B.S.,

AND

Fred W. Tanner, Ph.D.

URBANA, ILL.

(Contribution from the Laboratories of General Bacteriology of the University of Illinois, Urbana, Ill.)

The object of this investigation was to determine the numbers and types of microörganisms on the coins and currency being used in general circulation. The smaller values were used, since it was believed that these were passing more quickly from one person to another. The significance of contact infection and infection by means of the hand has been well emphasized by many recent investigations. Money is a medium which is received from all kinds of individuals, often with little regard that it may be a carrier of infection.

Very little data are available from which to draw conclusions with regard to the significance of coins in this relation. Most of the studies have been concerned with the pathogenic bacteria, and no study seems to have been made to determine just what types of organisms are present on the coins. Some of the information

has been deduced by analogy. Some have argued that money may be a carrier of disease bacteria simply because it passes through the hands and pockets of so many individuals in a short time. Realizing this danger, some banks provide disinfectants with which the hands of those who handle money are disinfected. On the other hand it does not seem to be true that bankers are more liable to infection than others who do not handle our mediums of exchange so constantly. The majority of reports on this subject are limited to investigations with pathogenic microörganisms.

It has been repeatedly shown by recent investigators that infection is very probable by handling contaminated materials. A similar study to the one reported in this paper was conducted on postage stamps by Keilty and McMaster.[1] They examined fifty postage stamps and found only two of them sterile. With the possible exception of two cases no pathogenic organisms were found. They state that it is dangerous to lick stamps, since they are laden with bacteria which might include some of the pathogenic types. Postage stamps bear somewhat the same relation to the public that money does, although the constitution of them is quite different from that of coins. Stamps are used but once and are not handled by so many individuals, although the adhesive applied to them might be a favorable abode for microörganisms for relatively long periods of time.

Park[2] reported a few interesting investigations to determine whether money could be a carrier of pathogenic bacteria. He was interested especially in that which was handled by persons known to have been infected with disease. Coins which were infected were found to carry living bacteria for a short time after infection. He took coins from children having diphtheria and tested them for living bacteria six hours later. Out of thirty-five pennies three had diphtheria bacilli. Out of seven nickels, streptococci were obtained from one and staphylococci from two. Out of four dimes, one contained streptococci and another staphylococci. Coins taken from tuberculous people and examined twenty-four and forty-eight hours later gave no living bacilli. Park's investigations were conducted on coins which were subjected to infection, while those used in this investigation were from general circulation.

Hilditch[3] studied the bacteria on paper money. While he does not say that soiled paper money may not spread disease, he asserts that there is not an authentic case on record in which such transmission has been accurately proved. His investigations were carried out on twenty-four dirty bills, with special efforts to identify the diphtheria and tubercle bacteria. His results were negative. The number of bacteria on the bills varied from 14,000 to 586,000,

[1] Med. Rec., July 22, 1916.
[2] Money as a Carrier of Disease, Current Literature, May, 1904, xxxvi, 547.
[3] Bankers' Magazine, 1908, lxxvii, 493.

with an average count of 142,000. He could notice no relation between the apparent dirt on the bill and the bacterial content. The cleanest bill had next to the largest number of bacteria while that which seemed to be the dirtiest had a very small number of bacteria. Such was not the case with the bills examined in this investigation. In general there seemed to be a relation between the condition of the bill and bacterial content. On the new bills few bacteria were found. Park found 135,000 bacteria on a dirty bill taken from a store. It seems probable that none of the materials used in the manufacture of paper currency are bactericidal.

A similar investigation has been reported in the *Medical Officer* for May 1, 1920, from Great Britain, where the ability of coins to spread disease was tested by the use of five common pathogenic bacteria. Under the conditions of the experiment, the life of the organism on coins (copper and silver) was very short. The chief factor accounting for this was the germicidal action of the metals. It is concluded that coins may be regarded as negligible factors in the transmission of disease.

The technic used in the investigation reported herein was as follows: Glass-stoppered bottles containing 25 c.c. of water and about 5 grams of sand were sterilized in the autoclave and proved to be sterile by subsequent culture. The coins were placed in these bottles and shaken on a shaking machine for five minutes. After shaking the sand quickly settled and aliquot portions of the wash water were plated out in the usual laboratory media. Special attention was given to the lactose broth tubes, since it was desirous of determining the presence of any of the indicators of pollution. After incubation at 37° C. the colonies were picked from the plates and transferred to dextrose broth and agar slants. In order to simplify the cultural study and yet be able to group the bacteria which would be isolated the group number of the Society of American Bacteriologists was used. This method allows the salient characters of the organisms to be shown without the use of some cumbersome cultural data or names. The following chart shows the meaning of each digit in the group number:

100.	Endospores produced.
200.	Endospores not produced.
10.	Aërobic (strict).
20.	Facultative anaërobic.
30.	Anaërobic (strict).
1.	Gelatin liquefied.
2.	Gelatin not liquefied.
0.1	Acid and gas from dextrose.
0.2	Acid without gas from dextrose.
0.3	No acid from dextrose.
0.4	No growth with dextrose.

.01   Acid and gas from lactose.
.02   Acid without gas from lactose.
.03   No acid from lactose.
.04   No growth with lactose.
.001   Acid and gas from saccharose.
.002   Acid without gas from saccharose.
.003   No acid from saccharose.
.004   No growth with saccharose.
.0001   Nitrates reduced with evolution of gas.
.0002   Nitrates reduced without gas.
.0003   Nitrates not reduced.
.00001   Fluorescent.
.00002   Violet chromogens.
.00003   Blue chromogens.
.00004   Green chromogens.
.00005   Yellow chromogens.
.00006   Orange chromogens.
.00007   Red chromogens.
.00008   Brown chromogens.
.00009   Pink chromogens.
.00000   Non-chromogenic.
.000001   Diastatic action on starch, strong.
.000002   Diastatic action on starch, feeble.
.000003   Diastatic action on starch, absent.
.0000001   Acid and gas from glycerin.
.0000002   Acid without gas from glycerin.
.0000003   No acid from glycerin.
.0000004   No growth with glycerin.

The genus according to the system of Migula is given its proper symbol which precedes the number thus:

Bacillus coli (Esch.) Mig. becomes B. 222.111202.

In Table I the group numbers for all of the bacteria which were found on coins are given. It is seen that most of the bacteria are aërobic spore formers. One hundred and ten strains were isolated from the coins examined, eighty-three of which produced spores. None were found which formed gas in dextrose or lactose. This is taken as evidence that the coins examined in this study were not contaminated or that the indicators of pollution used in microbiology were not living when the coins reached the laboratory. No special procedure was used to collect the coins. Some were secured from the teller at the bank while others were taken at random from general circulation.

In order to determine just how long bacteria could survive on coins, one hundred pennies and one hundred nickels were sterilized by shaking in 95 per cent alcohol and allowed to stand overnight. This treatment left the coins clean and in many cases bright and shiny. They were then rinsed in sterile water, placed in large Petri

TABLE I.

Number of strains with common group number.	Group number.	Culture number.[4]
6	111.2221012	26, 28, 46, B1, B24, B26
11	111.2221032	18, 45, 47, 50, 53, 63, 74, 76, 77, 79, 81
1	111.2221512	51,
1	111.2221532	37,
10	111.2221812	3, 6, 8, 15, 19, 36, 38, 43, 68, B13
1	111.2222012	B9
2	111.2222812	1, 12
1	111.2223012	49,
1	111.2232013	5,
1	111.2233033	52,
4	111.2321012	10, 39, B17, B21
2	111.2321032	B2, B6
2	111.2321812	9, B14
1	111.2321832	B7,
3	111.2322012	21, 22, B18
3	111.2322812	58, 75, 80
1	111.3221012	B23,
3	111.3221812	34, B4, B8
2	111.3231812	57, 82
4	111.3321012	40, 60, 61, B25
1	111.3331013	B16,
3	111.3331813	23, 24, 41
1	111.3331813	25
1	111.3333013	35
1	112.2221032	65
1	112.2223032	67,
1	112.2223033	64,
1	112.2233833	55,
1	112.3332933	2,
1	112.3333033	54,
1	121.1331012	27,
2	121.2221032	69, 70
3	121.2221812	B15, B19, B22
2	121.2221832	71, 72
1	121.2223012	13,
1	121.3231612	11,
1	121.3321012	14,
1	122.2221012	29,
1	211.2222032	74,
3	211.2223033	48, 56, 78
1	211.2223512	59,
1	211.2223532	B10,
1	211.2223912	68,
1	211.2321012	20,
1	211.2321812	16,
1	211.2331033	32,
1	211.2333033	42,
1	211.3222033	30,
1	211.3321032	B5,
1	212.2221012	B11,
1	212.2221932	66,
1	212.2223032	B3,
1	221.2221012	B20,

dishes, and sterilized in the autoclave. The coins in each dish were then inoculated with broth cultures of Bacillus prodigiosus, Bacillus typhosus, Bacillus colon and Bacillus anthracis. Every

[4] Those culture numbers marked "B" indicate bacteria isolated from currency.

three or four days one of the coins was tested for sterility by dropping it into dextrose broth and agitating for a short time. After the coin had remained in this first broth tube for a few minutes it was removed by sterile forceps and placed in a second tube. This was done in order not to secure any salts of the metals in the culture tubes to restrain development of the organism. The solutions in which the pennies were left indefinitely turned to a distinct green color, which indicated the presence of metallic salts. Bacillus anthracis was the only organism which remained alive for any length of time. It lived on pennies eighty days; on nickels seventy-one days, when the experiment ended. This organism is a spore-former, and the fact that it is able to survive on coins confirms the presence of so many spore-forming bacteria on the coins which were taken from general circulation and analyzed for types of micro-organisms.

From this it seems that the metallic composition of the coin acts as a bactericide. It has been known for a long time that copper and silver are toxic to microörganisms. Park in the paper referred to above stated that the metals used in the coin tended to destroy bacteria. He placed coins in broth and allowed them to remain for twenty hours, after which the broth was inoculated with bacteria. Park regarded the copper and nickel as good germicides, but the silver gave less activity. Coins which were placed on gelatin heavily inoculated give a halo of sterility about them which would indicate that the salts of the metal diffused into the medium and acted as disinfectants. Photographic illustrations of this were too unsatis-factory for reproduction in this paper. Similar data have been secured by other investigators. Friedenthal[5] stated that silver has a decided bactericidal action. Colloidal silver was found to be twice as active as silver nitrate. A penny is made up of 95 per cent of copper and 5 per cent of silver and tin. A nickel has 75 per cent of copper and 25 per cent of nickel. A dime has 90 per cent of silver and 10 per cent of copper. Lusini[6] states that although the disinfection activity of cations is not in direct relation to their atomic weights, the greatest disinfection activity belongs to those with high atomic weights. According to Lusini, then, all of the metals used in making coins would possess bactericidal activity. Their strength as disinfectants when applied to coins is probably determined somewhat by the solubility of the salts formed as the coins pass through the different channels of commerce. It must be apparent that coins are able to have small amounts of salts formed on their surfaces as they are passed from one person to another. These probably act as the disinfectants. The germicidal action of the metals of the coins was well shown by pouring agar heavily inoculated with certain pathogenic bacteria over silver and copper

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[5] Biochem. Zeit., 1919, xciv, 47–68.
[6] R. Acad. fisicrit, March 20, 1910. Chem. Absts., 1912, vi, 240.

coins in Petri dishes.   About each coin there was a halo where no growth occurred, while beyond this the organism grew abundantly. Diffusion of the metallic ions probably restrained growth in the near vicinity of the coins.

In order to determine whether the reaction of the medium in which the coins were placed exerted any influence on the amount of metallic salts which would be formed, pennies, nickels and dimes were placed in media having a neutral reaction and distinctly acid reaction.   The results were somewhat different than were expected. In the acid broth, in most cases, there was good growth, while in the neutral broth there seemed to be less development.

The number of organisms on coins is quite varied.   Table II shows the numbers of bacteria on pennies as they were taken from general circulation.   No attempt was made to secure them from people known to be infected with disease.   The coins were subjected to the same technic as described before.

TABLE II.—NUMBER OF BACTERIA FOUND ON THIRTY COINS TAKEN FROM GENERAL CIRCULATION.

Number of coin.	Number of bacteria.
1	2950
2	12
3	93
4	56
5	12
6	12
7	112
8	37
9	6
10	18
11	6
12	25
13	87
14	68
15	81
16	50
17	0[7]
18	0[7]
19	25
20	43
21	25
22	31
23	18
24	18
25	00[7]
26	224
27	62
28	18
29	31
30	18

Nine paper bills were examined by shaking in bottles containing sterile sand and water.   There was a marked difference in the numbers of bacteria which were enumerated.   The old bills were laden

[7] O indicates no bacteria in 1 c.c. of wash water.

with great numbers of organisms while the new bills contained only a few bacteria. As stated above, Hilditch did not secure such results. However, they are to be expected, since a new bill would have travelled through fewer hands and would not have had the opportunity for infection that an old bill would have. The definition of an old bill and a new bill is by no means satisfactory. Appearance is the only guide, and it is possible that a bill of recent engraving might by rough usage be made to look old. The group numbers for the bacteria isolated from the bills are included in Table I.

Summary and Conclusions. There seems to be little basis for the belief that coins bear any close relation to the spread of disease. The indicators of pollution used in sanitary investigations were entirely absent on the coins used in this investigation. Thirty-seven of the strains of microörganisms isolated from the coins were spore-formers, and probably spores are necessary before the organism may perpetuate itself for any considerable length of time on coins. This may explain why none of the commonly accepted indicators of pollution were found. They are not spore-forming organisms, and consequently are destroyed by the action of the metals. Since the flora of coins seems to be made up almost entirely of microörganisms which form spores it is reasonable to assume that coins might function in spreading diseases, the etiological agents of which are spore formers. It was shown in this paper that Bacillus anthracis was able to live for eighty days on pennies and seventy-one days on nickels when the experiment ended. The greatest factor tending to control the types and numbers of microorganisms on coins seems to be the metal of which the coins are made. Numerous instances are mentioned in the literature where it is shown that the metallic ions have a distinctly bactericidal effect. The same statement applies to certain of the salts of these metals. It is undoubtedly true that coins which are passing from person to person in general circulation come in contact with acids and alkalies which were the formation of soluble salts on their surfaces. These tend to keep down the bacterial flora and to probably exert a selective action, destroying the non-sporeforming organisms. Mold spores were isolated in a few cases. These probably are just as resistant as the bacterial spores, although they play a lesser role in the transmission of infection.

CASE OF MENINGITIS IN AN INFANT DUE TO A THREAD-LIKE DIPHTHEROID ORGANISM.[1]

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AND

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The case of meningitis here recorded is of interest because of the rarity with which diphtheroid organisms are definitely concerned in causing pathological processes and of the still greater rarity with which they have been found in the cerebrospinal fluid. In a review of the diphtheroid organisms, Mellon[2] quotes from the literature a case in which a diphtheroid had caused meningitis, and in a synoptic table (page 276), one of his forms of Bacillus hoagii was obtained from spinal fluid. More recently Dick[3] has described a case of meningitis due to a diphtheroid organism. The pleomorphic organism described below cannot be considered an important cause of meningitis, but it is an addition to the list of organisms causing this condition and illustrates the value of making cultures of spinal fluids when obtainable.

Clinical History. P. K., male infant, aged eighteen months. First seen by Dr. G. J. Geisler, of South Bend, Indiana, August 10, 1920. At that time he had had a cough for six weeks; diagnosis, bronchopneumonia. Early in the morning of August 13 he seemed much improved and sat up and played; later that morning he became rapidly worse, gradually becoming unconscious. Legs were very spastic. One of us (M.K.M.) saw the patient in consultation in the early afternoon. The child lay quietly in bed with a fixed stare, apparently unconscious. Temperature, 105.4° F. Typical Biot breathing with long periods of apnea. No strabismus; both pupils dilated; edema of both disks. Skin without eruptions; tissue turgor good. Slight general adenopathy. Slight cervical rigidity; no opisthotonos. Ears negative. Throat clear. Lungs showed area of relative dulness, suppressed tubular breathing and crepitant rales in the left interscapular region. Heart of normal size; sounds rapid and regular; no adventitious sounds. Legs extended and so spastic that reflexes could not be elicited. Kernig and Brudzinski signs doubtful because of spasticity. Blood leukocytes, 7000. Lumbar puncture revealed fluid under greatly increased pressure. About 20 c.c. of cloudy fluid removed. Last tube of four, each con-

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taining about 5 c.c., was much more cloudy than others and quickly formed a web. Antimeningitis serum was not given pending the determination of exciting organism. Patient died about a half-hour after puncture. Autopsy refused.

Microscopic Examination of Spinal Fluid. Enormous number of leukocytes, mainly polymorphonuclears, but lymphocytes present as well. Numerous Gram-negative bacilli of small size and with a tendency to bipolar staining, always extracellular. Their small size and behavior to Gram-stain suggested Bacillus influenzæ, especially in view of the previous diagnosis of bronchopneumonia; but influenza bacilli when present are ordinarily not found in spinal fluids in large numbers.
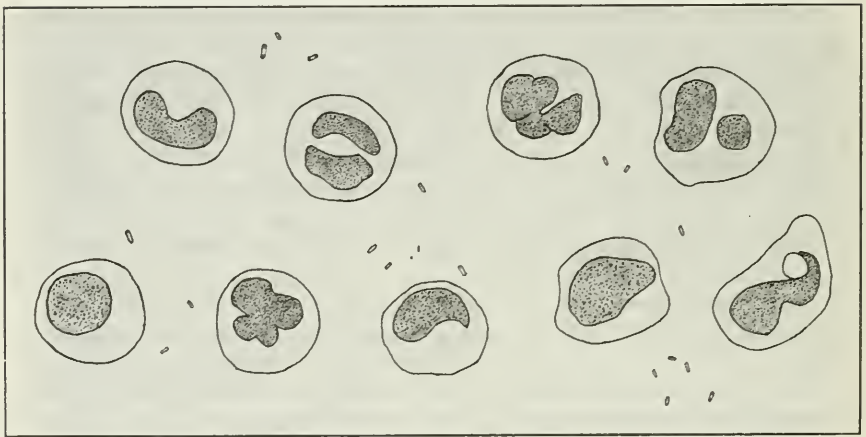
Fig. 1.—Free-hand composite drawing of stained smear of spinal fluid, showing leukocytes and small Gram-negative bacilli.

Culture of Spinal Fluid. The fluid in one of the tubes was planted on plain and on 10 per cent human blood agar and incubated aërobically. Within twenty-four hours on each medium there developed numerous fine (about 0.2 mm. diameter), nearly colorless, grayish, round colonies. The blood of the blood-agar culture remained unchanged. Microscopic examination of each of these cultures revealed curious long, twisted, irregularly-shaped Gram-negative threads with only a few bacillary forms. These thread-like forms were so surprising that the fluid of two other tubes was cultured similarly, and exactly the same results were obtained (Figs. 2 and 3).

Characters of Organism. Transfers from these cultures to blood agar, to plain agar and to Loeffler serum at first gave thread-like forms still Gram-negative, but at times containing Gram-positive

bodies within them and also bacillary forms with bipolar Gram-positive bodies (Fig. 4). Subsequent subcultures yielded bacillary
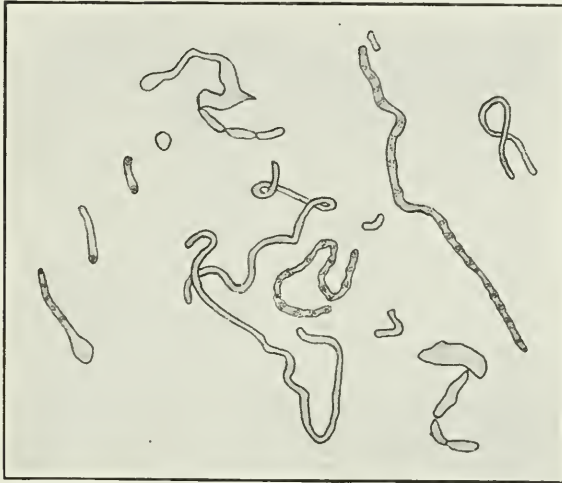
Fig. 2.—Free-hand drawing of smear from first culture of spinal fluid, Gram-negative irregular unbranched threads and other irregular forms.
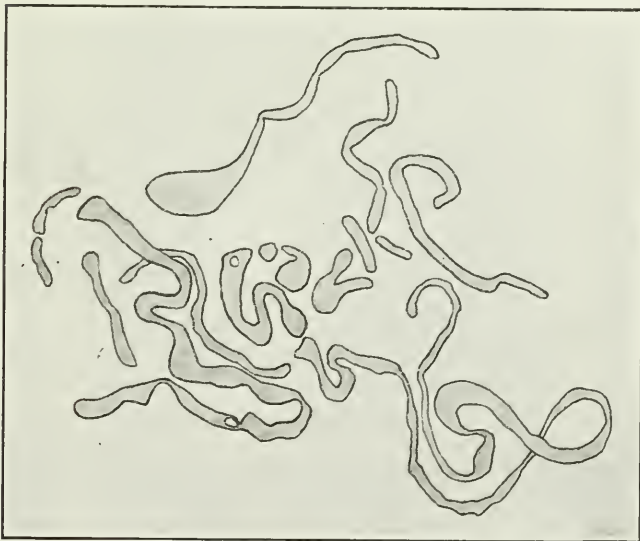
Fig. 3.—Free-hand composite drawing of smear from one of first cultures, Gram-negative irregular unbranched threads and other irregular forms. Some of the threads show Gram-positive bodies.

forms sometimes clubbed and slightly curved, nearly always with Gram-positive ends and segments: rarely forms not taking the

Gram-stain (Fig. 6). When stained with phenol-fuchsin and lightly decolorized by 10 per cent hydrochloric acid the ends and segments were acid-fast. The organism was kept alive for over two months
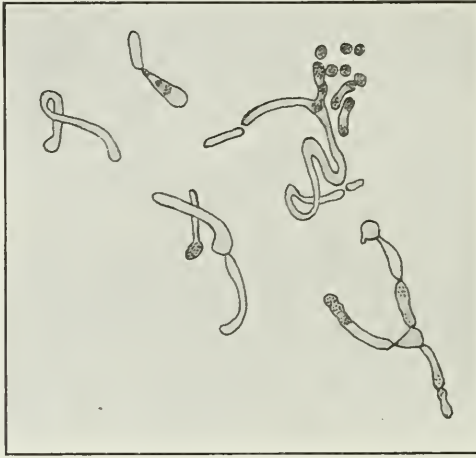
Fig. 4.— Free-hand composite drawing of smear from one of first subcultures showing Gram-negative threads, some containing Gram-positive bodies; some show apparent branching.
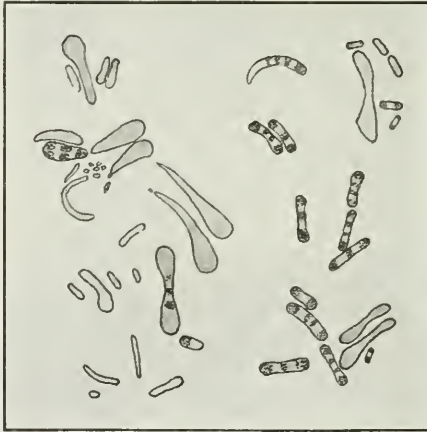
Fig. 5.—Left—Free-hand composite drawing of smear from one of later subcultures, showing clubbed Gram-negative bacillary forms, a few Gram-positive bodies.

Right—Free-hand composite drawing of late subcultures showing bacillary forms, often slightly curved or clubbed, usually with marked Gram-positive and slightly acid-fast bodies, occasionally Gram-negative forms.

on blood agar and plain agar, and it never reverted to the bizarre thread-like forms seen on first culturing.

The organism grew equally well aërobically and anaërobically.

It produced no changes in purple milk. It did not ferment dextrose, mannite, lactose or saccharose in broth with litmus indicator after ten days of incubation. It produced no changes in Russell double sugar medium with Andrade indicator. It did not cloud broth but formed a very slight sediment. It did not liquefy gelatin; grew along the entire needle track as small, discrete, yellowish-white colonies from about 0.2 to 0.5 mm. diameter. In its growth on solid mediums it never produced a confluent growth, always appearing as small, discrete colonies. It showed no motility in hanging-drop preparations.

Cultures from the original spinal fluid yielded no growth after having been kept at room temperature for three days. At first the subcultures were transferred daily, but some of the later subcultures remained viable for two weeks.

A Loeffler slant of one of the first cultures was inoculated intravenously into the ear vein of a rabbit and the animal remained perfectly well. A Loeffler slant of one of the first cultures was inoculated intraperitoneally. The animal remained well and at the end of a week was sacrificed. No pathology was seen in the peritoneum or elsewhere. Cultures from the peritoneum remained sterile. Subsequently another cavy was similarly inoculated with an agar slant of strictly bacillary forms. This animal remained well and was killed at the end of a week. It showed no pathology, and cultures from the peritoneum remained sterile.

Once the bacillary forms were planted in human cerebrospinal fluid. The fluid remained clear but contained a slight sediment, as in the case of broth cultures. Its morphology was unaltered in the spinal fluid or in cultures made from it.

Comment. As this organism does not appear to be strictly identical with any of the named organisms with which we are acquainted, or of which we have found descriptions, we suggest for it the name Corynebacterium trichodiphtheroide, in allusion to its original thread-like growth and its subsequent marked diphtheroid appearance. Even at the risk of making synonyms it seems better to bestow binomial names on unusual organisms than to refer to them as members of certain more or less evident groups. Bacteriological literature contains many examples of well-described species which have not been named by their describers. Corynebacterium trichodiphtheroide falls in Mellon's subgroup Bacillus hoffmanii, but it is certainly quite unlike the usual so-called Bacillus hoffmanii.

Bergstrand's[4] unnamed corynebacterium isolated from a case of lymphatic leukemia appears to be very similar to Corynebacterium trichodiphtheroide in its morphology. Spirillary forms, however, were not found in our cultures. There are marked cultural differences such as the absence of clouding and of pellicle formation in

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[4] Acta medica scandinavica, 1920, liii, 209–302, plates 1 to 4.

broth and the ready growth in gelatin stab and the ability to grow anaërobically in the case of the present organism. Bergstrand did not think his organism possessed pathogenic properties.

Italian literature[5] contains several articles describing cases of meningitis due to unnamed thread-like organisms. Most of them occurred in infants, but a few were found in older children as complications of epidemic cerebrospinal meningitis. The organism we have described above presents some points of resemblance to those of the Italian authors, differing chiefly in its marked production of bacillary forms and in the readiness with which it grew on plain agar. The Italian organisms were much more thread-like. It is not impossible, however, that they may represent stages of diphtheroid organisms.

Corynebacterium trichodiphtheroide appears to have certain points of resemblance to Smith's[6] Bacillus actinoides and to Actinobacillus lignieresi of Brumpt.[7] The diphtheroid organism recovered by Dick[8] from a case of meningitis was strictly bacillary and of the type so commonly referred to as "a diphtheroid."

We do not think that this and the other thread-like organisms found in cerebrospinal fluid constitute a primary cause of meningitis, but probably represent cases in which the organisms have gained access to the meninges from some focus elsewhere in the body and that the meningeal symptoms have dominated the clinical picture.

Summary. A diphtheroid microörganism named Coryenbacterium trichodiphtheroide was isolated as the causative agent in a case of purulent meningitis developing in an infant suffering with bronchopneumonia. It appeared as a small bacillus in the spinal fluid, grew into irregular thread-like forms on first culturing, later becoming bacillary with Gram-positive polar bodies and segments of diphtheroid type. It was not pathogenic for rabbits or cavies.

[5] Rutelli, A.: Pediatria, October, 1915, xxiii, 713–716, Figs. 1 to 3.   Fabris, S.: Pediatria, 1920, xxviii.   Khàrina-Marinucci, R.:   Pediatria, 1918, xxvi, 11. Sindoni, Maria: Pediatria, 1916, xxiv, 530–539.

[6] Jour. Exp: Med., 1918, xxviii, 333.

[7] Précis de parasitologie, 1913, 2d ed., pp. 963–964.

[8] Loc. cit.

REVIEWS.

THE pronounced changes that have occurred within the last few
years in the subject of dietetics would certainly seem to make it
essential that some authoritative discussion of this subject should
be made available to the physician. Within a comparatively short
time we have seen the introduction of marked variations in the die-
tetic treatment of diabetes and gout, the high calory diet of typhoid
fever and the newer knowledge of the deficiency diseases, to mention
offhand just a few examples of the changes that have occurred in a
comparatively short time, and which differ materially from the treat-
ment of a few years ago. Furthermore our knowledge of the chem-
istry of foodstuffs has also materially changed in the last few years.
We know more about the constituents of food and their metabolism
by the body than we did a short time ago, while our knowledge of
those indefinite substances known as vitamines has developed
entirely within the past few years. In spite of the fact that much
of this material is contained in the first edition, published three
years ago, yet such changes have occurred in this time that an
extensive revision is deemed necessary in order to keep the book
contemporaneous with present-day knowledge.

The book is divided into four parts. The first part deals almost
entirely with the subject of foods and normal nutrition. The second
part describes foods alone. The third part deals with feeding in

infancy and childhood, while the last part of the book presents the interesting subject of feeding in disease. The book is of undoubted value. The subject-matter is well presented, clear-cut and decisive. Criticism might be made of various minor points, for example, in the treatment of hyperacidity it is an open question whether proteins are not valuable in at least a certain number of cases. In the treatment of anemia much stress is paid to the free ingestion of milk, carbohydrates, and proteins and but minor note is paid to the iron-carrying types of food, the vegetables. The green vegetables are mentioned but with insufficient specificity to be of value in a book such as this. Likewise it would seem that the authors might have omitted some of the older dietetic regimina which have been largely discarded, in line with their expressed endeavor to delete obsolete matter.

The authors have done their work well. The previous edition was good but the thorough revision has enhanced the value of the work immensely. Particularly praiseworthy is the new chapter on feeding of children over two years of age; while also worthy of commendation are the numerous tables at the back of the book, time-consuming to compile but time-saving to the physician, because of the ease with which one may refer to them.   J. H. M., Jr.

DISEASES OF THE DIGESTIVE ORGANS, WITH SPECIAL REFERENCE TO THEIR DIAGNOSIS AND TREATMENT. By CHARLES D. AARON, Sc.D., M.D., F.A.C.P., Professor of Gastro-enterology and Dietetics in the Detroit College of Medicine and Surgery; Consulting Gastro-enterologist to Harper Hospital. Third edition revised. Pp. 904; illustrations 164; roentgenograms 48; plates 13, colored. Philadelphia and New York: Lea & Febiger, 1921.

Six years ago the first edition of this work had its introduction to the medical profession. The plan of the present edition, as before, follows the physiologic path of the digestive tract, beginning with diseases of the mouth and ending with those of the anus. Throughout, the author endeavors to reaffirm the intimate relationship between gastro-enterology and the other branches of internal medicine.

Several new colored plates and engravings have been added to this edition, while some changes and new material have been added to the text. The fractional method of investigating gastric function is rightfully noted without expression of opinion as to its diagnostic value. To the investigation of the duodenal contents is given a separate chapter, with sufficient detail and the inclusion of directions for the execution of duodenal content extraction and duodenal lavage. The popular subject of vitamines is not omitted and a good table of caloric food values has been added. In the preface a typo-

graphical error attributes a summary of our present-day knowledge of hepatic, gall-bladder and pancreatic diseases to chapters XXXIII, XXXIV and XXXV instead of XXXI, XXXII and XXXIII. A new chapter takes up the important question of flatulence, meteorism and tympanites, while another one discusses intestinal toxemia, intestinal stasis and ileal regurgitation.

The present edition still remains a splendid text-book on gastro-enterology. The sections on treatment are complete; there should be no faultfinding on this score. The whole story of gastro-enterology is told briefly and yet completely enough to make it a valuable book for all medical men.   T. G. S.

Epidemic Respiratory Disease. By Eugene L. Opie, M.D., Colonel, M.R.C., U. S. Army; Professor of Pathology, Washington University School of Medicine; Francis G. Blake, M.D., Major, M.R.C., U. S. Army; Associate Member of the Rockefeller Institute for Medical Research; James C. Small, M.D., formerly First Lieutenant, M.C., U. S. Army; Bacteriologist, Philadelphia General Hospital, and Thomas M. Rivers, M.D., formerly First Lieutenant, M.C., U. S. Army; Associate in Bacteriology, Johns Hopkins University. Pp. 398, 33 illustrations. St. Louis: C. V. Mosby Company, 1921.

The epidemic of hemolytic bronchopneumonia which followed the outbreak of measles in the various camps and cantonments in this country in 1917 and early in 1918 and the influenza epidemic which occurred in 1918 and with it the severe pneumonias that developed at the time, afforded an excellent opportunity for intensive study of these respiratory diseases. The military authorities at Washington appreciated this and selected a commission of medical men who were ably fitted to make these studies. Every facility was given them for complete work and they were afforded every opportunity to carry out extremely complete and scientific studies of these disorders. The authorities at Washington chose their men well and from their past record in civilian medicine probably no better men could have been selected to carry out this work. Their very extensive and detailed studies have been reported in part and are familiar to most medical men, but they have never been collected in a single volume so that they would be available for reference and where the more complete details of the work and the opinions of the authors in regard to the work could be readily reached. The present volume as it now appears fulfils these conditions. It records the laboratory studies, the clinical features, the pathology, the epidemiology and so on, of these two great causes of death in our civilian army, influenzal pneumonia and

bronchopneumonia after measles. The work is presented in a systematic, careful manner. Details of the methods employed in the study of the cases open a chapter, sample cases are reported, the work is then summarized and conclusions are drawn from what the commission has studied in this particular phase of the diseases. In this way we get an expression of opinion as to the various details of these diseases which make the work particularly valuable. Finally there is a concluding chapter by Doctor Opie in which the whole material is briefly summarized and conclusions are drawn from this summary. The book is completed by an appendix on experimental work on monkeys to determine the effect of inoculations of these animals with the Bacillus influenzæ and microörganisms that are isolated from the pneumonias of influenza.

The character of the men selected to compose this commission seems sufficient indication of the type of work they would produce, nor is this anticipation unfulfilled. The work is a clear-cut and authoritative exposition on the subject of respiratory tract infections after influenza and measles. J. H. M., Jr.

Manson's Tropical Diseases. Edited by Philip H. Manson-Bahr, Physician to the Hospital for Tropical Diseases, London. Seventh edition. Pp. 960; 462 illustrations. New York: Wm. Wood & Company, 1921.

The new edition of the manual has been revised by Dr. Manson-Bahr, with some very important changes. Perhaps the most noteworthy of these is the addition of very many illustrations, in fact, the number of these has been almost doubled. Of special excellence are the colored plates of malarial parasites; these were made from paintings done for this edition.

Several of the chapters have been rewritten, such as that on the enteric group of fevers; while in others, recently acquired knowledge, such as Noguchi's work on the leptospiræ, has been incorporated. In the chapter on plagues, the rats and fleas concerned in transmitting the disease are studied rather thoroughly.

There are now three large appendices to the work. The one on protozoölogy has been much amplified, while new sections have been added on metazoan parasites and on laboratory methods. These extensive additions will undoubtedly increase the value of the work to many practitioners. There is, however, a tendency already here manifested on the part of chapters on parasitology to grow in successive editions until they make the work exceedingly bulky and unwieldy. But this stage has not been reached by the manual; the insertion of much new matter has been made possible by

enlarging the pages without increasing their number. The book is still of very convenient dimensions.

Otherwise, the general make-up of this book follows that of earlier editions. The first section is on the fevers; the fullest treatment is accorded malaria, blackwater-fever (treated as a distinct disease), trypanosomiasis and leishmaniasis. The next part covers such diseases as beriberi, pellagra, with a new chapter on tropical scurvy. Next come the abdominal diseases, then leprosy and other granulomas, diseases produced by metazoan parasites, a new section on poisons (animal and vegetable), skin diseases and finally the appendices already referred to.

Manson's *Tropical Medicine*, while not the most complete, is probably the most generally useful work on the subject, giving all the essentials of the subject in a compact, handy and readable form. M. M.

MEDICAL CLINICS OF NORTH AMERICA. Boston Number, Vol. IV, No. 6. Philadelphia and London: W. B. Saunders Company, 1921.

PROBABLY the best feature of the Boston number of the *Medical Clinics* is the fact that each of the authors contributes an article on some subject with which he has familiarized himself and studied so carefully that his name is well known through the country as being an authority on that particular phase of internal medicine. I refer, for example, to the name of Doctor Joslin with diabetes, Doctor Christian with nephritis, Doctor Walker with hay fever, Doctor Minot with anemia, to mention but a few of the contributors on the subjects in which they are particularly interested. The intensive study that these men have made of the disease or diseases in which they are interested has made them more capable of writing with knowledge on these subjects than the average clinician who is interested in the whole broad realm of internal medicine. The presentation of such subjects by the contributors to the present number makes it extremely worth while and valuable.

J. H. M., JR.

OPTIMISTIC MEDICINE; OR, THE EARLY TREATMENT OF SIMPLE PROBLEMS RATHER THAN THE LATE TREATMENT OF SERIOUS PROBLEMS. ANONYMOUS. Pp. 302. Philadelphia: F. A. Davis Company, 1921.

A FORMER insurance man has presented to the medical profession, under the cloak of anonymity, a series of essays on things medical and medicosocial. These essays are found to be extremely inter-

esting and to present various subjects not strictly medical but with which the physician comes into close contact in his everyday life. He discusses such subjects as coöperation between doctor and patient, adolescence and the family doctor, the overworked business man, to quote just a few of the titles of the sixteen chapters which the book contains. The author's relationship with physicians has evidently been most cordial, as he is kind and generous to the physician. He avoids criticism of him and advises the person who is not on intimate terms with his doctor to become acquainted with him, and to secure his advice early, in order to obviate conditions which may cause trouble later in life. The book is intended not only for the physician but also for the layman. One might almost suggest that the author had in mind the physician's distribution of the book to the layman.   J. H. M., Jr.

DIAGNOSTIC AND THERAPEUTIC TECHNIC. By ALBERT S. MORROW, A.B., M.D., F.A.C.S., late Lieutenant-Colonel, M.C., U.S.A., Attending Surgeon to the City Hospital and to St. Bartholomew's Hospital; Consulting Surgeon to the Nassau Hospital, Mineola, L. I. Third edition. Pp. 872, 892 illustrations. Philadelphia and London: W. B. Saunders Company, 1921.

THE third edition of Doctor Morrow's book has been completely revised and entirely reset, but follows very closely the previous editions in the general scheme. Every type of modern therapeutic and diagnostic method is presented. For example, the author gives a complete section on the treatment of wounds by Carrel-Dakin method; he tells us how to do lumbar puncture; how to make the proper examination of the nose and throat, as well as how properly to insert a vaginal speculum. From these four examples it may be seen how many different types of specialties are presented. These do not include by any means all the specialties. Indeed, one might say that every type of specialty is dealt with which has anything to do with the use of instruments and in which there is not performed a major operation. The book is not sufficiently complete for a man doing any particular line of work, but will aid very materially those engaged in some other line at times called upon to wander from his beaten track, or the man in general practice in performing diagnostic or therapeutic procedures in which he is not thrown actively into contact or meets with frequently.   J. H. M., Jr.

PROGRESS

OF

MEDICAL SCIENCE

SURGERY

UNDER THE CHARGE OF

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On Ununited Fractures.—BERESFORD (*Brit. Med. Jour.*, 1921, p. 456), says that a fracture which shows no evidence of bony union at the end of twelve months may be regarded as a case of non-union. Normal bone—merely specialized connective tissue—is constantly undergoing steady processes of absorption and reformation, like all other tissues. There is, however, a special method for absorption—the osteoclastic. Moreover, factors which stimulate osteoclastic processes, increase in like measure bone-forming elements—the osteoblasts, which in early stages are not distinguishable from fibroblasts. It is, therefore, not surprising that fibrous union is not uncommon. Pituitary secretion particularly produces hypertrophy of interstitial bone while the thyroid gland also has an important influence upon bone formation. The chief features noted on examination of the ununited fractures are: atrophy of the bone, loss of vascular supply and sclerosis of surrounding soft tissues and the bone ends. The causes can be grouped as general and local. In the first group are included some upset between osteoclastic and osteoblastic elements, disuse and defective blood supply, while in the second group, non-apposition of fractured ends is the foremost cause. Movement between apposed ends and prolonged severe infections are other causes. The most important part of the treatment will be directed to the local state, although due regard should be paid to the general condition. Massage and electricity are important to improve and maintain nutrition, while movement and use should be encouraged whenever possible with special attention to all joints and soft structures. Infection must always be cleared up, and an interval of at least three months allowed after healing. It is sometimes desirable to perform two operations in cases of prolonged infection. At the first, scar tissue is excised and the sclerosed ends of bone removed. Complete suture is immediately performed, while

the main operation is done one month later. The operation consists in attaining apposition and retaining apposition without possibility of movement between the ends. The method of actually attaining apposition will depend upon the bone and the condition of the bone ends. The methods employed are the "slot" or "dovetailing" method, the "step" method, the sliding bone-graft, and bone transplantation, the slot being filled with an accurately fitting piece of bone cut from some other bone, usually the tibia. This last is the most successful type of bone transplantation. Speed is of importance as bone dries very quickly after exposure. The uncovered parts are bathed with warm saline. In every case, the ends are securely bound together by drilling holes and using thick thirty-day catgut. The whole limb is put up in plaster, paying particular attention to fixation of the joint above and below. A radiogram, taken through the plaster may be taken in a day or so to see that all is well. After bone grafting or transplantation it is wise not to remove the plaster before the end of three months and a protective splint used for further period. The length of time of non-union, even a period of years, should not deter one from operating with a reasonable certainty of a good result.

The Indications for Cholecystectomy.—MONSARRAT (*Brit. Med. Jour.*, 1921, p. 371), says that the problem in the treatment of cholecystitis whether associated with gallstones or not is to arrest infection and obviate its recurrence. The test of successful operation for cholecystitis, is whether the infection of the bile channels clears up, the liver function returns to normal with no recurrent symptoms from inflammatory reaction or adhesions in the operation area. It has been the author's experience that a considerable proportion of cases of cholecystitis treated by drainage fail to pass this test, for ill health is suffered referable to the persistence of the gall-bladder as a centre of infection. Chronic cholangitis with chronic pancreatitis, recurrent attacks of pain and tenderness in neighborhood of the wound, gastric distention, spasm and vomiting due to the angulation of the pylorus and duodenum by adhesions are resulting conditions. For these reasons, it seems advisable to remove a gall-bladder which has been attacked by cholecystitis of any type, because patients who have had the gall-bladder removed do not suffer any demonstrable disadvantage from its absence, while in calculous cholecystitis they are relieved of the double risk of reformation of stones and persistence of bile-duct inflammation. In cases of cholecystitis without calculi, patients are relieved of a diverticulum which would in all probability prove to be the source of a recrudescence of their intoxication. Granted that cholecystectomy is a cleaner performance and not a more serious operative risk than cholecystostomy—that the gall-bladder is of no particular functional value in the human subject, that it is, moreover, the nidus of persistent infections in the biliary channels—then argument for cholecystectomy as the normal operation in cholecystitis is overwhelming.

Treatment of Syphilis.—FELDMAN (*Amer. Jour. Syphilis*, 1921, v, 268) says that the results obtained in primary lues by treating the patient before his blood becomes positive is not much better than when treatment is instituted after systemic invasion. Salvarsan will clear

up symptoms much more rapidly than mercury. The chances for obtaining a negative Wassermann reaction in cases of latent lues even in very old cases are very good and they should be treated. All early cerebrospinal cases can be cured and a proportionately large number of old cases are favorably influenced by ordinary intravenous salvarsan and intramuscular mercury injections. The advantage claimed for intraspinal treatment does not seem to compensate for its disadvantage. A negative Wassermann reaction obtained after a single course of a few months of treatment does not indicate that a cure has been effected. A comparatively large proportion of patients returned to the positive Wassermann after a period of one year without treatment. Treatment therefore should be kept up for at least one year after the first negative result and if the Wassermann is still negative at that time, treatment may be discontinued and the patient watched.

PEDIATRICS

UNDER THE CHARGE OF

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Masked Juvenile Tuberculosis.—COOKE and HEMPLEMANN (*Am. Rev. Tuberculosis*, November, 1920), in attempt to show that it is during childhood that infection with tuberculosis occurs, studied 1556 children by the complement-fixation test. The results in 116 who had manifest tuberculosis including chiefly pulmonary, meningeal and bone involvement with some cases of generalized infection, were interesting. The tests were uniformly negative in infants under one year of age, and was positive in only one-fifth of the cases between the first and second years. From the third to the sixth year the percentage of positive reactions rose to 50 and with each succeeding year it increased rapidly so that between nine and fifteen years of age 82 per cent of children with such active tuberculosis gave a positive complement-fixation test. Another group of 556 cases with no evidence of infection with tuberculosis and with negative skin tuberculin reactions gave only 19, or 3.4 per cent, positive reactions to the complement-fixation test. Only twenty well children were examined, who had been observed during an obviously active tuberculosis some years before. These children were free from all signs for from two to six years, and only two gave positive complement-fixation tests. These rather striking figures in themselves indicate that positive fixation tests accompany evidence of clinical activity in tuberculosis, and are found in relatively small proportions of children with such infections. In 131 cases of masked juvenile tuberculosis no case was seen under one year of age, and only five in the second year. After two years of age there was an increasing proportion of positive reactions to 50 per cent from the second to the fourth years and to 95 per cent for from the twelfth to the fifteenth year. In 116 children

over four years of age, 76 per cent were positive.   In another group in which the only evidence of tuberculosis was a positive skin reaction only 16.6 per cent gave positive complement-fixation tests.   Roentgen-ray pictures in 117 children gave deviation from the normal in all.   The characteristic clinical picture of masked tuberculosis is history of frequent colds and coughs, attacks of unexplained fever, anorexia, loss of weight, and asthenia.   On physical examination more or less malnutrition, anemia, and chest signs referabe to enlarged tracheobronchial nodes are found.   In certain instances there may be in addition phlyctenular disease or skin tuberculosis.

Observations on the Capacity of the Stomach in the First ten Days of Postnatal Life.—SCAMMON and DOYLE (*Am. Jour. Dis. Children*, December, 1920) found that the average physiologic capacity of the stomach in the first day after birth is about 7 gm.   This practically doubles in the second day, quadruples in the third day, and increases almost seven times in the fourth.   After the fourth day the increase is much slower, and the average capacity on the tenth day is 81 gm., or over eleven times that of the first day.   The average maximum physiologic capacity increases in much the same manner as the average physiologic capacity.   It is about one-fourth greater than the average physiologic capacity on the first day, about two-thirds greater on the second day.   After that the difference between the two measures decreases rapidly until the sixth day, after which the average maximum capacity remains about one-third greater than the average capacity.   The relative physiologic capacity increases in much the same way as the absolute physiologic capacity.   It is equal to 0.21 per cent of the birth weight of the body on the first day, to 1.38 per cent on the fourth day, and to 2.43 per cent on the tenth day.   The relative maximum capacity is equal to 0.27 per cent of the initial body weight on the first day, to 1.96 per cent on the fourth, and to 3.17 per cent on the tenth day.   In the first ten days the parity has no constant effect on the physiologic capacities of children having an initial body weight of from 2000 to 4000 gm.   Sex has no effect on the physiologic capacity in this period. The average deviation in physiologic capacity rises rapidly from the first to the fourth day.   After that it increases slowly.   The percentage decreases rapidly until the fifth day, and after that continues to drop very slowly.   All indices of physiologic capacity indicate that there is a distinct change in the nature of this value after the fourth day.   Until this time the increase in capacity, in whatever manner it is calculated, is very rapid and afterward it is much slower.   In the first four days the average deviation in capacity is increasing rapidly, and percentage deviation is decreasing rapidly.   After this time both of these measures change very little.   The anatomic capacity of the stomach at birth averages 33 c.c.   This is increased about one-third in the first three or four days, and is little more than doubled in the second week.   There is no indication of two definite stages in the development of anatomic capacity in the neonatal period corresponding to the two phases of physiologic capacity.   Anatomic capacity and physiologic capacity approximate one another about the fourth day.   After that physiologic capacity runs parallel to the anatomic capacity, but is slightly greater. This agrees with previous findings regarding this relation throughout

the greater part of the suckling period. The curve representing average physiologic capacity in the first ten days of postnatal life shows two phases. The first segment, from birth to the fourth day, shows little relation to the actual capacity of the organ, but is rather a measure of the ability of the average mother to furnish nourishment in this period, and the ability of the average child to receive it. The second segment, extending from the fourth to the tenth day, is probably a fair measure of the actual increase in gastric capacity compared with similar increases of this value made at later times in the suckling period. The gastric capacities of children weighing 4000 gm. or over at birth are somewhat different from those of infants of lighter weights. Both the average and the maximum average physiologic capacities of this group are smaller than those of children of lighter weight in the first three or four days of postnatal life, but these values increase rapidly in the fifth and sixth days, and before the end of the period exceed those of smaller infants. Parity has a slight but distinct effect on physiologic capacity in this group of larger infants, and first-born children have a smaller capacity than do the later-born. The anatomic capacities of children of this group are somewhat greater absolutely, but smaller relatively than in children of the lighter group.

Empyema in Infants and Young Children.—SPENCE (*Am. Jour. Dis. Children,* December, 1920) says that the mortality in infants and very young children is high with all methods of treatment employed. About 11 per cent of all of the cases of pneumonia in the Babies' Hospital in New York during the past seven years either had empyema on admission or developed it during their stay in the hospital. The mortality rate decreased very rapidly as the age of the infant advances. Empyema was the sequel of pneumonia in every case of this series. When pneumonia is a complication of the common infectious diseases of childhood, the mortality is very high. Pneumococcus in pure culture was present in the pus from the pleural cavity in 70 per cent of the cases. The mortality from this type of infection was the lowest in the series. The degree of leukocytosis is no guide to prognosis or to diagnosis. In this hospital siphon drainage gave better results than any other form of treatment.

A Study of the Blood and its Circulation in Normal Infants and in Infants Suffering from Chronic Nutritional Disturbances.—UTHEIM (*Am. Jour. Dis. Children,* November, 1920) found in this study that the serum protein in normal infants was from 6 to 6.5 per cent. and remained at this level until the tenth or eleventh month, when the protein began to rise, and by the fifteenth month it had reached the same level as found in adults, about 8 per cent. Infants suffering from various diseases showed, with the exception of the exudative diathesis and nephritis no remarkable change in blood protein concentration, while infants with acute diarrhea or vomiting had a high percentage of protein, the result of blood concentration. Premature infants and athreptic infants showed a low protein percentage in the blood, in many cases as low as 4 per cent. This condition in premature infants is an expression of the influences of age and development on the water metabolism of the organism. As far as the athreptic infants were concerned, the low pro-

tein in some cases seemed to be due to lack of power on the part of the organism to build up protein, and in other instances to the overfeeding with carbohydrates. The high water content of the organism in both premature and athreptic infants must be regarded as an important factor in the low immunity they show, thus predisposing these infants to multiple infections. Besides this high water content of the organism, the athreptic infants showed a very low rate of blood flow, which in some instances was due partly to the diminished blood volume, and in other instances to constriction of the peripheral small vessels in order to accomplish the distribution of the blood to the internal organs. This constriction of the peripheral vessels is proved by the differences found in the blood count and hemoglobin content between capillary and venous blood. The low blood flow is not usually accompanied by a lowering of blood-pressure because of compensatory factors such as diminution of the blood bed by atrophy of the skin, subcutaneous tissues and musculature; by contraction of the small peripheral vessels; and by possible change in the alimentary bloodvessels. This low rate of blood flow will contribute in lessening the resistance of these infants by depriving the body tissues of the necessary food, and in this way contribute to the breakdown of the body cells. Experiments on rabbits have shown that during complete starvation with deprivation of fluid, the body volume falls below the normal value for the body surface as a result of water loss from the blood. By giving only food and water to prevent further weight loss the blood volume is rapidly restored and quickly reached a value above normal for the body surface. When these findings are applied to infants it can be seen that in athreptic infants who show a lowering of blood volume all the above-mentioned factors will still further affect the organism, and all factors will work together in lowering the oxidizing power of the body cells and favor a breaking down of body tissues.

A Method of Determining the Appropriate Dose of Tuberculin for the Individual Tuberculous Child.—Solis-Cohen (*Arch. Ped.*, November, 1920), in determining the appropriate dose of tuberculin for the individual child, first makes the test for tuberculin hypersensitiveness. He injects intracutaneously into the patient's forearm at the same time $\frac{1}{100000000}$ mg. distally, $\frac{1}{1000000}$ mg. medially, and $\frac{1}{100000}$ mg. proximally, the injections being made in a diagonal line. This is done to avoid the same lymph channels, and there is less danger of the lymphatics carrying tuberculin from the large injection to the smaller. Twenty-four to forty-eight hours after the injections are made, their sites are examined for the presence of a papule or for induration, either of which is regarded as evidence of a reaction. If no reaction occurs $\frac{1}{10000}$ mg., $\frac{1}{1000}$ mg. and $\frac{1}{100}$ mg. are injected into the other arm in the same manner in which the first injections were made, the smallest dose being distally and the largest dose being proximally. If still no reaction occurs, $\frac{1}{10}$ mg., and 1 mg. are injected, and, if necessary at a still later time 10 mg. are injected. The smallest dose that produces a distinct reaction is administered therapeutically either by mouth or subcutaneously. The initial dose determined in this manner has never produced any untoward reaction in the hands of the author, although in some cases it was as high as $\frac{1}{100}$ mg. If this dose produces

a favorable reaction such as increase of appetite, reduction of temperature, a general feeling of improvement it is repeated every three to five days until it loses its effect, when it is gradually increased until it again produces a favorable reaction. If it seems to produce no effect, it is repeated for several weeks and then increased. If any dose produces an unfavorable reaction such as rise of temperature, anorexia, malaise and the like, it is reduced. At intervals tests for hypersensitiveness are again made in the forearm, by injecting the dose that the patient is taking, and doses of $\frac{1}{10}$ of and ten times this amount. If no reaction occurs from any of these doses doses of one hundred times and ten thousand times the amount the patient is taking, are injected. If the amount producing the intracutaneous reaction is greater than the amount being given therapeutically, the latter is increased rapidly until it corresponds to the former. The writer has used the method mostly in children, and has given tuberculin Rückst (T.R.), because in his experience he has obtained the best reaction from this form. It does not seem to make any difference whether the tuberculin is given by mouth or subcutaneously. Some patients do better on one and some on the other method. He does not as a rule give tuberculin to patients who are doing well without it.

OBSTETRICS

UNDER THE CHARGE OF

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The Significance of Diphtheria Bacilli in the Body of the Mother Infecting the Child.—LÖNNE (*Zentralbl. f. Gynäk.*, 1920, No. 37) has made investigations in the clinic at Göttingen to determine the possibility of infection in newborn infants from diphtheria bacilli in the birth canal of the mother. It is well established that diphtheria bacilli are often present in the mouth and throat of persons apparently well. Very frequently patients suffering from slight sore-throat show the presence of these infected germs. Patients recovering from diphtheria frequently have the diphtheria bacilli in the urine. Evidently in both these cases it would be possible for the mother to infect the child. Regarding infants it must be remembered that nurses and attendants in hospitals and private houses may be diphtheria carriers. This has happened in a number of cases and it can readily be seen that under such conditions infants might easily become infected. As to the length of time during which diphtheria bacilli can exist in the human body after apparent convalescence, an instance is recorded where the diphtheria bacilli were found ninety-two days after a patient's recovery from the disease, and not infrequently from sixty-three to eighty-four days after the first positive result of examination for the diphtheria germ. As late as ten weeks after an attack of diphtheria, patients may pass the characteristic bacilli in the urine. In the case of infants, in two well-established instances, diphtheria germs gained access to the umbilicus after the separation of the cord. Again in

some cases, infants suffering from the presence of diphtheria germs in the umbilicus may be admitted to nurseries and thus infect other children. Sittler reports a case where diphtheria bacilli were found on the nipple of a nursing mother. It is more than probable that a diphtheritic infant might infect the nipples of a nursing mother. Cases have been observed where diphtheria bacilli were present upon ulcerated surfaces in the genital canal in women recovering from labor. Bumm and others have demonstrated the presence of diphtheria bacilli in the vagina in a pseudomembrane and the inference is a natural one that diphtheria bacilli in these cases could readily be conveyed to the newborn. In order to make further tests of the matter, the writers examined thoroughly a considerable number of patients in their clinic. In all 42 healthy patients were examined and from each one several smear cultures were made. In none of these cases could the characteristic diphtheria bacillus be recognized. Bacteria were found which at first sight very closely, at least, resembled the so-called diphtheria germ, but, on closer examination, these were classified as pseudo-diphtheria bacilli. In one case where a pure cultur- and smear preparations pointed to a positive diagnosis, inoculation on animals was practised without reaction. The growth on agar did not indicate diphtheria. The writers believe that a positive diagnosis of vaginal diphtheria or of the presence of the diphtheria bacilli in the vagina can be made only when smear cultures show positively the characteristic germ and when in unselected cases a pure culture can be obtained. They do not deny the possibility of the presence of diphtheria bacilli in the genital tract of healthy pregnant women, but they believe that such must be a rare occurrence. In their experience it is much more important to scan closely those persons who act as nurses and attendants in nurseries and hospitals containing infants. The throats of these persons should be thoroughly examined and oftentimes in them will be found the source of infection. They would have, if possible, an isolation room for all children brought to an infants' hospital, where a child could be retained under observation until it could be positively determined that infective disease was absent. It is, however, difficult on account of the expense and room required to carry out such a provision.

Syphilis in Pregnancy and Labor.—CORNELL and STILLIANS (*Am. Jour. Syph.*, 1920, No. 4, p. 342) draw attention to the fact that there is great difference of opinion concerning the frequency of syphilis. Some place it as high as 16 per cent, others as low as 3 or 4. Such differences can be explained by the kind of material which has been the subject of study. In a dispensary resembling private practice, every patient was examined by the Wassermann test. If syphilis is as frequent as indicated by the high percentages, there must be many mistakes in diagnosis. Sixty-nine patients were so examined, 2 giving a strong positive and 1 a weak positive reaction. The strong reactions were obtained in negro women and one-half of them were evidently syphilitic. Twenty-six per cent of these patients gave a history of abortion or stillbirth. The reason for this condition did not become evident in the investigation. Of the pregnancies occurring among these patients, one-third of all resulted disastrously. This is frequently caused by poor living conditions and lack of prenatal care

among the poor. Those who have no proper attention frequently possess poor teeth, tonsils which are infected, chronic appendicitis, chronic inflammation of the gall-bladder. Among private patients, about 20 per cent. gave a history of abortion or stillbirth. DOUGAL and BRIDE (*British Med. Jour.*, 1920, No. 1, p. 632) studied 100 unselected cases of abortion to ascertain the cause. In most of the cases pregnancy was interrupted during the first half. In about 40 per cent. between third and fourth months. There had been no previous pregnancy in 17 per cent; 80 per cent had born children at term and one-third of the patients had had more than three pregnancies. Previous abortion had occurred in 49 per cent., but most of them had but one abortion. In searching for the cause among 28 patients, there were mechanical causes in 13, the action of lead in 8, in 2 shock, in 1 a kick in the abdomen, in 1 an injury to the foot, in 2 the use of a syringe or some instrument and in 1 unusual disturbance. There were 22 cases in which a local condition seemed to be the cause. Among these 5 had an abnormal position or shape of the uterus; in 2 there were fibroid tumors; 3 had had abdominal sections previously; influenza had attacked 3 and 2 had placenta previa. There were 7 patients who had various medical conditions. In 12 cases, the positive Wasserman reaction was found and in 6 there was no other apparent cause. In over half of the cases what seemed to be an adequate cause for the accident could be determined. So far as the pathology of the condition was concerned, hemorrhage into some portion of the embryo or ovum was usually present. It is interesting to note that of the 12 cases giving a positive reaction for syphilis, 11 had already had children at full term. It could not be shown that there is any association between a positive Wassermann reaction and repeated abortion. Probably syphilis is not responsible for more than 10 per cent. of abortions. In summing up their observations, the authors find that in 18 per cent. there was an accidental or reflex cause; in 25 per cent. some constitutional condition of the mother or disease or displacement of the uterus or some pronounced change in the embryo and its appendages. Of all abortions 20 per cent. are produced by the patients themselves. When all things are considered, it becomes evident that the precise cause of abortion cannot be ascertained in about one-third of all cases.

The Relation of the Insertion of the Round Ligaments during the Expulsive Period of Normal Labor as Indicating Uterine Ruptures.—AUER (*Zentralbl. f. Gynäk.*, 1920, Nr. 38), in the clinic in Bonn has studied cases of labor to observe the position of the point of insertion of the round ligaments. He describes the case of a primipara, aged twenty-nine years, with flat and rachitic pelvis, who entered the hospital after the rupture of the membranes. The child was in second position, the head movable above the pelvis. On internal examination, the membranes had partly refilled and one could not make out the sutures and fontanelle. There was a double promontory and partial dilatation. The true conjugate was approximately 8 cm. During the night following admission very little progress was made in the labor. The head was still movable above the pelvic brim; the back was still to the right and the lower segment had distended, but

was not sensitive on pressure. The point of insertion of the round ligaments could be plainly felt on both sides, at a lower level than the umbilicus, the left two fingers' breadth higher than the right. As the head had not made its way into the pelvis, it was determined to use Walcher's position. After several hours, the lower segment on both sides became sensitive to pressure, the round ligaments were as large as the finger. On internal examination, the lower portion of the head was impacted at about the middle of the pelvic brim. The sagittal suture was near the promontory, the smaller fontanelle on the left side and toward the front. As there was no signs of spontaneous labor the patient was delivered by Cesarean section. The child weighed 38.7 grams, was 53 cm. long and correspondingly developed in all portions of the body. The point of interest in the case from the point of study made by the writers is the very high position of the round ligaments and the fact that when this can be recognized, it points to overdistention of the uterus and the danger of rupture. Further investigation shows that of 100 spontaneous labors, in 36 per cent the point of insertion of the round ligaments was above the umbilicus, either just before or actually in the expulsive period. Of these 100, 28 had the round ligaments higher on one side than on the other. In the majority of cases, the line made between the round ligaments was oblique. In most of the cases the line between these cases was oblique, in 71 primiparæ 48 times, 29 multiparæ 15 times and more often higher upon the left than upon the right side. Contrary to what is often believed, the same thing has been observed during the stage of dilatation and this at a time when actual delivery was still somewhat remote. In a series of 10 cases in which this phenomenon was very evident, the points of insertion of the round ligaments on both sides were three fingers' breadth above the umbilicus in an oblique direction more than three hours before the forceps was applied. In a case of spinal deformity, six hours before the patient was delivered by forceps the round ligament was two fingers' breadth above the umbilicus. In a case of highly deformed, rachitic pelvis, delivered by Cesarean section, in labor two days, twenty hours before the actual birth of the child, the same phenomenon could be observed.

The Causation and Diagnosis of Tubal Pregnancy.—HIRSCH (*Zentralbl. f. Gynäk.*, 1920, Nr. 38) draws attention to some points in the etiology and diagnosis of tubal pregnancy. He describes three different points of diagnosis: First, when the patient under observation is put into bed, an ice-bag over the abdomen, and given opium, it is possible to clear the outline of tumor made by the abdominal condition and thus to separate it from the surrounding tissues. The second point for diagnosis in tubal pregnancy consists in the muscular action produced by large doses of preparations of ergot. The writer used secacornin; some have employed preparations of the pituitary gland. If the pregnancy is tubal, these substances do not cause the bleeding to stop. If the pregnancy is intra-uterine, these injections will stop the hemorrhage. A third symptom of value is the frequent appearance together of tubal pregnancy and ovarian cyst. Frequently while the case of tubal pregnancy is under observation there may develop a cystic swelling of the adnexa. This may be thought to be an increase

in the size of the tubal pregnancy produced by hemorrhage into the tube and it may be considered as a tubal abortion. When the case comes to operation, it is found that this cystic swelling was a cyst of the corpus luteum. In 18 cases of tubal pregnancy, Opitz found 7 corpus luteum cysts and Fraenkel has observed one of these cysts to from three or four ectopic gestations. The writer has nothing to say concerning the reason for these phenomena, but has observed them and so have others.

GYNECOLOGY

UNDER THE CHARGE OF

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The Problem of Cancer Control.—One of the most earnest students in this country, perhaps in the world, of the subject of cancer control, especially from the statistical standpoint, is FREDERICK L. HOFFMAN, whose book on the subject of cancer statistics is a masterpiece, of which he may well be proud. In a more recent article (*Minnesota Medicine*, 1921, iv, 124), he states that the cancer problem is as baffling today, if not more so, as it has ever been. The subject is becoming more ramified as research in one direction or another proceeds and as new problems arise, or new discoveries are made. No one can today lay claim to a thorough grasp of the whole subject further than in broad outline, and even that is a task of considerable difficulty. When the Society for the Control of Cancer was formed, it was clearly realized that the main objective of its propaganda should be to arouse the general public to the menace of cancer increase and the hopeful effects of early diagnosis and surgical treatment in the early stages of the disease. It was for this reason decided not to call the society one for the prevention, but rather for the control of cancer. In other words, the aim of the society is to bring about a reduction in the death rate from cancer as the results of early methods of treatment, whether surgical or otherwise. Nothing of value is known at the present time that would justify the belief that cancerous processes can be prevented: but the knowledge of precancerous conditions leads to earlier diagnosis and treatment at a stage when the prognosis is generally quite favorable. Regardless of what the Society has done, and it has done much, there has not as yet been a marked effect on the cancer death rate. In some localities where the campaign has been most effective, the rate has unquestionably declined, on account of cases coming earlier to operation. But, in a general way, it may be said that the vast majority of cancer operations still take place when the disease has reached an inoperable condi-

tion. Cancer is not only one of the most important causes of death, but the disease is increasing from year to year practically in all civilized countries. In the continental United States it may be conservatively estimated that during the past year there were not less than about 90,000 deaths from malignant disease. On the basis of an earlier estimate, the approximate number of deaths from cancer is divided somewhat as follows: stomach and liver, 32,000: female generative organs, 12,500: peritoneum, intestine and rectum, 11,000: female breast 8500: cancer of skin 3500: cancer of the buccal cavity, 3500: and of other organs or parts, 13,000: a total of 84,000. This statement illustrates the wide diversity of the cancer problem and emphasizes the importance of considering the cancer question in detail, rather than in general terms, for methods of treatment applicable to one form of cancer may be wholly inapplicable, or partly so, to another form. The statement also illustrates the great importance of accurate death certification. It is lamentable that so many certificates should be sent in containing merely the term "cancer." It is obviously of the first importance that. the organ or part of the body affected should be stated, for it will not advance the cause of cancer control to deal with statistics limited to cancer mortality in general terms. It, no doubt, entails a certain amount of additional labor on the part of the doctor to fill out a certificate in detail, but by doing so much subsequent and more burdensome correspondence is avoided. The cancer death rate in the continental United States has been increasing from year to year, at the rate of about 2.5 per cent. per annum. There is no corresponding increase in the death rate of any other disease or group of diseases, and considering the vast amount of useful knowledge concerning the cancer problem, the increase reflects a lamentable apathy on the part of both the public and the medical profession toward the problem of the earliest qualified diagnosis, followed by the earliest radical method of treatment. Since the propaganda for cancer control is largely limited to urban communities, it will be of interest to point out that the cancer death rate of twenty representative American cities increased from a rate of 72 per 100,000 in 1904 to 89 per 100,000 in 1914 and to 94 per 100,000 in 1918. Hoffman insists that this increase is real and not apparent. In fact, he states that the true increase in cancer liability is much greater, for operative interference has in the meantime increased materially in efficiency. If it were possible to ascertain the number of successful cancer operations during the course of a year and, by means of a follow-up system, the number of successful cures within a given period of time, it would become clearly apparent that the liability to cancerous affections is possibly today 50 per cent. greater than it was fifteen years ago. The control of the cancer death rate is primarily a surgical question for unless the offending cancerous mass is promptly removed in the early stage of the disease, death is a foregone conclusion. Hoffman directs our attention to the fact that the negative side of the cancer question is as important as the positive side. It is as urgent that we know or understand why cancer does not occur in certain races or in certain sections, as why the rate should be one of extraordinary and exceptional frequency. Cancer, for instance, practically never occurs among our native Indian tribes and another most significant phase of the problem, also generally ignored by those who should give consideration to the question, is the very rare occurrence of cancer of the female breast among the Japanese.

Considering the question of heredity, the conclusions derived from animal experimentation are diametrically opposed to the facts, as far as known, for the human race. Cancer is certainly not inherited in human beings in the same sense as a hereditary predisposition is frequently apparent in tuberculosis. Cancer is now so common a disease of adult life that the occurrence of cancer in more than one individual in the same family may be looked upon as an unusual coincidence. The cases of exceptional frequency sometimes reported, even granting the absolute accuracy of the facts, are in the nature of abnormalities, with only a slight bearing upon the practical side of the question. There are no reasons why a cancerous predisposition should not be inherited, or, in other words, why persons living the same kind of lives, in the same kind of environment, subject to about the same external influences, should not suffer likewise from cancerous affections, but no statistical evidence is available to prove that cancer is inherited in the accepted sense of the term, all the experiments on rats, mice and guinea-pigs notwithstanding. Much is said of cancer villages, cancer streets and cancer houses. But all investigations by qualified experts have shown the fallacy of the assumption other than as previously observed, that the general environment, the topographic features, or perhaps the occupational pursuits may predispose to an excessive rate of cancer frequency. Occupational cancers are a fact and not a theory. Chimney-sweep's cancer is unquestionably a direct result of soot irritation, just as roentgen-ray dermatitis is a direct result of roentgen-ray exposure. Here also an extended discussion would be necessary to illustrate the problem from a practical point of view. Roentgen-ray dermatitis, however, may be referred to as evidence of external conditions, within our knowledge and understanding, acting as causative factors in malignant disease and there are no reasons for supposing that the true causative processes vary extensively from other forms of cancer than in occupational skin disease. An important phase of the cancer problem is the higher rate of frequency of cancer of the uterus among married than among single women. Investigation has also brought out the fact that cancer of the breast is relatively more frequent among the unmarried, and the same holds true of malignant ovarian tumors. Finally, Hoffman refers to the apparent difference in cancer occurrence according to economic status. There seems to be no serious question of doubt that cancer is more frequent among the well-to-do than among the poor: and since prosperity is practically the equivalent of hypernutrition, the conclusion seems justified that overnutrition is a predisposing factor of considerable importance. It is true that there is a divergence of opinion on this question, but Hoffman's investigations conclusively proved to him that cancer is more common among persons of overweight than those whose weight falls below the normal standard. Since poverty and undernutrition or malnutrition, go practically together there is here another neglected field where specialized research gives promise of useful results.

Incidence of Cancer in Retained Cervical Stump.—Paraphrasing Hamlet's famous soliloquy to the realm of gynecology, we might say, with respect to the type of hysterectomy that should be performed in removing uterine fibroids, "complete or incomplete" and indeed it is quite a question, since both sides have their noted advocates. POLAK

(*New York State Jour. Med.*, 1921, xxi, 45) reminds us that squamous-cell cancer primarily starts from the squamous epithelium covering the mucous membrane of the vaginal portion of the cervix; while adenocarcinoma either develops from cylindric epithelium covering the mucosa of the canal, or from that lining the glands of the cervix. These facts have a clinical significance when supracervical hysterectomy is employed as the routine procedure for the treatment of fibroid tumors of the uterus, for notwithstanding the habit of some operators to cauterize or cone out the cervical canal after supracervical amputation, the areas in the cervix from which cancer usually originates are not destroyed, and a review of the literature will show that epithelioma does occur in the retained cervical stump. The relative frequency with which this occurrence takes place should make any thinking gynecologist question the advisability of performing the supracervical procedure as routine, states Polak. During the past year, two cases of cervical cancer in the retained stump have occurred in his practice, both in married women who had borne children, after having had the supracervical portion of their uteri removed fifteen and five years before respectively, suggesting to him the idea of investigating the incidence of cancer of the cervix in fibroid tumors of the uterus. Unfortunately in this country but few clinics make serial sections of the uterus after its removal. This, however, is not the case in some of the foreign clinics where statistics show an incidence of about 2 per cent of undiagnosed cervical cancer, which more than counterbalances the increased risk which is charged against complete extirpation by those who favor routine supracervical amputation in fibroids. Comparing his own mortality in 100 supracervical amputations, against 100 total extirpations, the figures are 1.5 per cent for the supracervical procedure against 2 per cent for the total removal. In reviewing the reported cases and those reported in personal communications, the author finds that the occurrence of cervical cancer in the retained cervical stump is by no means uncommon, and as might be expected, it occurs at the age at which cancer usually attacks. As a result of his investigation into this subject, Polak concludes that cancer occurring in the retained cervix after supracervical operations for fibroids is a clinical and pathological entity and that it may be stated that cancer of the cervix occurs in approximately 2 per cent of all fibroid tumors of the uterus. The great majority of these cases occur at the cancer age, namely between forty and fifty, and in cervices that have been traumatized by childbirth operation or have been the seat of chronic cervical inflammation. The great majority occur in the portio or just within the external os and are squamous-cell cancer, hence their point of origin is not removed by coning out the cervix. The interval of occurrence, excluding those cases in which the cancer has probably co-existed at the time of the operation, has varied from five to twenty-one years after the original operation. Consequently one cannot state positively that a given case of fibroid where the tumor is removed by the supracervical method, has not or will not have cancer changes in the cervix. Polak believes, therefore, that the routine employment of supracervical hysterectomy in those fibroids which need operation should be abandoned, and that partial removal of the uterus should only be employed when the cervix is free from injury or disease in the nulliparous woman.

PATHOLOGY AND BACTERIOLOGY

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Experimental Streptococcus Empyema; Attempts at Prevention and Therapy by Means of Vaccine and Serum.—The importance of streptococcus empyema has not only decreased but has become intensified during the last year or so by its occurrence as a fatal sequel to influenza as well as in its previous relation to spontaneous bronchopneumonia and bronchopneumonia after measles. GAY and STONE (*Jour. Inf. Dis.*, 1920, xxvi, 265) undertook the present study, not simply in an effort to proceed toward a possible practical method of treating streptococcic empyema, but in a desire to contribute some information to the larger question of streptococcic immunity as a whole. The experiments were conducted on rabbits by means of a single pure strain isolated from the lung of a fatal case of bronchopneumonia complicated by empyema and pericarditis, and though culturally of the S. pyogenes group, was immunologically unclassified. Beef infusion broth, Ph. 7.2 to 7.4 and containing either 1 per cent glucose or 5 per cent sterile fresh rabbit serum was the medium employed. In counting the bacteria it was found that the Wright method, when checked by the gravimetric tests, gave accurate and consistent results. The particular strain was not markedly pathogenic for rabbits by intravenous inoculation. Attempts to increase the general invasive properties of the cultures for rabbits were unsuccessful, as were all attempts to produce bronchopneumonia by bronchial insufflation. Empyema could be produced, however, by injecting small quantities of broth cultures into the pleural cavity, particularly when subcultures from the pleural fluid of an animal with fatal empyema which had been passed through the pleura of several animals were employed. Death occurred in from one to seventeen days, the average being five days. Of 103 rabbits injected by a constant dose of a uniform passage culture, 102 showed involvement of one or both chests, with or without pericarditis. There was no evidence of an elective localizing affinity with the strain used. If sufficient amounts of killed and, subsequently, living cultures of streptococci were given over a considerable period of time, protection against empyema occurred. The total number of bacteria injected, rather than the number of injections seemed to be the decisive factor. The immune serums produced gave positive agglutination reactions at 55° C. in dilutions of from 1:400 to 1:12,800. The technical difficulties were surmounted by using a constant homogeneous suspension made by the addition of phenol in a final concentration of 0.2 to 0.5 per cent to a 24-serum broth culture. The serum of the animals in which

active immunity had been proved by intrapleural inoculation was found to vary in tropin content of from five to eighty times that of normal rabbit serum. Satisfactory precipitin reactions were obtained by the immune serums used for therapeutic purposes, the antigens consisting of extracts of ground and dried streptococci. It was shown that the immune sera which contained strong antibodies may have a preventive and curative action when given before, with and after the infecting intrapleural dose of bacteria. Attempted vaccine therapy of the localized empyema gave consistently negative results. The authors conclude that although distinct results in the prevention of experimental empyema and, in rare instances, the cure of empyema may be produced by the use of immune serum from rabbits, they have, as yet, no evidence of a sovereign or even encouraging serum therapy to offer and that no optimistic conclusions can be drawn from their results as to the possibility of protecting human beings against localized streptococcus infections or, specifically, against empyema, owing to the large amount of vaccine and the prolonged nature of treatment required.

Experimental Streptococcus Empyema; Eleven Attempts at Dye Therapy.—An interesting attempt to develop the value of dye therapy in the treatment of localized infections is described by GAY and MORRISON (*Jour. Inf. Dis.*, 1921, xxviii, 1) wherein the workers are eventually forced to conclude that "there is little certainty of the ultimate usefulness of dyestuffs as disinfectants in actual bacterial infections." The opportune availability of the pleural cavity for localized infections and the ready accessibility for any indicated subsequent manipulation were well known to the investigators so that their principal interest lay in developing an indisputable method for demonstrating the efficacy of the dyes in combating definite bacterial infection. Rabbits were the animals chosen for experimental purposes and these were injected intrapleurally with streptococci as the needs of the experiments required. The disinfectant and bacteriostatic effects of various dyes were tested out *in vitro*, not only upon the strains of streptococci but also upon B. typhosus and staphylococcus. It was shown by these means that streptococci succumb much more readily to the action of any one of a long series of dyes than does B. typhosus or even staphylococcus and that the most actively inhibitory dyes came from the triphenylmethane and acridine groups. This was true to a lesser degree when the dyes were introduced into tubes of active pus removed from involved thoracic cavities. But when introduced into the pleural cavities of living animals suffering from empyema the sterilizing powers of the dye, in dosage and concentration many times that employed *in vitro*, were insignificant and readily offered the menace of toxic action from the dye itself. It may be that the dye inhibits or kills many of the organisms but probably some are held deep in the meshes of the fibrin and these subsequently proliferate. This latter hypothesis presents because there is no reason to believe that the organisms became dye-fast. As correlative problems, the authors proved that acriflavine, the most potent dye against streptococci, does, in strong concentration inhibit phagocytosis and that the reaction upon bacterial culture is the same in the presence as in the absence of oxygen, thereby eliminating a ques-

tionable feature in the intrapleural use of the dye. The value of the dye as an adjuvant to immune serum is of such insignificant quantity as to render it almost totally impractical.

The Experimental Transmission of Encephalitis Lethargica to a Monkey.—Following the production of a hemorrhagic encephalitis in a monkey by V. Wiesner and of epidemic encephalitis by Strauss, Hirshfeld and Loewe in both monkeys and rabbits with brain emulsions and nasopharyngeal secretions, McIntosh and Turnbull (*British Jour. Exp., Path.* 1920, i, 89) reported the successful transmission of encephalitis lethargica to a Patas monkey after more or less indifferent results were obtained when material from eight fatal cases was inoculated into monkeys. In the present experiments, filtered and unfiltered human brain emulsions, which had been immersed in 33 per cent. glycerin for fourteen days were injected intracerebrally and intraperitoneally. A Macacus rhesus monkey received the unfiltered emulsion and the Patas monkey the filtered. Although the rhesus monkey showed evidence of drowsiness in about two weeks after inoculation, no inflammatory lesions in the brain could be demonstrated on necropsy. The Patas monkey, however, recovered from the inoculation in a week, but several weeks later developed a severe fit, dying nine days later. The histological changes reproduced, in exaggerated form, the chief characteristics of human encephalitis lethargica. This consisted of inflammatory infiltration, confined to the areas chiefly affected in the human disease. An emulsion of the cord and basal nuclei of the Patas monkey were inoculated into three other monkeys, one of which was developing symptoms not unlike those of the Patas monkey. The results of the inoculation of brain emulsions, from the Patas monkey were further reported upon by McIntosh (*British Jour. Exp. Path.*, 1920, i, 257). The one animal which showed symptoms, presented at autopsy acute inflammatory changes, consisting of glial proliferation, slight perivascular infiltrations of glial cells and lymphocytes as well as congestion, hyaline thrombi and multiple hemorrhages in the perivascular sheaths along with such degenerative changes as chromatolysis and protoplasmic vacuolation of the ganglion cells. Emulsions of the spinal cord and brain from this monkey were then inoculated under the dura and subcutaneously into two monkeys and three rabbits. One monkey showed no abnormal signs while the baboon appeared to be out of sorts nine days after inoculation, which condition persisted for a week and then disappeared. The animal died four months later, after a fit. Two of the rabbits presented choreiform movements. The brain sections of one of these showed a few small cellular infiltrations. At the same time a monkey, kept as a control with an inoculated monkey, developed symptoms identical with those of the inoculated animal. The author believes the spontaneous case is additional proof " that the successful transmission in series of experimental encephalitis to monkeys and rabbits has completed the experimental proof necessary to show that the disease is caused by a living virus."

The Viability and Growth of B. Typhosus in Bile.—Various workers have held conflicting views regarding the action of bile and bile salts

on the members of the colon-typhoid group of organisms, some believ-
ing the material to be bactericidal, some thinking that it is not inhibi-
tory, while others believe that some of the organisms are killed at first,
with a subsequent proliferation of the survivors. BECKWITH and LYON
(*Jour. Inf. Dis.*, 1921, xxviii, 62) attempted to ascertain the viability
of a given strain of B. typhosus in bile, as well as its ability to multiply
in bile. Seven specimens of bile, including five human, one rabbit and
one beef, were sterilized at fifteen pounds' pressure for fifteen minutes
and were seeded with two 2 mm. loopfuls of a twenty-four-hour broth
culture of a strain of B. typhosus which had been isolated from a
carrier. It was found that this organism was long-lived in the human,
rabbit and ox bile. To determine the rate of growth, four specimens
of beef bile were pooled, autoclaved as before and 100 c.c. quantities
were inoculated with 0.5 c.c. of a twenty-four-hour broth culture.
Plate determinations, according to the methods for counting milk and
water, were made at intervals of one-half, one, one and a half, two,
three, four, six, eight, twenty-four and forty-eight hours. As a control,
beef broth of the same reaction as the sterilized bile (P_h 8.4) was
inoculated and similarily examined. It was noted that the bacteria
suffered a high mortality in the early hours of incubation in the beef
bile. This was followed by a bacteriostatic action with a later "slow
but progressive proliferation,"—facts, as the authors indicate, which
confirm some of the observations of Jordan and Ecker.

**Fate of Microörganisms Introduced into Isolated Loops of the
Intestine.**— In order to test the validity of the assumption that patho-
genic organisms are killed or inhibited in the intestinal tract—particu-
larly "by the antagonistic action of the normal intestinal flora—"
EISKAMP and PARK (*Jour. Inf. Dis.*, 1921, xxviii, 67) introduced by
means of a hypodermic needle, 5 c.c. of various bacterial suspensions
into the ligated loops of both duodenum and jejunum of 26 dogs.
From within two to five or even twelve hours the animals were killed
and aërobic plated determinations were made by the dilution methods
of milk and water analysis. It was found that S. lutea completely
disappeared from both loops within two hours and B. violaceus within
five hours. S. aureus became greatly reduced in number in the jejunal
loop within three hours and disappeared from both loops within twelve
hours, as did the spores of B. subtilis, while red yeast disappeared from
the duodenal loop in twelve hours. B. typhosus was markedly reduced
in numbers within five hours. The experiment with streptococci were
inconclusive and the spores of B. anthracis were not killed. Samples
of the intestinal contents withdraw from each loop immediately after
infection of microörganisms were incubated aërobically and anaërobi-
cally and counts of these were made at the time of necropsy. Practically
no bacterial destruction was found in the incubated contents, except
in the instance of S. lutea. There was an appreciable multiplication
of S. aureus after longer incubation "in spite of the presence of
numerous, presumably antagonistic forms." The authors conclude
that many bacteria injected into isolated loops of the intestine of dogs
are destroyed in from two to seven hours, that the destruction is
not due to the antagonistic action of the normal intestinal flora and that
there is evidently a distinct antibacterial mechanism in the intestine,
the nature of which is at present unknown.

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

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The Comparative Toxicity of Thymol and Carvacrol (Isothymol).—
LIVINGSTON (*Public Health Rep.*, 1921, xxxvi, 1317) found that for rabbits
there was but little difference between thymol and the isomer,
carvacrol, though the indications were that the latter was slightly more
toxic. Work on earthworms and paramecia gave results showing no
material difference in the toxicity of the two substances. Carvacrol
can be produced much more cheaply than can thymol and has the
advantage of being readily produced in any quantity from materials
of domestic origin, while thymol is obtained abroad.

**Bacteriologic Studies of the Upper Respiratory Passages (the Influ-
enza Bacilli (Pfeiffer) of the Adenoids and Tonsils)**—PILOT and
PEARLMAN (*Jour. Inf. Dis.*, 1921, xxix, 55) state that Gram-
negative, polemorphic, hemoglobinophilic bacilli, showing a preference
for heated blood agar and revealing the characteristic property
of symbiosis, were isolated and identified in 40.9 per cent of
extirpated adenoids and in 53.9 per cent of the excised tonsils from
115 persons. In the nasopharynx they were present in 40 per cent
of 25 persons and in fewer numbers. The tonsils and adenoids, there-
fore, are foci in which influenza bacilli (Pfeiffer) commonly flourish.

**The Incidence of Pneumococci, Hemolytic Streptococci and Influ-
enza Bacilli (Pfeiffer) in the Nasopharynx of Tonsillectomized and
Non-tonsillectomized Children.**—MEYER, PILOT and PEARLMAN (*Jour.
Inf. Dis.*, 1921, xxix, 60) found that pneumococci, hemolytic strepto-
cocci and B. influenzæ were often found in the nasopharynx of normal
children. The incidence and numbers of hemolytic streptococci
and influenza bacilli in the nasopharynx is decidedly less in the
children whose adenoids and tonsils had been removed. In case of
the pneumococcus the numbers are less in the same children than in
those whose tonsils were present. The removal of tonsils and adenoids
reduces the number of certain bacteria in the oropharynx and naso-
pharynx, but does not cause their disappearance.

**The Diphtheria Bacilli and Diphtheroids of the Adenoids and
Tonsils.**—PILOT (*Jour. Inf. Dis.*, 1921, xxix, 62) studied cultures
made of the excised adenoids of 100 children and revealed B.

diphtheriæ in 12. The crypts of the extirpated faucial tonsils of the same persons harbored the bacilli in 12. When present in the tonsils the bacilli also occurred in the adenoids of the same person. In the tonsillar crypts the diphtheria bacilli were usually more numerous than in the adenoids. Two of the twelve strains were virulent; one showed attentuated virulence; three were pathogenic in large doses of the first culture while subsequent cultures were without virulence; the remainder were totally avirulent. Diphtheroids occurred in 30 of the adenoids and in 17 of the tonsils; when present in both they were decidedly more numerous in the nasopharyngeal vegetations than in the tonsillar crypts.

The Standard Treatment for Malaria.—Bass (*Public Helth Rep.*, xxxvi, 1502) regards as "most effective and practical" the following method which has been recommended by the National Malaria Committee and approved by the U. S. Public Health Service: "For the acute attack, 10 grains of quinine sulphate by mouth three times a day for a period of at least three or four days, to be followed by 10 grains every night before retiring for a period of eight weeks. For infected persons not having acute symptoms at the time, only the eight weeks' treatment is required. The proportionate doses for children are: Under one year, $\frac{1}{2}$ grain; one year, 1 grain; two years, 2 grains; three and four years, 3 grains; five, six and seven years, 4 grains; eight, nine and ten years, 6 grains; eleven, twelve, thirteen and fourteen years, 8 grains; fifteen years or older, 10 grains." The advantage of such a uniform treatment are set forth.

Some Suggestions Concerning the Bacteriological Diagnosis of Human Botulism.—Meyer and Geiger (*Public Health Rep.*, xxxvi, 1313) report the result of attempts at isolation of the botulimus organism from feces and organs of those sick of this disease or who have died of the poisoning. Details of technic are given and the prediction made that fecal examinations will prove of diagnostic value.

Suggestions for a Broader Application of Gambusia for the Purpose of Mosquito Control in the South.—Hildebrand (*Public Health Rep.*, xxxvi, 1460) calls attention to the usefulness of top minnows (Gambusia) in the control of mosquitoes. The fish are particularly useful in standing or sluggish water, but vegetation and floatage interfere with their activities. A plan is outlined for popularizing them.

ORIGINAL ARTICLES.

THE PATHWAYS OF INFECTION IN THE NERVOUS SYSTEM.

A PRESIDENTIAL ADDRESS TO THE NEW YORK NEUROLOGICAL SOCIETY.[1]

By Foster Kennedy, M.D., F.R.S. (Edin.).

Something less than eleven years ago I came to New York to undertake the duties of chief of clinic at the Neurological Institute. I had then a few American friends, whom I had made in London, but none were here; yet the amazing kindness of this country has since made the number of my friends here legion, and the honor you have done in making me your president is an index of the generosity and gentleness of your hearts toward those of different antecedents and training from yourselves.

There is a host of resemblances in the customs of the two great branches of the English-speaking peoples, but one might say with justice that the attitude toward the stranger differs on the two sides of the Atlantic—in Great Britain he is to be viewed socially with suspicion until he proves himself innocent, while in this kindly country he is accepted at something more than his face value until his actions betray him. It is a nice point, therefore, whether my position in this honorable society is to be attributed to my subtlety or to your goodness, nor should I wish for personal reasons to press these researches too closely. Instead I thank you in all gravity

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[1] Delivered February 1, 1921.

for the trust you have shown me, which I shall do what in me lies to deserve.

A few weeks ago there was held a meeting of the newborn Association for Research in Nervous and Mental Diseases, an organization fathered by this society, which will be regarded, we trust, in the next couple of decades as a really constructive effort in our branch of medicine. In this concerted attempt to investigate thoroughly a single disease picture, we discovered our strength as clinical observers and as pathological anatomists, and our need of aid from those with knowledge in other fields than our own. From the collected evidence, we gleaned the idea that epidemic encephalitis was an organismal reaction rather than a specific clinical entity; that its picture was drawn and colored probably more by the physiological function of the structure attacked than by the specificity of the virus. We examined carefully the morbid tissues of fatal cases; we explored the battlefields, but made little mention of the roads by which those stricken places were reached by the invading armies. We found that the bulk of individuals with encephalitis had evidence of an injury to the mesencephelon, to the striate bodies and to the red nucleus; we found that, most usually, the first sign of infection other than general malaise was diplopia dependent on a disintegration of function in the oculomotor nuclei, a district at first sight not easily accessible to exogenous poisons. Without speculation on this anomaly of disease incidence, those of us, who consciously deliberated on this phenomenon at all, were content weakly to ascribe to the poison, or group of poisons, responsible for the disease, unknown properties of specific chemiotropism for the nerve structures initially damaged.

This has seemed to me, therefore, an appropriate occasion on which to examine, even without detail, some of our knowledge regarding the routes by which bacteria and toxins, organic and inorganic, can achieve admission to the highways and byways of the central nervous system. In doing so, I cannot hope to tell you any new thing, but rather to refresh your memories of work done in the past and overlain by the accumulations of more recent times. It is well occasionally that we take stock of our possessions; those we have had for long grow dusty and unrecognizable, and we often fail to see how they complement and illumine our baubles acquired but yesterday. The Minotaur was found and slain in the labyrinth only by the aid of Ariadne's guiding threads, and in our searchings we must see to it that some of these be held unbroken.

The bases of our knowledge of the properties of nervous tissue, laid down almost entirely in the lifetime of our senior members, were of necessity anatomical and physiological. The notion of the ancients had to be dispelled—not so many centuries ago—that the purpose of the brain was but to cool the hot and noisome vapors

arising from the heart! Analysis of centers, tracts and functions have given us a storehouse of knowledge incredibly large indeed, when one considers the short time that has elapsed since groups of men seriously began to apply themselves to neurological problems. When, however, these were beginning to be solved little or nothing was known of infection, bacteriology was still unborn, and to explain morbid processes, men were oriented toward innate degeneration and deficiency of vital forces rather than to the guerrilla warfare, which we now know to be waged unceasingly in our bodies, between our cells and humors on the one hand and an implacable host of microscopic and ultramicroscopic organisms on the other.

The assumption of death of specific tracts and centers before the rest of the organism, of a simple vital lack in a few cells or fibers satisfied us when we were unconscious of the roles capable of being played by insidious infections; so amyotrophic lateral sclerosis, among other ills, was explained by an abacadabra charm called abiotrophy, and the great group of the myopathies was similarly incanted, though we feel ourselves now on the threshold of knowledge of their morbid courses by the portal of the endocrines.

In the presence of your retiring president it might be an impropriety in me to dilate much on this last notion, but I may submit that a consideration of the pathogenesis of the infections of the nervous system may reveal a unity of morbid process in many ailments clinically unlike, a pathological synthesis at least as valuable as the meticulous analyses of symptoms to which we have been accustomed to bend our minds.

The reaction of each of us to a given infection varies (could we but notice the variations) with the different physical personalities which we possess; perhaps—though this is a seven-league step—with the different kinds of endocrine balance in each of us! Our senses require training to detect differences between similar-appearing objects; I remember my difficulty in Russia in distinguishing one acquaintance from another, and on my return, for the first few days the feeling that I knew all the passers-by on a London street because of their general racial and facial resemblance to my friends and relations. So I believe that in the future we shall be able to perceive small individual reactions to toxins from without, reactions which we now look at but do not see. Further, just as one man differs from another in his reaction to infection, so in a single organism there is a host of unknown and little thought of circumstances which determine the incidence and distribution of the lesions—a case of Addison's disease has tuberculosis of the adrenal glands, but one would like to know why he has not a tabes mesenterica or a fibroid phthisis instead.

But such problems at present are merely exasperating, though they will be solved, and some, not improbably, in our day. A

statement of such an example, however, shows our modern wish
to be dissatisfied with the mere nomenclature of disease and our
desire to dig into the basic study of the conditions of liability and
resistance to infection in the various tissues and organs of the body.

The sentry guarding the gate by which infections most commonly
reach the central nervous system is the cilia of the mucosa of the
airways and especially, perhaps, the mucoid material with which
the mucosa is lined. Bayliss has stated that it is mucin which
protects the digestive tract from the effects of its own juices, and
it is likely that ferment action from dead or living bacteria effects
the first rent in the epithelium, giving access therefrom to the
lymphatic and blood systems. Benians has demonstrated that
Shiga's bacillus can be held alive and harmless in the organism
for months if surrounded by mucilage of tragacanth, and this with-
out the production of antibodies in the host against the bacillus.
It has been shown that bacteria in carriers are always interned in
a mass of mucus, nor have carriers usually developed an active
immunity against their potential parasite. In the British training
camps and barracks an unduly high carrier rate for the meningo-
coccus invariably preceded the outbreak of an epidemic of cerebro-
spinal fever, and a task still to be done would be to discover if there
be any relationship between susceptibility to infection and naso-
pharyngeal disease, involving a defect of mucoid secretion—an
objective to be gained not alone in cerebrospinal fever but in
epidemic encephalitis and poliomyelitis as well.

I have just said that epithelial destruction of mucous membrane
is the prelude to invasion of the lymphatic and blood systems by
bacteria and their toxins; over the respective roles of these two
systems, in conveying noxious material to the nervous system,
much recrimination has occurred. As in most controversies there
is some truth on both sides, but I believe that an examination of
the evidence will in our day dispose of neutrality of thought in the
matter. Despite the state of philosophic doubt in the minds of
Alford and Schwab, it would appear that the defensive mechanism
of the choroid gland in excluding all hematogenous material unsuited
to its purpose coupled with the anatomical continuity of the lymph
system with the cerebrospinal pons—a continuity accepted by
such observers as Halliburton and Starling—make it more than
a working hypothesis that, by the perineural and endoneural lymph
channels of the cranial and spinal nerves, toxins can reach with
unfortunate ease the cerebrospinal axis.

Twenty years ago experimenters were struck by their utter
failure to produce characteristic brain and cord lesions by the
intravenous injection of bacteria of high virulence; we are now
aware of the role played in elective filtration, to use Mestrezat's
phrase, by the choroid plexus, whereby large colloid molecules are
forbidden access to central nervous tissue—the whole group of

albumenoid toxins are thus cut off from direct invasion of the brain space; I have said *direct* invasion for these large molecules can pass easily through the walls of the capillary vessels, so breaking from the blood to the lymphatic economy. This permeability of the capillary wall is an important factor in the mechanism of many of our infections; Marie, confirmed by Meyer and Ransome, showed that tetanus toxin passed to the lymph vessels from the initial lesion, thence to the blood, thence to the motor end-plates, thence by efferent nerves to the spinal cord—and it has further been shown that if these same nerves be cut an otherwise lethal dose of tetanus can be given without any cord involvement at all; the incubation period in experimental tetanus varies in warm-blooded animals with the length of peripheral nerve tissue to be traversed, a few hours in rats to several days in the horse. When the lower segments of the cord were already the seat of experimental tetanic irritation, it has been always possible to prevent cervical implication by dorsal section, and it is interesting to note, further, that dolorous tetanus, produced by the injection of the posterior roots proximal to the ganglia, was in no instance accompanied by any sign of ventral horn irritation.

However, tetanus intoxication takes place through both the blood and lymph systems, and in experimental intoxication the poison can be demonstrated in the blood even in the earliest stages, but in a state of high dilution; it reaches the subarachnoid spaces of the lumbar enlargement in a much higher concentration through the lymph spaces of the peripheral nerves. One must notice, however, that trismus is one of the earliest signs of the onset of generalized tetanus even when the initial lesion has been in one of the lower extremities. This would seem to be an evidence of a blood-borne toxemia, though the mechanism by which the motor root of the fifth nerve is thus early irritated is by no means clear.

Might I bring to your attention in this connection that in diphtheritic nerve intoxication oculomotor palsy is a constant feature of the disease wherever the infecting focus may be in the body, and we have referred already to the very usual early infection of the third nerve nuclei in epidemic encephalitis. This special susceptibility, to react to general infection on the part of the mes-encephalic nucleus of the motor fifth nerve and on the part of the mesencephalic oculomotor nuclei, may not be due simply to an undue delicacy of these structures but may depend on anatomical avenues for invasion as yet not comprehended.

A consideration of the mass of diphtheritic infections occurring in the course of the Palestine campaign has led Walsh away from the idea that this virus is exclusively blood-borne with special affinity for discrete areas of nerve tissue, and toward a notion of the part played by the process named by Orr and Rows lymphogenous toxi-infection of the nervous system. Among the troops operating against the Turks there was an outbreak of so-

called desert sores, which in certain units of the Egyptian expeditionary forces affected 40 per cent of the men. These sores were thought to have some connection with the horse manure laid down on the desert roads, for they ceased to be a military anxiety when the army had attained the fertile plain of the Promised Land. From almost all of these sluggish ulcers Klebs-Loeffler bacilli were recovered in nearly pure culture, and a vast number of cases of peripheral neuritis ensued. The most important observation made by Walsh on this material was that invariably there was an initial local paresis related anatomically to the site of the infective focus—a circumstance in itself disposing of the idea that in such conditions the poison is entirely carried by the blood to the nervous elements; the poliomyelitic virulence of the mesenteric lymph glands of subjects, whose blood is innocuous, is another circumstance of moment in the same connection. At least two of these diphtheritic cases should be quoted here briefly: One, an artillery driver, who suffered from multiple septic sores on the thighs and buttocks and a large ulcer in the perineum also of ten weeks' duration. In the seventh week of his illness he began to experience numbness around the anus and on the buttocks. This sensation of deadness spread to the penis, scrotum, and to the backs of the thighs; a few days later there was loss of control of the bladder and rectum. Not for weeks after the appearance of these conditions did the signs and symptoms of a mild subacute toxic polyneuritis occur, by which time there was also a ready fatigue of visual accommodation. On examination, this man was found to have complete loss to all forms of sensation over the skin areas supplied by the fourth and fifth sacral roots and severe loss of sensibility over the second and third sacral root areas. It was noticed that the segmental symptoms were improving *pari passu*, with an increase in those referable to the terminal nerve twigs.

The second case I ask your leave to quote is that of a medical officer, who infected his right thumb when performing a tracheotomy upon a fatal case of laryngeal diphtheria. In seven weeks the digital wound had healed, but he began to notice numbness and loss of feeling in the affected thumb, signs and symptoms which spread to the radial part of the hand and subsequently were present in the entire hand and forearm. At the same time ataxia and loss of power developed in the right upper extremity. After these disabilities had occurred in the limb he sustained a generalized multiple neuritis, but did not experience accommodation paralysis.

Neither of these patients had any affection of the palate, in which circumstance they were identical with the other cases of paralysis following extrafaucial diphtheria.

Perhaps I might be allowed to correlate with this material, those cases described by myself as acute infective neuronitis. These occurred as a minor epidemic among soldiers in the field and were characterized by fever, peripheral neuritis and ascending signs of

involvement of the spinal roots and ganglia. In some of them the posterior roots suffered vastly more than the peripheral nerves, so that root zones of grossly altered sensibility were easily demonstrated. A constant feature of these cases was peripheral paralysis of the face and the lower muscles of deglutition. The pathological picture produced was extraordinarily akin to those obtained experimentally by Orr and Rows in their work on lymphogenous infections and the gross involvement of the spinal ganglia in my cases gives point to the suggestion that these structures may act as blocks to the centripetal transportation of lymphogenous poisons.

Severe damage to the cells of the posterior ganglia was a feature also of a series of ascending neuritides of the cauda equina, which I described with Charles Elsberg in 1913, and the arguments for the lymphogenous nature of the virus in tabes through the changes in the dorsal root entry zone are sufficiently familiar to warrant no more than a passing mention in an address already growing overlong. We should notice, however, the interesting fact that degeneration of exogenous fibers invariably begins at the point where the neurilemma leaves off and that, in fatal cases of diphtheritic poisoning, where the palate has been entirely disabled, the vagal nuclei have been found destroyed without any evidence of injury to the vagi themselves. Whether the influence of the neurilemma on the axis-cylinder be protective or nutritive, whether it be vital or mechanical or whether its role is an integral part of neural conduction is one of the major problems of neurology today. Before turning from these surface speculations on some of the avenues of infection of the central axis, we should refer suggestively to Collins and Armour's autopsied case of acute bulbar palsy in a child with mumps; and especially to a series of cases described by Wilfred Harris of chronic bulbar palsy immediately following diphtheria, clinically resembling myasthenia gravis, but differing from that condition by the absence of ptosis, dyspnea or variability of disease picture, and by the presence of muscular atrophy and the reaction of degeneration. Dr. Dana has described amyotrophic lateral sclerosis directly produced by lues; a group of patients with chronic lead poisoning suffering from the same disease has come under my own observation, and Stanley Barnes has recorded a number of patients with a chronic toxic affection of the lower motor neurone, having a tendency to slow improvement following acute specific fevers.

It is fair to suppose, therefore, that further investigation of the routes, by which infections attain the brain and cord, may reveal much regarding the pathogenesis of some nervous ailments. We can hope, however, to illuminate only a few problems by any one method. Thus an attempt, and one somehow appealing, has been made recently to show that the location of the lesion in the combined spinal sclerosis of anemia and marasmus depends ultimately on a depreciated adrenal activity operating on the spinal pial ves-

sels through the thoracicolumbar sympathetic chain. One may add that some such synthetic imagining is required to account for the so-frequent incidence of spinal tuberculosis in the fifth or sixth dorsal vertebræ. The clinical phenomena of acute multiple sclerosis suggest a perivascular outpouring of fluid into the nervous elements, to study which adequately requires more than a notion of the conditions governing osmotic pressures in living organisms, and possibly also of colloidal chemistry and the specific action of calcium ions in producing abnormal permeability of capillary vessels. Indeed, the whole question of radio-active salts on cell function might well have to be determined before a satisfactory explanation of such a well-recognized clinical process as I have just mentioned can be forthcoming.

The development of all branches of medicine has led to diversion of talent into a variety of areas as separated from each other as though each observer were in a kite balloon by himself—nor have we evolved any adequate headquarters where reports from each can be received and correlated. The modern student receives instruction in animal physiology from physiologists who never enter a ward, in chemistry from chemists often without interest in either physics or biology; structure and function in his mind are in different water-tight compartments so that in the beginning of his clinical years he is in travail to apply his knowledge to the problems before him, and must needs explain a hemianopia by a possible lesion of the bundle of Vicq d'Azyr. The same segregation of different branches of knowledge is continued into our adult professional lives. As a society for the advancement of learning we must try to arouse interest in our problems among physiologists and biological chemists, among pathologists and anatomists; we should seek to include them in our body. Their science would be more humane, our medicine more scientific. I should go even further than this, for I can see no disability but a great gain, through a new orientation, if sometimes we were to choose to lead us, a man, not of our specialty, but one of erudition in some cognate sphere, with sympathy for our state of darkness. No one can play equally sweetly on all the instruments of an orchestra and the conductor should be changed with the kind of music to be played.

In all civilizations known to us there has been a fairly regular sequence in the flowering of thought: First, there develops carving and painting and building as expressions of the human spirit, then comes literature and, last of all, science strides forward. For us, this last cycle is but beginning, and there will be time enough before the great changes are rung in the world to lay down principles, the knowledge of which may with fortune be stored up for the peoples who will come after ours. Let there be but coöperation among all kinds of us and then, "Turn you to any cause of policy, The Gordian knot of it you will unloose, Familiar as your garter."

THE EFFECT OF TREATMENT FOR SYPHILIS ON SEVERE ANEMIAS

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FOURNIER in reviewing the anemias of syphilis states that the disease causes a diminution in the percentage of hemoglobin, a decrease in the number of erythrocytes and an increase in the number of leukocytes. He recognizes five types of anemia in association with the disease: (1) the simple secondary anemia (by far the most common), (2) chlorotic anemia, (3) chlorotic anemia with leukocytosis, (4) leukemia and (5) (infinitely rare) syphilis imitating the picture of pernicious anemia.

Fournier refers to the difficulty in some cases of deciding whether syphilis is the direct cause of these modifications or whether they are the result of associated symptoms (the febrile state, symptoms of dyspepsia, nervous troubles, superimposed infections or the influence of misguided therapy). He quotes the old saying that "mercury is the iron of syphilitic anemia." However, after having corrected the syphilitic changes, mercury becomes, in turn, an alterant of the blood. For a time it does good, later it becomes harmful. Mercury cannot be given over a prolonged period without damage. Fournier instituted, therefore, the "method of successive or intermittent treatments."

Since Fournier's time little has been added to our knowledge of the mercurial therapy of syphilitic anemias. The advent of arsphenamin has brought new possibilities, which, although extensively discussed in the abstract, have been reinforced by only a small body of clinical material. This paucity of clinical discussion may be ascribable to the comparative rarity of pernicious anemia in combination with syphilis. The total number of cases with or without syphilis treated with arsphenamin which have been collected from the literature is thirty-six. To this are now added the twenty-five cases of severe anemia which form the basis of the present study. Primary emphasis is laid on the effect of arsphenamin therapy, since the cases were originally approached from this angle.

REVIEW OF LITERATURE

Arsenic was first used in treating pernicious anemia with gratifying results in 1875 by Bramwell. In 1911 he began using arsphen-

amin, one to four injections of 0.3 gm. each intramuscularly, because he desired to secure a gradual and prolonged action of the arsenic constituent of the drug. In 1913 he reported his experience with twelve patients, of whom two showed no change, three showed slight improvement and seven were greatly benefited, although one had a relapse later.

Leede, in 1911, treated five patients with pernicious anemia *in extremis*. Four of them died in from thirty-six hours to fourteen days, and Leede therefore concludes that arsphenamin is directly contraindicated. He also reported a case that gave the impression of pernicious anemia, atypical however. A diagnosis of anemia with a syphilitic basis was made. After one injection the hemoglobin rose from 15 per cent to 60 per cent and the erythrocytes from 900,000 to 4,000,000 in two months. The hemoglobin fell to 50 per cent and a second injection was given; the hemoglobin then rose to 70 per cent in eight days. Leede pointed out the need for splitting up pernicious anemia into further groups (due to *Bothriocephalus latus, Ankylostoma, and so forth*).

Steyrer, in 1912, after treating a patient for some time with Fowler's solution and seeing no improvement, gave several injections of arsphenamin. The hemoglobin rose from 20 per cent to 70 per cent, and the erythrocytes from 700,000 to 4,500,000, with the disappearance of megaloblasts and poikilocytosis.

Friedlander, in 1912, reported a case in which the patient had received large quantities of arsenic and iron. The erythrocytes numbered only 887,000 with 20 per cent hemoglobin, giving an index of 1.1. After two injections of 0.3 gm. arsphenamin and injections of 1 gr. of cacodylate of iron on alternate days for twenty-seven days the erythrocytes rose to 3,200,000, the hemoglobin to 52 per cent, with an index of 0.7, the picture of only a mild anemia.

Hobhouse, in 1912, added one case to the list. His patient had been anemic for more than a year and had improved under large doses of arsenic. In October there was no sign of pernicious anemia, but in May the count showed 800,000 erythrocytes and 18 per cent hemoglobin, with an index of 1. Two intramuscular injections of 0.3 gm. of arsphenamin were given and in October the erythrocytes numbered 4,704,000, hemoglobin 110 per cent, with an index of 1.05.

Boggs, in 1913, reported eleven cases. Three of the patients died. One was moribund at the time of injection and one died eleven days after the administration of 0.2 gm. of arsphenamin. The reaction was not marked and the blood count did not drop more than 200,000 erythrocytes. The third patient improved, the count rose from 1,100,000 to 3,400,000 in twenty days, eventually reaching 4,800,000, with 85 per cent hemoglobin; the patient, however, died later. The picture was never free from the qualitative changes of pernicious anemia. Five patients improved with an initial drop of never more than 200,000 erythrocytes. One received 0.3 gm. intravenously

every four weeks. In sixteen weeks the erythrocytes rose from 500,-000 to 5,000,000 and the hemoglobin from 23 per cent to 90 per cent. Two other patients had an average rise of 2,000,000 erythrocytes. Although all precautions were observed a sharp febrile reaction after each injection lasted from six to twelve hours, in contrast to the very mild or absent reactions in syphilitics. Boggs concludes that the drug may be given without serious risk, and the results justify its use in pernicious anemia.

Maynard, in 1913, noted a slight increase in erythrocytes after a first injection of arsphenamin; after a second, however, there was a decrease, and he did not use it further.

Weicksel (1913) thinks that syphilitic pernicious anemia is not the result of syphilis, but that under certain predisposing conditions syphilis sometimes leads to this disease. According to him syphilitic anemia is seen in general in latent syphilis. He reports one case, that of a man, aged fifty-two years, with a moderately positive Wassermann reaction and a typical pernicious anemia. The patient was given two injections of arsphenamin and reactions followed which confined him to bed. The erythrocytes subsequently rose from 1,680,000 to 3,700,000 and the hemoglobin from 45 per cent to 85 per cent; the index fell from 1.34 to 1.08. This, however, brings up the question of whether arsphenamin produced the improvement or the collateral treatment for the pneumonia which developed. In the syphilitic pernicious anemia the situation is more favorable, because there is a remedy against the syphilis. Weicksel, in a second article (1913), reported the death of the patient and the pathologic findings of pernicious anemia. Either the old syphilis had no connection with the anemia and the condition was a so-called cryptogenetic form of pernicious anemia or the anemia was the result of a former syphilis for which insufficient arsphenamin had been given to remove the cause. Weicksel inclines to the latter view and advises the use of arsphenamin in further cases.

Lämpe, in 1916, treated three patients suffering from pernicious anemia by the intravenous injections of small doses of arsphenamin, 0.05 gm. to 0.15 gm.; the hemoglobin rose 40 or 50 per cent and the erythrocytes were increased 2,500,000. One of the patients had a remission and died. Lämpe states that he has never seen similar favorable results in cases of pernicious anemia that have been treated in other ways.

Lowrey, in 1917, reported a case in which pernicious anemia developed some time after treatment with arsphenamin, and he decided that there is probably no causal relation.

It will be noted that all the foregoing cases had been diagnosed pernicious anemia and only in a few instances was there any mention of syphilis. Other than these reports we have been unable to find any series which dealt primarily with the effect of arsphenamin on anemia associated definitely with syphilis. Hirschfeld (1918) makes

the general statement, however, that in a few cases syphilis in its tertiary stage may present the symptom-complex of pernicious anemia. Treatment of syphilis, preferably with arsphenamin, "cures the disease, without a remission." Each patient with a positive Wassermann reaction, however, should not be regarded as syphilitic. Old syphilis is more often an associate than a cause of pernicious anemia. Hirschfeld has repeatedly seen cases of this type in which treatment was given for syphilis without success. The question concerning the syphilitic etiology is determined only by the success of specific therapy. It is always possible that the anemia has progressed so far that in spite of the control of the syphilis a normal regeneration of blood can no longer take place. This must be considered, particularly if during treatment the Wassermann reaction becomes negative and the blood findings are not improved.

EFFECT OF ARSPHENAMIN ON THE BLOOD PICTURE

Numerous investigators have studied the blood picture of syphilitics under treatment with arsphenamin. In most cases the examinations were routine and made without particular reference to anemia. Lévy-Bing, Duroeux and Dogny, however, confined their reports to cases presenting definite anemia.

Von Besaiss, in 1911, noted, besides a hyperleukocytosis, marked increase in erythrocytes under arsphenamin treatment. In one case of tertiary syphilis the erythrocytes were unaltered, and in this case the preparation failed therapeutically.

Magat, in 1910, studied the blood and urine in three cases of recurrent fever, fifteen of syphilis and several of malaria treated by Georgyewsky. He speaks of the increase in erythrocytes and in hemoglobin with a decrease in leukocytes the first day after injection of arsphenamin.

Evdokimow, in 1911, observed a more or less distinct improvement in the blood picture under arsphenamin. The fluctuation in hemoglobin was transitory and rarely exceeded 8 per cent. Usually there was a slight increase in erythrocytes, a more or less marked leukocytosis with increase in eosinophils and a more frequent increase in neutrophils.

Baugher and Vaughan, in 1911, treated eighteen patients with syphilis, the erythrocytes and hemoglobin showing no constant change. There was an initial drop in leukocytes in the first few hours after the injection, a rapid increase during the first twenty-four hours, reaching a maximum in from two to four days, becoming normal or slightly above normal in from six to ten days.

Dorn, in 1912, stated that following intravenous injection of arsphenamin there is a hemolysis of short duration, with a decrease in hemoglobin, sometimes as great as 20 per cent, and a drop in

erythrocytes with the presence of urobilinogen and urobilin in the urine. The blood count returns to its former level or even a little higher in twenty-four hours.

Thevenot and Brissaud (1912) believe that arsphenamin causes an excitation of hematopoiesis. The erythrocytes show at first a diminution of sometimes 1,000,000. In fifteen days there is an increase of from 500,000 to 2,400,000.

Schwaer, in 1912, treated twenty-four syphilitic patients with positive Wassermann reactions whose blood pictures varied but little from normal. The hemoglobin showed but little change, from 5 per cent to 10 per cent either way, usually down, irrespective of the dose, 0.2 gm. to 0.6 gm. There was no definite alteration in the erythrocytes. Schwaer used small doses, 0.05 gm., in anemias of different etiology with practically no effect, and concludes that as then employed arsphenamin did not seem to have a place in the treatment of diseases of the blood in general.

MacKee, in 1912, investigated twenty-one cases before and after treatment and noted a very definite relation between the systemic reaction and the fall in erythrocytes, when, as he believed, the reactions were produced by the use of stale distilled water. In his opinion arsphenamin itself plays no part in reducing the count, for if there was no systemic reaction there was no substantial reduction in the number of erythrocytes and no reaction occurred with proper technic.

Lévy-Bing, Duroeux and Dogny used from one to three injections of 0.3 gm. of arsphenamin in neutral suspension in ten cases of secondary syphilis. All the patients were moderately anemic, 3,200,000 to 3,800,000 erythrocytes. No appreciable change in hemoglobin was noted. There was a varying diminution in erythrocytes, 300,000 to 500,000, returning to the former count. There was no amelioration of the preëxisting anemia.

Wawiorowski, in 1912, using subcutaneous and intravenous injections of arsphenamin, found only a slight effect on hemoglobin and erythrocytes.

Heden (1913) gave from three to eight intravenous injections (average six of 0.4 gm. arsphenamin or its equivalent) in fifteen cases. After the first treatment there was a slight decrease in hemoglobin, 10 per cent at most, less after the second and third treatments and none later. The same held true for erythrocytes.

Yakimoff, in 1911, from experimental work on rats, normal or infected with *Spirochæta duttoni* and *Trypanosoma gambiense,* concludes that arsenobenzol causes first an inhibition of the hematopoietic organs and later an excitation. The reaction in monkeys is similar.

Kolmer and Yagles' work (1920) on the hemolytic activity of solutions of arsphenamin and neoarphenamin shows that hemolytic activity depends on (1) the direct action of arsphenamin, (2) the

use of nonisotonic solvents, and (3) the use of sodium hydroxide, especially in excess of that needed to produce the disodium arsphenamin salt.

It appears from the foregoing *resume* that of nine clinical investigators six report favorable results from arsphenamin in anemia, one is opposed to the treatment and two are undecided or give qualified opinions. Among investigators of the laboratory aspects of the problem of the influence of arsphenamin on the blood, five are in favor of the drug as a means of producing a rise in hemoglobin and erythrocytes and seven are against or give qualified opinions. In general it appears that there is a transient destruction of erythrocytes followed by a rise whose degree and permanence vary in different opinions.

CASES OBSERVED IN THE MAYO CLINIC

During the last four years approximately 4800 patients with syphilis have been treated in the Section on Dermatology and Syphilology of the Mayo Clinic. These are largely patients with late or latent syphilis who have come to the Clinic on account of nervous, cardiac or gastric symptoms, although there is a fair percentage with primary or secondary manifestations. In the examination of the records of these patients it was found that in the majority the hemoglobin was 70 per cent or more. It seemed advisable to study only those with 55 per cent or less. Only twenty-five patients were available for such a study. These were all patients in whom the diagnosis of syphilis was either unquestionable or in whom it was sufficiently plausible to warrant a therapeutic test. Patients with proved or suspected syphilis were chosen because if arsphenamin will help any type of anemia it should help the type with a possible syphilitic basis.

Three types of cases are possible in this group of anemias:

Type 1, true pernicious anemia, giving a nonspecific positive Wassermann reaction.

Type 2, true pernicious anemia in association with syphilis.

Type 3, severe anemia due directly or indirectly to syphilis.

Cases were regarded as proved syphilitic, in which there was at least a definite history, a positive Wassermann test and remnants of an old infection or signs at the time of examination of involvement in any system. Cases in which there was either no history or only a doubtful history of a primary lesion, with no clinical evidence of syphilis, or in which only one positive Wassermann reaction had been obtained were regarded as doubtful. Cases were classified as a pernicious type of anemia in which the blood picture showed a decrease in erythrocytes out of proportion to the fall in hemoglobin with the presence of anisocytosis, poikilocytosis, nucleated erythrocytes and clinically by weakness, dyspnea, sore-tongue, gastro-

intestinal disturbances, pigmentary changes (lemon tint) and sometimes nervous manifestations. Obviously little may be expected in the first two groups from treatment for syphilis, *per se*, except insofar as the drugs used primarily against syphilis may also have a direct beneficial effect on the anemia, either by stimulating hematopoiesis or by preventing blood destruction.

METHODS AND TREATMENT

Schamberg's preparation of arsphenamin, obtained from the Dermatological Research Laboratories, Philadelphia, was used in most cases in increasing doses, 0.3 gm. to 0.5 gm., at weekly intervals. In a few cases Lowey's solution of arsphenamin was used. Novarsenobenzol was substituted when the patient's condition indicated. Occasionally the dosage was reduced. After the patient had been given a course of six injections, during which time his tolerance for mercury was ascertained, he was sent home for from one to three months with or without mercurial treatment in the form of 4 gm. 33 per cent inunctions, or *hydrargyrum cum creta*. Second and even third courses were given to some of these patients.

Transfusions were given to certain patients prior to, concomitant with, or following specific therapy. They were given by the citrate method, the donor and recipient usually belonging to the same group, although in emergency a Group IV donor was used irrespective of the recipient's group. The usual quantity given was 500 cc.

The Dare hemoglobinometer was used throughout. The recent work of Senty, in which he showed that readings above 70 per cent were subject to error, needs mention. Below this, however, the estimations are accurate. In this series, then, the readings may be considered correct apart from the variations due to personal equation. We have arbitrarily taken increases or decreases of 5 per cent as legitimate error and have paid attention only to greater changes.

The Wassermann technic as carried out at the Clinic under the direction of Dr. A. H. Sanford is a slight modification of the original Noguchi system. In the preparation of the amboceptor, dogs instead of rabbits have been used. Human corpuscles have been sensitized by adding a definite amount of amboceptor to the washed corpuscles and placing the mixture overnight in the ice-box. The sensitized cells are then titrated against various amounts of 40 per cent diluted guinea-pig serum. The standard antigen for routine work is an acetone-insoluble fraction of heart extract.

We have been more interested in the effect of arsphenamin on the course of anemia from day to day and from week to week than in the immediate effect on the blood picture. No attempt has been made to learn whether there was an initial drop in the first few minutes or hours with a subsequent rise to the original count or

above. This has been the object of study by several investigators, and the results have been uniform.

Tables 1, 2, and 3 classify our material from various standpoints.

TABLE I.—EVIDENCE OF THE PRESENCE OF SYPHILIS IN RELATION TO THE BLOOD PICTURE

Evidence of syphilis.	Pernicious anemia.	Secondary anemia.	Undetermined,[1] (hemoglobin only.)	Total.
Indisputable	5	5	1	11
Wassermann test and history	1	1		2
Wassermann test only	6	3	1	10
History only	1	..	..	1
No history. Wassermann test negative	..	1	..	1
	13	10	2	25

It will be seen that about half the cases in this series presented the picture of pernicious anemia. A positive Wassermann reaction as the only evidence of syphilis was encountered twice as frequently in pernicous anemia as in secondary anemia, perhaps supporting the theory that this disease may of itself yield a positive Wassermann reaction in the absence of syphilis (Sanford).

TABLE II.—CLINICAL DIAGNOSIS

Pernicious anemia:
    Definite 6
    Probable 4
    Atypical 1
    Associated with gastric syphilis 1
    Associated with hepatitis and cutaneous tertiary syphilis . . . 1
                                                    ———
                                                    13
Secondary anemia:
    Anemia prominent 3
    Associated with hereditary syphilis 1
    Associated with aortitis 1
    Associated with gastric syphilis 1
    Associated with syphilitic splenomegaly and enlarged liver . . 1
    Associated with chronic arthritis 1
    Associated with gastric syphilis and osteitis 1
    Associated with periostitis (syphilis of the ribs?) and empyema . 1
                                                    ———
                                                    10
Undetermined (hemoglobin estimation only) (clinically secondary in type):
    Tabes dorsalis 1
    Hypertension 1
                                                    ———
                                                    2

In cases presenting the picture of pernicious anemia the anemia was the outstanding feature and only infrequently were other conditions suggesting syphilis present. Secondary anemia, however,

[1] Clinically secondary in type.

was more commonly associated with some syphilitic involvement of other systems.

TABLE III.—THE EFFECT OF TREATMENT FOR SYPHILIS ON SEVERE ANEMIAS

	Pernicious anemia.	Secondary anemia.	Total.
Patients received mercury	9	9	18
Patients with proved syphilis	3	6	9
Patients sent home on mercury treatment	7	2	9
Patients with proved syphilis	2	1	3
Patients sent home on mercury treatment, hemoglobin fell from 12 per cent to 35 per cent	4		4
Patients with proved syphilis	2		2
Patients received arsphenamin	13	12[2]	25
Patients with proved syphilis	5	6	11
Patients without change under arsphenamin	3	6	9
Patients with proved syphilis	1	5	6
Patients improved under arsphenamin	5	5[2]	10
Patients with proved syphilis	2	1	3
Patients became worse under arsphenamin	5	1	6
Patients with proved syphilis	2		2

Mercury was given with arsphenamin and therefore it was often difficult to estimate its effect, which is best judged by watching the results when it is given to patients during their rest period between courses of intravenous injections. In four of nine patients a reduction in hemoglobin of from 12 to 35 per cent and a decrease in erythrocytes of from 500,000 to 2,000,000 were noted under inunctions. In all of these patients showing a decrease the blood picture had approached that of pernicious anemia from the start. They had previously improved from 18 per cent to 30 per cent under arsphenamin therapy. The relapses may, of course, have been purely a coincidence. While long experience may have shown mercury to be "the iron of syphilitic anemia," it must evidently be used with caution in the more severe grades, particularly when the picture approximates that of primary pernicious anemia. In two of the patients who reacted unfavorably to mercury, arsphenamin barely maintained the blood picture, while transfusions maintained it at a slightly higher level. One patient's hemoglobin continued to fall from 56 per cent to 36 per cent under three arsphenamin injections, but one month after a single transfusion the hemoglobin had risen to 67 per cent, the erythrocytes to 4,280,000, giving an index of 0.7, compared with hemoglobin 36 per cent, erythrocytes 1,530,000, and an index of 1.1. The fourth patient was apparently improving

[2] Including two indeterminate cases (hemoglobin only) clinically secondary, one with definite syphilis.

under arsphenamin therapy when a reaction, following an intravenous injection of the drug, resulted in a rapid decline, and only by repeated transfusions was the hemoglobin raised from 33 per cent to 46 per cent and the erythrocytes from 1,750,000 to 2,510,000. It is apparent at least that the patients reacting unfavorably to mercury showed evidence of a tendency to an unfavorable course.

With regard to the effect of arsphenamin in our series the drug has been given with reasonable safety even in patients whose hemoglobin is 20 per cent, although it seems a better policy to increase this to 30 per cent by transfusions, if possible, before starting specific therapy. Every precaution must be taken to prevent reactions, for accidents which may be only disagreeable in otherwise healthy persons assume dangerous proportions in persons whose condition is already grave.

In six cases a drop in hemoglobin of from 10 per cent to 20 per cent and a decrease of about 500,000 erythrocytes occurred during arsphenamin therapy. To these may be added one case in which an increase had previously been shown following intravenous therapy. In two of these unfavorably affected cases transfusions were of no value. In another the blood count continued to drop for a time even with transfusions, but ultimately, after seven transfusions, the picture improved. The hemoglobin in this case rose from 18 per cent to 48 per cent and the erythrocytes from 1,470,000 to 3,150,000. Despite this improvement the patient died shortly after reaching home. An initial drop in hemoglobin from 70 per cent to 50 per cent with a decrease in the number of erythrocytes from 4,600,000 to 4,000,000 was observed in the fourth case following two injections of arsphenamin. Throughout three subsequent courses in this case the erythrocytes fluctuated between 3,000,000 and 4,000,000 and the hemoglobin between 50 per cent and 60 per cent. In the fifth and sixth cases there was a 5 per cent increase in hemoglobin but a decrease of 500,000 erythrocytes. One of these patients died shortly after transfusion.

In nine cases no definite effect from arsphenamin was noted. Two of the patients received only three injections, a toxic erythema in one rendering it necessary to discontinue the arsenic preparation. The other presented the blood picture of such an advanced pernicious anemia that a transfusion was given but without improvement. He returned home and a letter indicated that his condition was unchanged. Seven patients received from four to fourteen injections without definite effect. Two of these had pernicious anemia with a questionable syphilis and five had secondary anemia; all but one of the latter were proved to be syphilitics.

In ten patients an improved blood picture (an increase of from 8 per cent to 35 per cent in hemoglobin and from 200,000 to 2,000,000

in erythrocytes) followed arsphenamin treatment. Five of them had pernicious anemia. In only three of the ten who improved was the evidence of syphilis indisputable. We are surprised in comparing this group with the foregoing to find the relatively high proportion of patients with pernicious anemia and the relatively small proportion with proved syphilis.

Transfusions were resorted to at some period of the treatment of sixteen patients, either to reinforce those who had made only moderate improvement or as treatment for those who had not responded. If patients did not improve under arsphenamin treatment only it was often combined with transfusion, and later transfusions were given alone. In patients whose initial hemoglobin was 25 per cent or under transfusions were used to bring the hemoglobin above 30 per cent. The estimation of the relative value of arsphenamin and transfusions is more difficult in cases in which the transfusions had been resorted to during the arsphenamin course. For example, one patient during the second course received four injections of arsphenamin and three of novarsenobenzol. Transfusions were given before the first and fourth injections. The hemoglobin at the beginning was 30 per cent and at the end 49 per cent, with a reading of 64 per cent following the second transfusion. Arsphenamin had no appreciable effect during the first and third courses. We therefore would feel justified in this case in concluding that the rise was merely due to the temporary beneficial effect of the transfusions rather than that the subsequent arsphenamin injections had counteracted the good effect of the transfusions.

In four instances transfusions gave more gratifying results than did arsphenamin. One of these patients had continued to improve under arsphenamin, the hemoglobin increasing from 40 per cent to 70 per cent. He relapsed under mercury and the third course of arsphenamin sufficed only to hold the hemoglobin at 40 per cent. By repeated transfusions the hemoglobin was maintained between 45 per cent and 50 per cent. In a similar case the hemoglobin dropped from 70 per cent to 56 per cent under mercury and continued to drop from 56 per cent to 36 per cent under arsphenamin. One month after a single transfusion the hemoglobin was 67 per cent. Another patient's hemoglobin improved under specific treatment from 35 per cent to 45 per cent. After receiving a transfusion the patient was sent home. In two months his hemoglobin estimation read 75 per cent, and this was maintained during the next course of arsphenamin. The fourth patient received one course of arsphenamin with slight improvement. Transfusions were combined with arsphenamin during the second course. After the second injection of the third course he had a violent reaction with a rapid fall in hemoglobin. Repeated transfusions raised the hemoglobin from 33 per cent to 46 per cent and the erythrocytes from 1,750,000 to 2,510,000.

In three other cases transfusions improved the blood picture, but the patients died. Transfusion had no effect in four instances and only a temporary beneficial effect in two. In another case following a relapse transfusions were successful in maintaining the count at a higher level, but not so high as it had been previously. In two cases transfusions were used with success before beginning specific therapy.

If, as Hirschfeld says, the proof that a pernicious type of anemia is due to syphilis depends on cure without remissions by means of treatment of the syphilis, no cases of syphilitic pernicious anemia have been recognized in the Mayo Clinic since the organization of the Section of Dermatology and Syphilology. The nearest approach to such a case is that of a man, aged thirty-eight years, with a history of infection and with leukoplakia in the mouth. His spinal fluid and his blood Wassermann test were negative, even with a provocative test. His symptoms and findings, interpretated by several competent observers, were those of a typical primary anemia. His hemoglobin was 55 per cent, the erythrocytes numbered 2,560,-000, with a color index of 1. After three transfusions the hemoglobin estimation was 70 per cent with 4,000,000 erythrocytes and an index of 0.8. After two courses of intravenous therapy the patient had 4,750,000 erythrocytes and 85 per cent hemoglobin, and following the third course the erythrocytes increased to 5,040,-000. He is the picture of health, has gained 50 pounds and has been well for two and one-half years. Whether his improvement was due to transfusion or to the arsphenamin injections, and whether he is merely having a long remission, cannot be stated. Stockton (1919) recently reported a case of pernicious anemia in which the patient had a remission after twelve years of apparently good health

SUMMARY AND CONCLUSIONS

1. Severe anemia, either primary or secondary, associated with late or latent syphilis, is apparently rare, twenty-five cases appearing in approximately 4800 records in the Section on Dermatology and Syphilology in the Mayo Clinic.

2. Pernicious anemia may be seen in association with syphilis, but no case exhibiting an incontestable etiologic connection has appeared in our records.

3. One patient with the clinical picture of pernicious anemia and a doubtful syphilitic infection has been apparently well two years as a result of treatment.

4. Pernicious anemia in the apparent absence of syphilis may yield a positive serum Wassermann reaction.

5. Mercury by inunction, used alone, produced an unfavorable reaction in four of nine patients with anemias who had pre-

viously improved under arsphenamin, but all had primary anemia and subsequently showed evidences of a relapsing unfavorable course.

6. We believe, therefore, that in syphilis with anemia mercury should be used with caution, especially if the picture suggests the primary type.

7. Five of thirteen patients with primary anemia improved under arsphenamin. Of these two who improved and three who did not had demonstrable syphilis.

8. Five of thirteen patients with primary anemia became worse under arsphenamin; of these two had syphilis.

9. Five of twelve patients with secondary anemia improved under arsphenamin treatment. Of these only one who improved and five who did not had demonstrable syphilis.

10. Only one of twelve patients with secondary anemia became worse under arsphenamin.

11. In our experience, then, arsphenamin has been much more effective in secondary anemia than in primary anemia, but curiously disappointing in secondary anemia with associated manifestations of syphilis.

12. Twelve of sixteen patients improved under transfusion, four of them after arsphenamin had failed. Two of these patients showed only temporary improvement and three others died notwithstanding the improved blood picture. The effect of transfusion could only be judged with difficulty because of the conditions under which it was employed.

13. In four of sixteen cases transfusion was without effect.

14. Transfusion should be a preliminary to arsphenamin when the hemoglobin is below 20 per cent.

15. Reactions to arsphenamin injections must be carefully avoided since they may produce an alarming drop in hemoglobin.

16. No satisfactory rule for determining which case would improve on treatment for syphilis and which case would not could be arrived at. In general half the cases may be expected to improve.

17. The degree of improvement is not necessarily proportional to the demonstrability of syphilis. The pernicious anemia associated with undoubted syphilis which we have seen has run the ultimate course of pernicious anemia regardless of treatment for syphilis.

18. Hemoglobin estimations alone are not sufficient to indicate the progress of the patient. The hemoglobin may rise and the number of erythrocytes fall at the same time.

19. Arsphenamin treatment is safe if carefully used in anemia and should be employed in patients with undoubted evidence of the disease, and, as a therapeutic test, when reasonable suspicion of its presence exists.

20. Transfusion must remain the ultimate resort in primary

cases, and in those cases associated with syphilis in which arsphenamin has failed, even in the presence of syphilis, the best effect will be secured by both together.[3]

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[3] Another case in the Mayo Clinic was brought to our attention after the completion of the paper.   As it does not alter any of the conclusions we have not thought it advisable to recast the article.

The case is one of definite syphilis with hepatic cirrhosis and splenomegaly.   Weekly tappings were necessary.   The blood picture was that of a moderate anemia, with hemoglobin 68 and erythrocytes 3,980,000.   After a six weeks' course of mercury inunctions with potassium iodide by mouth, the patient improved greatly and did not require tapping throughout this period.   His hemoglobin, however, dropped to 50 per cent and his erythrocytes to 2,880,000.   The improvement in his general condition continued through three months' treatment with *hydrargyrum cum creta* and with potassium iodide.   A course of arsphenamin, 0.2 to 0.4 gm., was given, at the end of which time the hemoglobin had risen to 60 per cent and the erythrocytes to 4,560,000.   Splenectomy was then performed.   The patient died early the next morning.

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LEUKEMIA IN CHILDREN, WITH SPECIAL REFERENCE TO LESIONS IN THE NERVOUS SYSTEM.

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The recent occurrence of two rather unusual cases of leukemia in children admitted to the pediatric service of the Mount Sinai Hospital has prompted me to go over the hospital records of the past ten years and to collect therefrom the cases of leukemia admitted during that time. In tabulating these cases, twenty-three in number, several interesting points are brought out and seemed to me worth while recording. It is distinctly not my purpose to review all the symptoms and signs of leukemia as this disease occurs in children, as this has been ably done by others, especially by Benjamin and Sluka in their monograph *Die Leukæmie im Kindesalter*, 1907, and by A. Strauch in an article published in the *American Journal of the Diseases of Children* in 1913, where a good bibliography may be found. In the review of the cases in the present paper I shall therefore not make any attempt at completeness in describing leukemia clinically, but will stress especially the following points: (1) The type of disease as it attacks children; (2) the common physical findings; (3) the diagnosis of the disease; (4) the symptoms referable to the nervous system.

As our cases well show, leukemia in children is essentially an acute disease. The longest duration of any of our cases was one year (Case 22). Benjamin and Sluka refer to a chronic case of the myeloid variety which lasted two years. All the cases which last

more than a few months are of the myeloid type, chronic lymphatic leukemia apparently not occurring in childhood. Case 9 in our series died after an illness of ten months. This, like Case 20, however, was an atypical one in which, as we shall point out later, a stage of grave anemia without a leukemic blood picture preceded the stage of lymphocytosis. It must also be emphasized that cases like the above are prolonged by transfusion and radiotherapy. Occasionally the entire course of illness is limited to a few days. Case 5, aged seven months, was sick only four days. It is, of course, true that these brief periods of illness may be preceded by symptoms or blood changes not noticed by unobservant parents.

The course of leukemia undoubtedly resembles that of an acute infectious disease. Fever was present in almost every case, and was often the first symptom to be noted.

In this connection the article of Gordon Ward is of interest.[1] The author has collected and grouped 1457 cases of leukemia and has examined these in reference to their resemblance to acute infections. His conclusions are: "(1) There is a congenital form of leukemia which occurs in children whose parents are not leukemic. (2) Leukemic parents have never been known to transmit the disease to the newborn child. (3) Instances in which the actual infection of one person might seem to have occurred are very few, although not devoid of significance. (4) In having a marked preference for a particular age and sex, leukemia differs from the infective class of diseases and resembles the metabolic diseases and cancers." For these reasons the author believes the disease is not an infectious one.

That the leukemic blood picture may develop in the course of an infection is known, and it is naturally difficult to decide whether the leukemia is an added condition or part and parcel of the infection. As an example of the development of the lymphocytosis late in the illness, consider Case 20, whose detailed history follows:

R. B. (Med. No. 196608), aged four years, was admitted to the hospital November 17, 1919. He was one of five children. The four other children were living and well. The family history was negative. The boy had never before been ill and had had none of the acute diseases of childhood.

The present ailment had commenced suddenly one month before with chills, high fever (104°) and a purpuric eruption on the trunk. These symptoms subsided after a week, the rash gradually fading nad leaving only a yellowish discoloration. One week later the boy began to have very severe abdominal pain unrelated to meals and accompanied on three occasions by vomiting. At the same time he developed severe pain in his ankles and legs. These symptoms all

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[1] British Jour. Dis. Children, January, 1917.

subsided until three days before admission, when the fever and abdominal pain returned and the purpuric rash again appeared, especially on the face. No blood was noted in the stool or vomitus. There had been a marked loss in weight.

Physical examination on admission showed an extremely pale, weak, sick-looking child. Over both cheeks were purplish-black ecchymoses which gave the boy a most grotesque appearance. On the arms, buttocks and legs were numerous hemorrhagic spots varying in size up to that of a twenty-five-cent piece. There were a few moderately enlarged, tender lymph nodes in the groins, axillæ, neck and the epitrochlear regions. There was a short, rough, systolic murmur heard along the left border of the sternum. The liver was felt one finger below the free border of the ribs and the spleen three fingers below. There was a small ulcer on the left anterior faucial pillar. Retinoscopy revealed numerous retinal hemorrhages. The urine examination was negative. The blood count was as follows:

Hemoglobin, 18 per cent.

Red cells, 1,200,000. Slight poikylocytosis and anisocytosis.

White cells, 1800.

Differential count: Polynuclear neutrophiles, 27 per cent; lymphocytes, 64 per cent; eosinophiles, 0; basophiles, 0; transi-tionals, 1 per cent; myelocytes, 2 per cent; metamyelocytes, 6 per cent.

Platelets, 72,000.

Coagulation time, 9 minutes.

Bleeding time, $2\frac{1}{2}$ minutes.

Fragility of the red cells begins at 0.4 and there is complete laking at 0.325.

Von Pirquet and Wassermann tests negative.

At this time the diagnosis of aplastic anemia was suggested. The extremely low cell counts of both the red and the white cells pointed to a severe hypoplasia of the bone-marrow. Purpura hemorrhagica was another diagnosis suggested, in view of the hemorrhages, the diminished number of the blood platelets and the profound anemia.

Several transfusions of citrated blood obtained from the child's mother apparently caused a considerable improvement in the boy's condition, the hemoglobin rising to 32 per cent and the red cells to 1,912,000. The white cell count, however, at this time (two weeks after admission to the hospital) showed the following figures:

White cells, 4000;

Polynuclear neutrophiles, 4 per cent;

Lymphocytes, 86 per cent;

Large mononuclears, 10 per cent;

Subsequent counts confirmed these findings.

The interpretation of this cell count showed that the case was in

reality one of lymphatic leukemia, the diagnosis being based on the relative and absolute lymphocytosis. The low total white cell count does not militate against this diagnosis, for many cases are now on record in which the so-called aleukemic blood picture is found in the course of leukemia.

This particular case developed an abscess of the cheek, due to the breaking down of one of the hemorrhagic areas. This caused a retrogression in the progress which had been made, and when the child was taken home against advice the blood count had changed to: Red cells, 880,000; hemoglobin, 18 per cent; white cells, 2600.

This case is of interest in demonstrating how difficult it may be to make the diagnosis of leukemia in the absence of a characteristic blood picture. It is, of course, important to decide the diagnosis for prognostic reasons, since we know that all cases of leukemia in children are almost without exception fatal.

The above case is very closely resembled by one reported by Gunewardene.[2] A boy, aged three and a half years, showed a red cell count of 760,000, hemoglobin of 11 per cent and a white cell count of 8400. Polynuclear neutrophiles, 9.5 per cent; lymphocytes, large and small, 85 per cent; hyalines, 2 per cent; myelocytes, 2 per cent. This case was diagnosed as one of aplastic anemia, but when, after a remission, skin nodules appeared with many myeloblasts in the blood the diagnosis of leukemia was entertained. The postmortem examination showed myeloblastic changes in the bone-marrow.

To recur to the aleukemic blood count it is of interest to note that the white blood cells in our group of cases varied from 1400 to 720,-000. In 9 cases the count on entering the hospital was above 50,000; in 7 it was between 11,000 and 50,000; in 2 it was between 5,000 and 10,000; and in 3 it was below 5000 cells. In several cases great changes took place in a few days. In some cases this was apparently due to roentgen therapy (Cases 16 and 17). The criterion of leukemic blood is the presence of abnormal cells in the circulating blood or a very definite change in the distribution of the normal cells. Apparently aleukemia is not a disease entity, but merely a stage in the course of the disease leukemia.

As we mentioned at the outset the lymphatic form of leukemia is much more common than the myeloid in childhood. In the present series the proportion is 20 of the lymphoid to 3 of the myeloid. It is, however, possible that some of the cases of lymphatic leukemia occurring in the earlier part of our series would now be classed as myeloid, owing to the recognition of the myeloblast cell which may easily have been mistaken for a lymphocyte. This cell, which is one of the progenitors of the myelocyte, is a mononuclear cell, the nucleus of which shows a finely reticulated structure, with

[2] British Jour. Dis. Children, January-March, 1920.

prominent nucleoli, and cytoplasm, non-granular, confined to a narrow peripheral zone. Naegeli[3] points out that the more acute the disease the more does this unripe type of cell displace the myelocyte. The acute myeloid leukemias, the existence of which was at one time doubted, are therefore accompanied by the extrusion into the blood not only of myelocytes but also of myeloblasts, sometimes almost to the complete exclusion of the former. Such cases often run an extremely acute course. Of this type is our Case 11, in a child, aged three years, showing 160,000 white cells, of which 57 per cent were myeloblasts. Such cases are usually accompanied by a very grave anemia and the presence of many abnormal red cells in the blood. Case 11 showed a red cell count of 1,480,000 with 21 per cent hemoglobin. The entire course of this case lasted four weeks.

In contradistinction to this form I would call attention to Case 22. A girl, aged eight years, previously in good health, began to complain of loss of weight and anorexia one year ago. Since that time she had been growing progressively weaker. Two months before entering the hospital an irritating cough had developed and continued. On admission, examination showed a pale, sallow, undernourished child, moderately dyspneic. All the superficial lymph nodes, but especially the cervical and submaxillary, were enlarged, hard and discrete. The left chest showed physical signs of a large pleural effusion. There were no enlarged superficial veins. The liver was felt 14 cm., the spleen 15 cm. below the free border of the ribs. Neither organ was nodular nor tender. The blood examination showed: Hemoglobin, 41 per cent; red cells, 2,080,000; white cells, 134,400; lymphocytes, 15 per cent; polynuclear neutrophiles, 5 per cent; myeloblasts, 80 per cent. The urine was negative. The temperature ranged from 99° to 101.5.°

The chest was aspirated twice but refilled rapidly. The pleural fluid was sterile, contained relatively few cells and had a specific gravity of 1012.

Clinically this case was one of chronic leukemia, though from the blood examination one would expect an acute history. Dr. N. Rosenthal, the hematologist at the hospital, was inclined to consider this case an acute one in spite of the history, believing that the leukemic process had been recently engrafted upon an old infection. The fact that myelocytes were entirely absent in the blood led us to exclude a so-called myeloblastic crisis, in the course of a myelogenous leukemia; for in such cases, notwithstanding the fact that great numbers of unripe cells (myeloblasts) are poured into the circulation there are present a certain number of maturer cells, myelocytes.

In this case then the blood findings pointed to an acute condition,

[3] Leukæmie und Pseudoleukæmie, 1913.

whereas the large, hard spleen and liver, the very large lymph nodes, the duration of symptoms and the slight fever were all in favor of the chronic type of the disease.

Of further interest was the hydrothorax. Radiograms of the chest taken before and after aspiration of the fluid failed to show any intrathoracic masses that might account for the pleural effusion. This is in accord with the findings in the other cases of our series in which chest radiograms have been taken. Apparently involvement of the intrathoracic nodes is rare, even in the chronic cases. These are quite contrary to the findings in cases of Hodgkin's disease, where, as pointed out by Wessler and Green[4] the bronchial and paratracheal nodes are regularly involved.

The participation of the nervous system in the leukemia of children is of considerable importance, and more attention should be directed toward it. In the present series Cases 5, 11, 12 and 23 showed involvement of the brain.

Case 5 was an infant aged seven months, admitted to the hospital July 26, 1915, in a moribund condition. The child had been taken ill four days before admission with restlessness, fever, a hemorrhagic eruption over the neck and shoulders and great prostration. Physical examination showed a dying child, extremely pale, with a hemorrhagic eruption, greatly enlarged liver and spleen and signs of meningeal irritation. The infant died before a careful examination was possible. Autopsy findings showed the lesions of acute leukemia, with a large hemorrhage over the surface of the brain.

Cases 11, 12 and 23 were all typical cases of acute leukemia which ended fatally with convulsions, delirium and coma. In two of them (11 and 23) lumbar puncture gave evidence of recent hemorrhage into the cerebrospinal fluid. The fluid was sterile.

In some cases the very first symptom of the disease is a convulsion. Such is a case seen by me, but not included in this series: An infant was brought to the hospital in coma, having been ill two days with high fever and convulsions followed by unconsciousness. Examination revealed an extremely pale child with numerous petechial spots scattered over the legs and trunk. There were a few enlarged lymph nodes in the neck. The spleen was not felt. On account of the fever, petechiæ and convulsions the case had been diagnosed as one of acute cerebrospinal meningitis, although all the classical signs of meningitis were absent. The lack of signs of meningeal irritation and the extreme pallor led me to diagnose a probable acute leukemia with cerebral symptoms. Lumbar puncture was performed and normal fluid under slight pressure was obtained. The differential blood count revealed 99 per cent lymphocytes.

Quite recently a similar case in a girl, aged seventeen years, has

been reported by Munro[5] under the heading, "Acute Myelogenous Leukemia Simulating Meningitis." Here symptoms and physical signs of meningeal irritation were present. The acute illness lasted but ten days and was ushered in by headache, fever and delirium, which passed to a stage of coma, during which there were present rigidity of the neck, positive Kernig and Babinski signs, mild opisthotonos, a slight external strabismus and twitching of the right side of the face. Lumbar puncture yielded blood-stained fluid under increased pressure, smears and cultures failing to show any organisms. The blood count showed the findings of acute myelogenous leukemia. Postmortem examination failed to reveal evidence of inflammatory condition or gross hemorrhage anywhere in the central nervous system. The vessels of the meninges were markedly engorged and an acute edema of the brain and cord was present. The cord and cerebellum showed infiltration with mononuclear cells. The meningeal symptoms were here not due as in the first case to hemorrhage, but apparently to acute congestion and microscopic leukemic infiltration.

Leukemic infiltration in the brain may, moreover, affect considerable areas before causing symptoms. In a case diagnosed as septic diphtheria in a girl, aged fifteen years, upon whom I performed an autopsy, large brick-red masses varying in size up to that of a cherry were found scattered through the cerebrum. These masses proved to be deposits of leukemic tissue. The girl had died in coma, having shown no cerebral symptoms until a few days before death.

Tapie and Cassar[6] in an article on the nervous complications in leukemia comment on the fact that leukemic infiltration of the nervous system may be present without causing any symptoms whatever. In their article, which contains a very good review of the literature bearing on this subject, they report a case of hemiplegia due to capillary hemorrhage and leukemic infiltration of the internal capsule. They classify the nervous lesions which may occur in leukemia under the following heads:

1. Medullary degeneration: small foci of sclerosis or capillary hemorrhage in the brain or cord.

2. Leukemic infiltration: this may or may not cause symptoms.

3. Hemorrhages in nerve centers.

4. Nerve lesions due to compression.

5. Zoster.

To summarize my own experience, I have seen 6 cases of leukemia in children in which symptoms referable to the nervous system were prominent. Four of these gave the picture of cerebral hemorrhage. Three were proved cases: 1 by postmortem examination, 2 by lumbar puncture. The fourth case neither came to autopsy nor had a puncture performed; from its clinical picture, however,

[5] Jour. Am. Med. Assn., No. 9, vol. lxxiv, p. 603.
[6] Arch. de mal. du cœur, 1919, xii, 218.

cerebral hemorrhage could with probability be diagnosed. I have described a case of acute leukemia mistaken for cerebrospinal meningitis, the clinical findings of which pointed to a leukemic infiltration as the cause of the symptoms. A very similar case with autopsy is reported from the literature. Finally, I have described a case with terminal cerebral symptoms in which areas of macroscopic leukemic infiltration were found at postmortem examination.

I wish to express my indebtedness to Dr. Henry Heiman for permission to make use of the material from the pediatric service of Mount Sinai Hospital.

PERICARDITIS: INCIDENCE AND DIAGNOSIS.[1]

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Inflammation is prone to develop in the serous sacs of the body, in some, seemingly, more than in others. The inflammatory reactions demonstrate nicely the various types of inflammations; in fact, in no situation in the body is one able to observe a more distinct set of reactions than are met with in the different forms of serositis. With the exception of direct wounds, infection in serous sacs is always a secondary manifestation of some primary focus, even though, at times, this focus may be so completely hidden as to escape recognition. One usually does not regard epidemic meningitis exactly in this light, but really the invasion from the upper respiratory tract of the meningococcus with a subsequent meningitis or of the Streptococcus salivarius with its accompanying arthritis or pericarditis is theoretically the same. There is no reason to believe that serous sacs are not infected in the usual ways—namely, by the blood stream, the lymphatics or by direct extension. It is, however, impossible in some instances of pericarditis to be certain of the manner of infection, hence the term idiopathic has been applied to certain clinical forms of the disease. On general medical grounds this term is a poor one, and even though, from the point of view of proof, it is at times correct, still it is probably better to drop the word idiopathic. The pericardium is subject to four types of acute inflammation; the acute fibrinous and the serofibrinous are the common forms while the purulent and the hemorrhagic forms are less frequent. The chronic inflammations are indicated by fibrous adhesions, localized or general in distribution, and a rather unusual form in which a diffuse thickening of the pericardium is observed. Tuberculosis produces an inflammatory reaction which

at times shows characteristics typical of both acute and chronic inflammation in addition to the granulomatous reaction.

It is quite apparent from clinical and pathological observations that the different serous sacs are by no means numerically equally involved in infection. There is no reason to believe that any inherent variability in the power of the resistance is possessed by one and not by the other. It would seem, rather, that the anatomical position in the body on the one hand and the type of bacterial infection on the other suggests the explanation. For example the acute inflammations of the peritoneum are practically always purulent, because they are secondary in most instances to a ruptured or leaking hollow viscus containing pus-producing bacteria. The pericardium, however, has choicer surroundings as the rupture of a viscus into it is extremely unusual; while, further, the Streptococcus pyogenes is not the prevailing organism in inflammations of the chest, the possible regional source of pericarditis. On the other hand the frequency of pericarditis in the Streptococcus viridans infection and the infrequency of any peritoneal involvement by this organism, at least that can be recognized as such, would appear to indicate that the type of bacterium is a factor of importance in inflammations of serous membranes. In the same way, Streptococcus viridans infection of the meninges, except in an occasional case of chorea, is very unusual; but it undoubtedly occurs in the pleura. It is not our purpose to become entangled in the bacteriological question of specific localization of bacteria which, in a certain sense, is correct as the localization of the meningococcus in the meninges, the tendency for Streptococcus viridans to be present in carditis, while the absence of these bacteria in the peritoneum certainly would suggest specificity in location. This, however, under no condition means that Streptococcus viridans isolated from a pericardial sac will always produce a pericarditis. Holman, McMeans and others have settled this point. The prevalence, therefore, of acute fibrinous or serofibrinous inflammations in the pericardium would appear to be due, firstly, to the fact that the most frequent bacterial invader is the Streptococcus viridans, and, secondly, the pericardium is not especially subjected to the influence of the usual pus-producer, the Streptococcus pyogenes. That the pericardium is readily available for a purulent infection if the pus-producing organism is present, is clearly shown by the considerable number of purulent pericarditis cases found in streptococcic pneumonias and to a lesser extent in the pneumonia of pneumococcic origin.

It is my purpose to deal with the pericardium in inflammatory conditions as recognized at the bedside and at the autopsy table. It must be kept in mind that acute pericarditis, with or without effusion, has not a high mortality and therefore the cases that come to autopsy, dying from acute pericarditis *per se*, are unusual. Further, much of the acute pericarditis found at autopsy is but a

terminal part of the picture of infection in that individual. Chronic pericarditis is of interest in indicating the number of cured acute forms and also in calling attention to clinical difficulties of diagnosis in this condition, for it still seems to be a fact, as Osler remarked many years ago, that chronic pericarditis is more often found in the autopsy room than in the ward. I thought it would be of some interest to review our autopsy records on this subject and to collect from them any data which seemed to have a pertinent bearing on the subject of pericarditis.

The subject of pericarditis is an old one, and in the literature it has been thoroughly covered as the reports, which are legion, on this disease would indicate. Our pathological findings are in accord with what has been shown in the past, our figures bearing a striking resemblance to those published about twenty years ago by Wells. One is also forced to say there is little further to add to the diagnosis; but as we are still going to have pericarditis with us it is possibly not out of place to occasionally submit a review. The number of autopsies examined was 975; in 100 of these pericarditis was present in some form. For the opportunity to study these records and for the helpful discussion with reference to them I wish to thank Dr. Oskar Klotz.

There are two conditions to which brief reference should be made, although neither of them is classed under inflammation. Hydropericardium has clinical significance in that some degree of this transudation is present when edema is a characteristic of certain chronic diseases, especially nephritis and primary anemias. A well-marked increase of fluid in the pericardial sac without other signs of pericarditis, or the presence in the body of edema in the tissues or fluid in the cavities, should be held in suspicion as probable evidence of the inflammation, the reaction being principally of a serous character. This differentiation, however, does not appear to be a difficult problem to decide, either from the clinical or the pathological point of view. A milk spot on the surface of the heart is, to say the least, a rather common finding. About the origin of these spots there is considerable debate, as the question has been raised as to whether they represent the end-results of inflammation or merely the effects of long-continued rubbing of the pericardial surfaces. It is not my intention to attempt to settle this problem in one way or the other, notwithstanding the fact that I have observed at least some milk spots to be of an inflammatory nature. They occur at all ages. Our records show 2 examples in infants, but they are undoubtedly more common past the middle period of life. It seems rather strange that we should not know exactly why these plaques develop as they are certainly accessible to study.

Under this heading we have the acute fibrinous, serofibrinous and purulent forms of pericarditis. The first two types predominate; gradations in the purulent forms occur from the slightly turbid

fluid to a frankly purulent one. The latter type has been unusually infrequent in our series of cases. There are several points brought out in the table which would bear some analysis. It is at once seen that a little over 5 per cent of the autopsies showed an acute pericarditis, and of this number the males were more than three times as numerous as the females, bearing out the general known sex incidence of this disease. Rather strangely, however, more cases occur after the age of forty. This is likely due to two facts, the number of children in our series was relatively small and acute pericarditis, *per se*, is not often fatal. It should be kept in mind that there is a difference in the group of acute pericarditis cases met with in the wards and in the autopsy room, especially in regard to the age. As a clinical disease, acute pericarditis is more often observed in young adults and children; further, it has a relatively low mortality, and hence is not frequently seen at autopsy. On the other hand, there are many instances of acute pericarditis appearing as a terminal infection with some other acute disease which was the cause of death. The involvement of the pericardium in this type of case is frequently not recognized before death; while it may be present at any age, our results indicated the tendency of this form to develop more often after middle life.

TABLE I.—ACUTE PERICARDITIS.

Cases.	Sex.			Age.			Amount of fluid.				
50	Males .	.	39	up to 10 .	.	2	5 c.c. .	.	.	.	1
	Females	.	11	10 to 20 .	.	6	10 c.c. .	.	.	.	1
				20 to 30 .	.	7	15 c.c. .	.	.	.	1
				30 to 40 .	.	9	20 c.c. .	.	.	.	2
				40 to 50 .	.	10	50 c.c. .	.	.	.	12
				50 to 60 .	.	7	60 c.c. .	.	.	.	1
				60 to 70 .	.	8	70 c.c. .	.	.	.	1
				70 to 80 .	.	1	100 c.c. .	.	.	.	5
							150 c.c. .	.	.	.	2
							200 c.c. .	.	.	.	2
							300 c.c. .	.	.	.	1
							400 c.c. .	.	.	.	1
							600 c.c. .	.	.	.	1
							Stated as not increased .	.	.		19

Acute pericarditis does not necessarily produce an increase in the amount of fluid in the pericardial sac. Almost three-fourths of our cases showed 50 c c or less fluid in the sac, while but one-seventh of the number had more than 100 c c of fluid present. This would seem to indicate, from the autopsy point of view, that the majority of acute infections in the pericardium are not associated with a large amount of fluid; but, as we mentioned previously, it is well to keep in mind that the acute serofibrinous pericarditis seen in the younger individual rarely comes to the autopsy table by reason of that disease alone. The reliance on increased cardiac dulness, assuming that it is due to fluid, as a point of diagnostic value may

not have an anatomical basis; in fact, I seriously doubt that it is possible to recognize with any method of physical examination an amount of fluid less than 100 cc. In only one-seventh of the cases, therefore, would the amount of fluid present have been of diagnostic aid.

One is not always able to demonstrate the etiological factor of this disease. It is our impression that acute rheumatic fever, chorea and tonsil infection with the endocardial and myocardial complications account for the majority of our acute clinical pericarditis. Streptococcus viridans infection is closely associated with this group, whether as the primary infecting agent or not, it is difficult to say, but certainly it is a factor; eliminate this streptococcus and there is nothing left. Until proved otherwise let us regard this infection as the etiological one for this group. Our actual findings, however, would indicate that acute endocarditis was present 10 times with acute pericarditis; but on 32 other occasions no pericardial lesion was associated. This merely shows that endocarditis is the more common lesion of the two. On 6 occasions during the acute stage of rheumatic fever with arthritis and twice associated with acute chorea a pericarditis was found, and in all of these instances there was other cardiac involvement. Two acute infections of the throat in chronic heart and kidney disease completes the list of this etiological group, comprising thus two-fifths of the cases.

It was somewhat surprising to find that in 128 cases of lobar pneumonia there were only 10 associated with pericarditis, and in one-third of these the inflammation was purulent. It is of interest to remember that a considerable amount of suppurative pericarditis was found in the pneumonias of streptococcic origin; but this bacterial finding has been practically unknown in the lobar pneumonia of our community. The pneumococcus seemingly is not especially prone to develop a pericarditis (7 per cent), but when this condition does occur it is liable to become purulent. In all probability if the duration of pneumonia were longer more purulent exudates likely would be found in the pericardial cavity. There were 13 other cases in which some inflammatory focus was present in the lung, as foreign body with mediastinitis, empyema, abscess and gangrene, tuberculosis and cancer; about one-half of these were of streptococcic origin. Suppuration in the pleural sac is certainly a commonplace complication of pneumonia as compared with pericarditis in the same disease. One case of pericarditis was present in 50 autopsies on epidemic influenza.

Infection arising from the peritoneal cavity, particularly from the gall-bladder with liver or subdiaphragmatic involvement, accounted for 7 cases of pericarditis. In this instance the infecting organism is almost always a streptococcus pyogenes.

Recently, Libman has called attention to the association of acute pericarditis with coronary embolism and infarction of the heart.

I have confirmed this on one occasion during the past few weeks and there is one other case in our records. This observation would bear further watching, as it may be of considerable value in diagnosis.

It was not possible to get an accurate estimate of the bacteriology, as certain difficulties were present which would have to be considered before laying too much stress on the autopsy bacteriological findings. To put any reliance upon these findings it is necessary to have the cultures made within as short a time as possible after death, as postmortem contamination in the thorax occurs very quickly. In our opinion, however, the Streptococcus viridans and pyogenes are the two common invaders while the pneumococcus ranks next. A word possibly would not be out of place regarding the fibrin deposited on the pericardial surfaces. It is often present in very small amounts. The surface over the right ventricle and at the base between the larger arterial trunks appears to be the most frequent situation for fibrin, especially when it is very sparingly distributed. In this connection it is of interest to remember that this is also the situation (anterior wall of right ventricle) favored by milk spots to which we previously referred. One has often to look carefully to see the fibrin on the surface of the right ventricle even where in life a well-marked friction sound had been heard. I have had the opportunity of following this point in several cases within the past year, and must admit being surprised to find so little fibrin in certain instances where very definite friction rubs had been present.

TABLE II.—CHRONIC PERICARDITIS.

Cases.	Sex.		Age.			General adhesions.	Local adhesions.
40	Males .	. 31	Up to 10 .	.	1	17	23
	Females	. 9	10 to 20 .	.	5		
			20 to 30 .	.	9		
			30 to 40 .	.	10		
			40 to 50 .	.	5		
			50 to 60 .	.	6		
			60 to 70 .	.	2		
			70 to 80 .	.	2		

The presence of fibrous adhesions in the pericardial sac indicates a chronic pericarditis. These adhesions may be localized as a few fine fibrous strands more often noted at the base of the heart, but also present anteriorly near the apex; or they may be diffusely present, forming the so-called general adhesive pericarditis. The localized fibrous adhesions in all probability in the majority of instances are little more than interesting pathological findings, as they are not only impossible to diagnose clinically, but there seems to be, further, little evidence to indicate that they actually produce any mechanical disturbance. Of course, a heavy isolated band in certain situations might produce considerable impairment in function leading to compensatory changes, as hypertrophy of the heart.

But these instances in our opinion are rather the exceptional findings. Table II shows that a little more than 4 per cent of the autopsies presented evidence of chronic pericarditis, and of this number a little less than half were of the general adhesive type. The male predominates, the relation being about the same as it is in the acute form of the disease. It is of interest to note that in one newborn child a diffusely adherent pericarditis was found. The infant presented some suggestive signs of congenital syphilis, although positive proof was never established. Over a half of the cases occurred under the age of forty, which is exactly opposite to what was found in acute pericarditis. The amount of fluid in the pericardial sac does not appear to have any relation to this form of pericarditis, as in the adherent form there is, of course, no fluid present, while in the localized type there is nothing in the adhesions themselves to call forth an effusion. It is my impression that one rarely sees chronic pericarditis with effusion, as this condition is either a persistent acute serofibrinous form or a tuberculous process. The latter is by no means rare.

It is a very difficult matter in many cases to identify the etiological factor responsible for chronic pericardial adhesions. This is but to be expected, as fibrous adhesions indicate an end-result, and it is always difficult to follow the course of a disease, especially pericarditis, a disease so often of an indefinite character. As a general principle, it would seem to us that the best explanation for the production of chronic adhesions is the organization of an acute fibrinous pericarditis and, therefore, the etiology would be the same for the chronic as for the acute form. Wells has suggested that a certain number of the adherent types of pericarditis are of a tuberculous nature, many possibly never existing in the state of a tuberculous pericarditis, but representing the fibrous tissue reaction induced by the tuberculous toxin developing in an adjacent active lesion such as the mediastinal lymph nodes. According to Wells the adhesive forms show nothing which would indicate tuberculosis either in the gross or in sections. We agree with this statement. It is possible that some obliterated pericardial sacs develop in the way suggested by Wells, but it is our impression that they form only a very small percentage of these cases. In but 3 of our 17 cases does it appear likely that tuberculosis was the etiological factor. At least it was the only disease present, the heart being perfectly normal. It should be added that there was nothing in these 3 cases in the pericardium itself to indicate morphologically a lesion characteristic of tuberculosis. According to our records this form of pericarditis is more often associated with endo- and myocarditis or what we may term the rheumatic-fever-cardiac group. This, in our opinion, is the etiological factor of first importance for any form of chronic pericardial adhesion but actual proof of this is not always forthcoming. That the other acute infections, as pneumonia, play

a part is but logical. There is nothing to indicate why general pericardial adhesions develop in some instances and local adhesions in others, although it would seem most likely that a massive acute inflammation would be more prone to develop general adhesions. On the other hand, however, it is quite possible that a recurrent infection could produce the identical result; while localized adhesions most likely would indicate single infections, probably not of an intensive character. As these are points which, even at the best, are debatable, one should not lay too much stress upon them.

Heart changes are not always associated with chronic pericarditis, and *vice versa*, pericarditis is not always present in heart disease; the endocardium and myocardium are undoubtedly more vulnerable than the pericardium. This fact is brought out in our records which show no pericardial involvement in 43 autopsies in which the cause of death was due to heart disease. In 11 of the chronic adhesive pericarditis cases there was evidence of chronic endo- or myocarditis, thus leaving 3 cases of this type in which the etiology was most indefinite, as tuberculosis was not present. The relation of kidney and arterial disease to chronic pericardial changes is approximately the same as that of the heart, in that these three vital structures are so commonly associated in disease. The actual size of the heart does not appear to depend entirely upon mechanical difficulties thrust upon it by an adherent pericardium, as there were several instances with little or no cardiac hypertrophy. Enlargement of the heart in this condition is seemingly related more to the myo- or endocardial changes, to nephritis with hypertension or to extensive adhesions to the adjacent structures outside of the pericardial sac. There were no typical examples of Pick's disease in our series.

TABLE III.—TUBERCULOUS PERICARDITIS.

Cases.	Sex.						Age.						
10	Males	.	.	.	.	9	Up to 10	.	.	.	.	.	0
	Females	.	.	.	.	1	10 to 20	.	.	.	.	.	2
							20 to 30	.	.	.	.	.	3
							30 to 40	.	.	.	.	.	2
							40 to 50	.	.	.	.	.	2
							50 to 60	.	.	.	.	.	1

In this table one sees again the predominance of the males in pericarditis and it further indicates an earlier age level, as three-fourths of the number were met with before the age of forty. Tuberculous pericarditis usually produces a very large sac, containing a great deal of fibrin and often a large amount of fluid. This fluid may be blood-tinged, but more often it is clear and straw colored. The largest pericardial sacs, according to our records, have been the tuberculous ones. One rarely sees at autopsy the development alone of miliary tubercles on the pericardial surfaces in the same manner as one observes them in the pleura. Certainly, there is probably

a stage in the development of tuberculous pericarditis when it is likely that only tubercles are present; but the production of fibrin is soon so extensive that, at first glance, the characteristic appearance is that of an acute fibrinous pericarditis. At autopsy this fibrinous character is always evident, and it is by no means improbable that a certain number of tuberculous pericarditis cases are labelled acute fibrinous pericarditis. The tubercles are readily enough seen when the fibrinous exudate is scraped off so as to expose the deeper layers, and once in a while it is necessary, when the tubercles are indistinct, to wait for a microscopic section in order to be quite sure of the diagnosis. The term bread-and-butter heart may apply equally well to both the acute fibrinous and the tuberculous forms of this disease. At times one sees in the deeper portions of the exudate the development of a moderate amount of caseation, although this feature has not been prominent in the materials which we have studied.

The question has been brought up as to whether some of the diffuse adherent pericardial sacs represent healed forms of tuberculosis. Although this is a possibility it is my impression that such a fortunate sequence of events rarely occurs. The healed tuberculous lesions of the pericardium which present unmistakable signs of this disease are extremely unusual if one is to consider calcification as an evidence of healing. Wells observed calcification on 4 occasions, but he is inclined to look upon this deposit as being secondary to a suppurative condition in the sac. We did not see any example of calcification in our series, but agree with Wells that this change and probably also what has been described as calculi in the pericardial sac represent the end-result of a purulent pericarditis. Calcification following chronic empyemas secondary to lobar pneumonia with tuberculosis ruled out at autopsy, in which a cast of the chest wall had formed, have occurred several times in our records. So by analogy it would appear that the same process is possible in the pericardial sac. We mentioned before Well's conception of the relation of tuberculosis to certain of the adhesive forms of chronic pericarditis. He admits that it is a difficult thing to prove, and we follow him in this matter.

A similarity of origin is quite possible between adherent pericarditis and chronic adhesive pleuritis. It is the general conception that tuberculosis is the most common productive factor in this latter condition, although by no means the only factor. Anatomically these adhesions represent nothing but fibrous tissue, and only rarely is one able to demonstrate in them histological evidences characteristic of tuberculosis. There is, therefore, some ground for considering chronic adhesive pericarditis as having a tuberculous etiology, but as we have seen this condition associated more often with the rheumatic group it is our impression that tuberculosis accounts for but a minimum number of these cases. It would be interesting to observe

the final result in the cases of tuberculous pericarditis which have been apparently cured by drainage of the sac. My experience with this disease has led me to regard it as a very severe form of local tuberculosis possibly as malignant as its kindred infection of the meninges.

The relation of pericarditis to tuberculosis elsewhere in the body is of considerable interest. It is in fact always a secondary infection. There was only one case in which we were unable to find the primary focus of tuberculosis, but this by no means indicates that the pericarditis was the primary disease; it merely shows that the original focus was probably very small, likely a hidden lymph node lying so close to the pericardium that it could not be clearly identified. A point of considerable interest is that the development of a tuberculous pericarditis seems to have little relation to the extent of the tuberculous process elsewhere. In other words this disease in the pericardium is often purely a local entity in the same way as tuberculosis of the peritoneum or meninges. Remembering how prone endothelial lined cavities are to involvement in a process of general miliary tuberculosis, it was of interest to record but 3 cases where a pericarditis was present in this general infection. The pleura, peritoneum, meninges and solid organs may be studded with tubercles and yet the pericardium escape; while, on the other hand, a marked pericarditis may be present with only the mediastinal lymph nodes presenting the primary lesion. It appears to us that tuberculous pericarditis has a more intimate etiological relationship to tuberculosis in the mediastinal lymph nodes than to this disease in any other situation, and that the infection is lymph-borne or possibly by direct extension. This view is in agreement with what has been previously expressed by many writers on this subject. A blood-stream infection in general miliary tuberculosis does occur, but this we regard as the rare method of infection of the pericardial cavities. In only 5 cases out of a total of 37 dying of pulmonary tuberculosis was there any evidence of a tuberculous pericarditis. This would seem to indicate that the pericardium very often escapes even in fatal forms of tuberculosis of the lung. As latent or healed tuberculosis of the lung is such a common finding, its relation, therefore, to the pericardium must be practically *nil*. As was just stated, in 3 instances of general miliary tuberculosis there was a tuberculous pericarditis, but in 20 others, comprising miliary tuberculosis of the peritoneum, meninges, pleura and bowel, the pericardium was negative. Both the peritoneum and the meninges are more often involved while the pleura is rarely missed in a tuberculous death.

Diagnosis. *Acute Pericarditis.* Pericarditis is often not diagnosed, as the clinical record of any service, where autopsies are made with moderate regularity, will show. It is no doubt a difficult diagnosis to make in many cases. Further, some of the very recent

inflammations of the sac found at autopsy are probably of relatively few hours' duration, hence they could be very easily missed. It is also possible and probable that some of these infections do not give any physical sign. At the same time, however, we are quite certain that many acute pericardial cases which are unrecognized, at some stage of their course do present the classical signs, and if one is on the watch for this disease, positive results will be more often forthcoming. We have nothing new to add to the method of diagnosis; the symptoms and signs have been described in detail in text-books and in numerous articles.

In the diagnosis of acute pericarditis the friction rub is by far the most important sign. We do not need to go into its character or its situation, but suffice it to say that the to-and-fro grating sound, heard usually outside of the left sternal border below the third rib, is pathognomonic of a fibrinous pericarditis. The rub may be localized to an area not larger than the end of the stethoscope or it may be well heard over the whole of the precordium. Cessation of breathing and slight pressure on the end of the stethoscope are aids in bringing out this murmur. Its demonstration is worth all of the other symptoms and signs combined. The fleeting character of the friction sound should be kept in mind, as it may be present when the intern makes his night rounds and yet be absent when he attempts to demonstrate it to his chief in the morning. This is the reason why careful and frequent observations are essential if we are going to recognize the majority of the acute fibrinous pericarditis cases. I am not sure that the development of fluid is the only reason to explain the disappearance of the friction rub. It is possible that where very little fibrin has formed, absorption may readily occur. A very loud rub can be produced by an unusually small amount of fibrin, so small, in fact, that it may be readily missed by a careless gross inspection of the heart at autopsy. The next sign of value appears to be the size of the cardiac dulness. The increased dulness is due to the presence of fibrin or fluid, or both. One must keep in mind, however, that an increase of fluid is by no means a regular finding in acute pericarditis. Half of our cases had less than 100 c c, and I doubt very much that this amount could be appreciated by physical examination. Possibly as small an amount of fluid as this might be recognized by a roentgen-ray plate or fluoroscopy. Where larger amounts of fluid are present the well-known pear-shaped cardiac dulness can be readily demonstrated by percussion, but we should always confirm this with roentgen-ray examination. This form of pericarditis with its sudden onset and rapid accumulation of fluid, as shown by the increase in the cardiac dulness, can be readily followed in its development. Associated often with this rapid distention of the pericardial sac, one may observe cyanosis and dyspnea accompanied by pain.

The change in the intensity of the cardiac sounds from the very

distinct to the faint or muffled character, as the fluid and fibrin accumulates can, at times, be observed, and when present is of great value.

The presence of the precordial pain, associated with a febrile condition and an increased pulse-rate, is seen in about a third of the cases. McKenzie believes that all pain accompanying acute pericarditis is a manifestation of myocardial involvement, as the lesions of the pericardium itself are painless. This is a very interesting point, and may be the explanation, although McKenzie in his typical way does not force us to accept his conclusion. Might it not also be possible to explain the pain in some cases of pericarditis as being due to an associated involvement at the base of the aorta? Klotz has called our attention to the fact that an aortitis is not an infrequent sequela of an acute rheumatic fever. As it is following this disease that most of our acute clinical pericarditis develops, it would seem reasonable to believe that aortitis, which is very often painful, may share with the myocardium as being the source of this important symptom. There is one other explanation to be considered: the sudden stretching of any moderately rigid sac is liable to cause pain, and, therefore, in those cases of acute pericarditis associated with the rapid accumulation of fluid the presence of pain may be due to the stretching of the pericardium. This, however, does not appear to apply if enlargement of the sac has not been brought about rapidly, for we have seen enormous pericardial sacs in tuberculous pericarditis which clinically were quite devoid of any suggestion of pain. These accumulations, however, are always of a more gradual development.

There are many other minor signs described, but it is unnecessary to repeat them here, as Robey has recently written on this matter in detail, to which work the reader is referred.

Chronic Pericarditis. The diagnosis of chronic pericarditis is a very difficult one to make, much more so than the acute form. It may, in fact, be impossible to recognize this condition. We can see no clinical method which could possibly help us to diagnose local isolated fibrous adhesions. This form of pericarditis is purely an autopsy finding, but where the adhesions are general, or massively developed at one point, they may produce in a certain number of instances signs by which they can be recognized. In view of the fact that some cases of general adhesive pericarditis are found at autopsy without evidence of their having produced any change in the gross appearance or function of the heart, it can be readily seen that there are difficulties ahead when one attempts to speak on the diagnosis of chronic adhesive pericarditis. There are no pathognomonic signs or symptoms of this condition, but there are some suggestive points which when present, are of value, but their absence is not of much significance in ruling out adhesive pericarditis.

The retraction of the lower ribs, posteriorly on the left side, with

cardiac systole (Broadbent's sign) is probably of most value in diagnosis although it must be kept in mind that this sign has been found in other conditions than adhesive pericarditis. The retraction of the lower end of the sternum and the pulling in of the costal margins in inspiration, as pointed out by Hoover, are at times noted. There are a number of other points that have been suggested, and possibly on certain occasions they are of value. The diastolic shock at the apex and the diastolic collapse of the distended veins in the neck have been given as signs of clinical worth, but I doubt if anyone would like to rely too much on such evidence. It is our impression that fluoroscopic examination of the diaphragmatic movements in a certain percentage of cases may offer some suggestive points of value. It might also be of importance in roentgen-ray examinations to lay more stress on the appearance of the mediastinal tissues which usually show some alteration when the pericardial sac is involved. No reliance is placed upon the quality of the heart sounds, but cardiac derangement out of keeping with the apparent valvular lesions has been advanced as possible evidence of adhesive pericarditis.

There is a point which I believe may be of great value in making this diagnosis, but it is neither a sign nor a symptom. To be able to prove without any question of doubt that the individual had a previous attack of acute pericarditis is of extreme value, and in our opinion may be the only factor present which would lead one to the diagnosis of adhesive pericarditis. We have but recently seen an excellent example of this very condition. Five years ago, in the medical ward, I observed a very extensive acute fibrinous pericarditis following an acute rheumatic fever and associated with an endocarditis and in all probability a myocarditis. The patient recovered and graduated as a male nurse a few years afterward. He was in good condition and worked regularly at his occupation. He had some suggestive signs of a mitral stenosis with regurgitation; the heart was hypertrophied, but the action was regular. In April of this year, five years after the original infection, he developed tonsillitis with an acute pleurisy and atrial fibrillation was recognized. It was not present a short time previous to this acute attack of infection. He made a perfect recovery from his acute conditions and after a month's rest had his tonsils removed under local anesthesia. He died suddenly a month later. At autopsy a general adhesive pericarditis with hypertrophy and dilatation of the heart and a slight thickening with but little stenosis of the mitral valve were found. There was nothing whatever in this case, in the way of physical sign, pointing to an adhesive pericarditis except that we known positively that some years previous he had an acute fibrinous pericarditis, and on this ground alone an adhesive pericarditis had been suggested along with the myo- and endocardial changes.

Tuberculous Pericarditis. The form of tuberculous pericarditis which we especially refer to is a serofibrinous exudate implanted

upon a tuberculous base. Some of the largest pericardial sacs and some of the best examples of the bread-and-butter heart are of this type. Clinically, tuberculous pericarditis very often proceeds as an individual process which early has the appearance of an acute pericarditis, but which later passes into the subacute or chronic form. In our experience they have all been fatal and not necessarily associated with marked or extensive tuberculosis elsewhere. In a chronic pericarditis with effusion one should always think of tuberculosis, and here, of course, it must clearly be understood that a hydropericardium is not to be mistaken for this condition. The diagnosis of tuberculous pericarditis is not always easy, and at times is made only at autopsy. The chief point in diagnosis is the chronicity of the process in a lesion which presents the physical signs of an acute serofibrinous pericarditis.

In the early stages the signs are like those of acute fibrinous pericarditis. The friction rub is usually well heard over a considerable portion of the precordium, and it often persists for a considerable period of time. On two occasions I have been able to hear the rub for almost a month. There is rarely any pain in this condition, although it may be present. A diffuse, persistent friction rub over the heart without the slightest evidence of pain, as is seen in many of those cases, rather supports McKenzie's statement that the pericardial sac is devoid of pain. As fluid is nearly always present, and at times in very large amounts, the cardiac dulness consequently is much increased. The presence of dulness behind at the left base is noted in this condition with some regularity. It is not diagnostic of the tuberculous pericarditis, as it may also be present in any type of sac containing a large amount of fluid. The change from day to day in the character of the heart sounds is of considerable value, and I have been able to follow this sign on several occasions from clear, loud cardiac sounds to those which became distinctly muffled. The accumulation of fluid and fibrin is responsible for this change in the heart sounds. The febrile reaction is of a tuberculous type. The pulse-rate is rapid, and as the disease advances the temperature elevations become greater and the rapidity of the pulse increases. The course is progressively downward.

Conclusions. 1. Ten per cent of our autopsies showed pericarditis; 5 per cent were acute, 4 per cent were chronic and 1 per cent were tuberculous.

2. The principal etiological factor, in the acute and chronic forms of pericarditis, seems to be associated with the disease acute rheumatic fever.

3. Acute pericarditis was present in 7 per cent of the acute lobar pneumonias. The majority of these appeared probably shortly before death. The streptococcus in thoracic infection is more prone to produce suppuration in the pericardial sac than the pneumococcus.

4. In 54 cases of death due to tuberculosis there was no evidence of tuberculous pericarditis.

5. Tuberculous pericarditis is usually of the serofibrinous variety; it may be present in the absence of other clinical signs of tuberculosis; pathologically there is always a primary focus, usually in the lymph nodes of the thorax or in lung. The pericardium is often missed in a general miliary tuberculosis.

6. Tuberculous pericarditis should always be considered when the signs of acute pericarditis persist for an unusually long time, and especially when there is considerable cardiac enlargement and a progressively downward clinical course.

7. The presence of a friction rub is the most valuable diagnostic sign of acute pericarditis.

8. Chronic adhesive pericarditis can be diagnosed only in a small percentage of cases, as there are no distinctive signs. It is of real value to know of a previous undoubted attack of acute fibrinous pericarditis when considering the possible presence of a general adherent pericarditis.

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BALANTIDIUM COLI AND PERNICIOUS ANEMIA: REPORT OF FOUR CASES.

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Balantidium coli is a flagellate parasite inhabiting the colon, common in animals, especially the pig, but rare in man. The work of Strong, Bowman, Bel and Couret, and Manlove, shows that the parasite is capable of invading all layers of the intestinal wall. It has been found in the bloodvessels of the intestine and in other organs. With the accompanying bacteria superficial and deep ulcers are formed which cannot be distinguished from ulcers due to ameba until the microscope differentiates the parasite. The parasite also possesses the power of encysting.

The clinical symptoms of invasion by *Balantidium coli* bear a great similarity to those produced by ameba. Both present an acute and chronic form. In the acute form there is severe bloody dysen-

tery, with great loss of fluid and marked toxicity. Perforation may occur. Death follows usually in from a few days to one or two weeks. The chronic form often exists for years with alternating constipation and diarrhea. As with many other parasites the acute form seems to develop chiefly in warm countries and the chronic form in colder regions.[10] The symptoms and findings of pernicious anemia seem to accompany the chronic form of the infection.

The prognosis in the acute type is very bad, even if the case is seen early. In the chronic type it seems to be bad only when the syndrome of pernicious anemia is added. Our patients have died from the pernicious anemia rather than directly from the dysentery.

Schwartz finds a hemolytic agent in *Ascaris lumbricoides* and *Trichuris trichiura*, which he believes accounts for the anemia in these infections. Under certain conditions, supposedly including a decomposition of the segments of the worm, *Dibothriocephalus latus* produces a picture of pernicious anemia. If the worm is expelled the blood picture returns to normal.

Glaessner has found a hemolytic agent in *Balantidium coli*. It seems probable that the constant subjection of the blood-forming organs to the poison is the cause of the pernicious anemia syndrome in the chronic type of case. The removal of the *Balantidium coli* and its hemolytic agent is a far different problem than the removal of the Dibothriocephalus latus. Since *Balantidium coli* penetrates the intestinal wall and its bloodvessels and other organs in the body and also encysts we cannot be sure when the organism is eradicated from the stools that it is not harbored somewhere in the tissues of the body with its hemolytic agent still active. Thus if the pernicious anemia complex persists after treatment we cannot be sure whether the toxin of *Balantidium coli* is still active or whether once the complex is started it becomes an entity.

The treatment resolves itself into ridding the intestinal lumen and the body tissues of the organism. The literature indicates that most of the drugs used against intestinal parasites are without effect on *Balantidium coli*. In our experience in the Clinic with the flagellate *Lamblia intestinalis* we found that the only drug that gave any satisfaction was put into the blood in sufficient quantity to act as a direct poison when ingested by the parasite; in a large number of cases arsphenamin proved of great value. In our latest case of infection with *Balantidium coli* we employed arsphenamin with apparently very good effect. An enema with vinegar and tannic acid also was given every day or every second day with the idea of producing an acid medium in the colon and of giving a direct parasiticide. On account of encystment the treatment must be carried out a long time, just how long I do not know, since the length of time the organism may remain encysted and become active again has not been determined. That the living organism is very resistant is shown by Klein, who found actively motile *Parame-*

cium coli in sewage which had been bottled for three weeks. In the case treated by five intravenous injections of arsphenamin at weekly intervals, nine stool tests were negative for the parasite, the diarrhea was entirely checked, and the patient felt very much better; yet the neurological symptoms of pernicious anemia still persisted. Jennings reports one case with the pernicious anemia syndrome which was apparently cured after two relapses.

It is interesting in connection with the family histories of three of our patients that death of one or more parents, brothers or sisters, persons in the same household living under similar conditions and eating the same food, occurred from pernicious anemia or anemia. This may explain the family tendency to pernicious anemia in many cases.

Case A52257, Mr. W. T. L., aged forty-two years, a farmer for the past five years, came for examination April 26, 1911. The patient had had a spell of diarrhea for two months when working in a butter and cheese factory twelve years before. The diarrhea had recurred off and on until five years before, when it became more constant and severe; blood was passed at intervals. During the past one and one-half years the patient had lost 10 to 15 pounds in weight and had become weak and dyspneic on exertion. One year before sore-mouth developed, at times severe enough to make eating difficult. During the past one and one-half months numbness and tingling had been noticed in the hands and feet.

Examination. The examination of pus from around the teeth revealed many motile ameba and two organisms from the Flagellata, one evidently Trichomonas, the other narrower and much longer than Trichomonas. The total gastric acidity was 8; free hydrochloric acid 0. In the examination of the stool large numbers of *Balantidium coli* but no ameba were found. The blood picture is shown in Table I.

Treatment. Blaud's pills, Fowler's solution, and rectal injections of vinegar and tannic acid were given. For six months there were marked improvement and gain in weight with a great reduction in the number of *Balantidium coli* in the stools. Reëxamination after nine months showed no *Balantidium coli* in one stool test, but the clinical symptoms and blood picture of pernicious anemia were still present.

Case A185278, Mr. G. A., aged thirty years, a farmer who had never been outside of Illinois, Minnesota, and Iowa came for examination February 9, 1917. The patient's father had died of pernicious anemia one year before. Nine years before and two years before the patient had had short attacks of diarrhea. Five weeks before he had had "grippe" and one week later he had had a sudden attack of pain at the right costal margin running up into the chest

BLOOD FINDINGS IN FOUR PATIENTS HAVING BALANTIDIUM COLI

	A52257		A185278			A215036		A21480			
	4/26/11	1/2/12	2/19/17	3/12/17	9/28/17	11/27/17	12/21/17	5/5/20	5/19/20	8/19/20	9/16/20
Hemoglobin (%)	35	43	35	70	40	44	48	25	39	58	55
Erythrocytes (millions)	1.6	1.97	2.1	3.14	1.66	1.6	2.76	1.97	2.14	2.86	2.84
Color index	1.1	1.0+	0.8+	1.1+	1.2+	1.3+	0.8+	0.6+	0.9+	1.0+	0.9+
Leukocytes	10,400	9,700	11,800	9,400	3,600	4,600	5,900	9,800	6,000	4,400	4,900
Cells counted	300	300	300	300	300	300	300	200	200	200	200
Polynuclear neutrophils	58.6	66.7	66.3	64.3	54.7	55.3	44.3	67.0	39.0	48.5	36.0
Small lymphocytes	32.4	29.0	26.0	29.3	37.7	33.7	45.3	29.0	53.0	41.5	58.0
Large lymphocytes	4.0	1.7	6.3	4.7	4.3	1.7	6.3	4.0	7.0	7.0	3.0
Eosinophils	5.0	1.7	1.3	1.7	2.7	8.7	3.7	....	0.5	2.0	2.0
Basophils	....	1.0	....	....	0.3	0.7	0.3	....	0.5	1.0	1.0
Neutrophilic myelocytes	....	....	....	....	0.3	....	....	....	....	....	....
Normoblasts	4.0	1.0	....	....	8.0	....	....	....	1.0	....	....
Megaloblasts	8.0	....	1.0	....	....	....	....	....	....	....	....
Poikilocytosis	Marked	Marked	Moderate	Moderate	Marked	Moderate	Marked	Moderate	Moderate	Moderate	Moderate
Granular degeneration of erythrocytes	Slight	....	Moderate	Slight	Marked	Moderate	Moderate	Moderate	Slight	Slight	Slight
Polychromatophilia	Slight	....	Moderate	....	Slight	....	....	....	....	....	Slight

and right shoulder and difficult breathing. Diarrhea had been constant since the attack of grippe, with from four to five loose stools in the early morning and at night.

Examination. The patient was pale and sallow. He had pyorrhea and much bridge-work in his mouth. The systolic blood-pressure was 116, the diastolic 54. The urine was negative for bile and urobilinogen, but urobilin was present. Roentgenograms of the chest and teeth were negative. The blood picture is shown in Table I. The duodenal contents showed a brown trace of bilirubin, urobilinogen 1000 units, and urobilin 1400 units, indicating increased blood destruction. The examination of the central nervous system was negative. Six stool tests showed *Balantidium coli* but no other parasites.

Treatment. Thymol and Blaud's pills by mouth and enemas of kerosene were given; in three weeks this man eliminated almost all of the *Balantidium coli* and raised the hemoglobin from 30 per cent. to 70 per cent. The patient went home feeling much improved.

Examination six months later showed the *Balantidium coli* still in the stools and the clinical picture and blood findings of pernicious anemia. Examination of the central nervous system showed the cord changes usually found in pernicious anemia. The patient was again treated with thymol, salol, Blaud's pills, and Fowler's solution, but he left for home after three weeks, unimproved. He died the following summer.

Case A215036, Mr. G. H. B., aged fifty-two years, a farmer, was examined November 26, 1917. The patient's father, brother, and sister died of similar trouble, "thin blood." For twenty years past the patient had had spells of pain in the upper abdomen lasting for from one to two hours, with vomiting. He had had malaria at the age of fifteen. During the past year diarrhea had been persistent, five to six stools daily. He had lost about 60 pounds in weight; he had lost strength progressively and in the past three months numbness over the entire body with tingling in the extremities had come on. His appetite was poor; he had not had a sore tongue. His memory had failed for two months and recently he had been irritable, and had had crying spells.

Examination. The blood picture may be seen in Table I. The systolic blood-pressure was 150, the diastolic 100; the pulse 84. Examination of the urine was negative. The total gastric acidity was 10, free hydrochloric acid 0. Roentgenograms of the stomach were negative. Two blood Wassermann tests were negative. Proctoscopic examination showed very slight proctitis for 14 inches. The stool test revealed *Balantidium coli* but no other parasite. Examination of the central nervous system showed subacute combined sclerosis.

Treatment. The patient was treated for two months with thymol, chloroform, Blaud's pills, and hydrochloric acid without improvement. The *Balantidium coli* persisted in the stools and the blood picture remained the same. The patient died two months after leaving the Clinic.

Case A21480, Mr. F. L. S., aged fifty-seven years, a farmer, was examined in the Clinic May 4, 1920. One sister had died of anemia at forty-eight. The patient had come to the Clinic eleven years before on account of weakness and loss of strength with spells of diarrhea, at times severe. One stool test had showed occult blood. The protoscopic examination had been negative. During the following years the patient had had spells of diarrhea every ten days, lasting four or five days, with four or five watery stools a day, usually in the morning. Between attacks the stools were normal. Eight months before examination the patient had returned from the state fair with diarrhea and abdominal cramps. He noticed numbness in the extremities, his feet felt "asleep, or as if varnished," and had some weakness of the anal and vesical sphincters.

Examination. The patient's systolic blood-pressure was 116, diastolic blood-pressure 78, pulse 84. The test of the urine and the Wassermann test on the blood were negative. The total gastric acidity was 46, the free hydrochloric acid 0. Foci of infection were not found in the teeth or tonsils.

After tests on the stool and blood were made in the Clinic the patient went away for two days to visit relatives; he was brought back on a cot, with hemoglobin of 25 per cent.

Treatment. The patient was treated with distilled chenopodium and he improved in every way. The number of Balantidia was greatly reduced. The patient was given enemas of vinegar and tannic acid every second day and arsphenamin intravenously once a week for five weeks. After the last treatment nine stool tests, August 5, 6, 12, 13, 19 and 20 and September 16, 17 and 18, failed to show any Balantidia. The clinical symptoms of pernicious anemia are still present and the last blood test, September 16, showed 55 per cent. hemoglobin.

The examination of the central nervous system on three occasions is interesting in showing progressive involvement. May 11, when the hemoglobin was 30 per cent, the neurologist reported slight subacute combined sclerosis, hardly as extensive as in the average case of pernicious anemia of the same severity. July 14 the neurologist reported evidence to be insufficient for a diagnosis of a central nervous system lesion, but findings of combined sclerosis. August 21 the report was subacute combined sclerosis of the pernicious anemia type. This last report was made by a consultant who had not examined the patient previously.

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SOME EXPERIENCES WITH THE MELTZER-LYON METHOD OF DRAINING THE BILIARY SYSTEM.

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INVESTIGATIONS have been conducted during the past year with clinical cases, operation observations and animal experimentation pertaining to the Meltzer-Lyon method of aspirating duodenal contents after the installation of a solution of magnesium sulphate. This was done for the purpose of proving, if possible, the premises of Meltzer and Lyon as to the accuracy of published statements on the physiological phenomena of gall-bladder function and of this method of treating biliary conditions.   We feel that experimental studies on the physiology of influencing motor phenomena of the gastro-intestinal canal or the associated organs in animals cannot be applied, except in a general way, to the physiology of the digestive tract in man.   It follows then that clinical and operative experience, when these are obtainable and carefully controlled and deducted from, are more accurate and worth the while, and therefore none of our animal experimentation is presented.

S. J. Meltzer[1] published an article in which he drew attention to the supposed function of the sphincter at the papilla of Vater and

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[1] AM. JOUR. MED. SC., 1917, cliii, 469.

the interrelation between the contracting gall-bladder and the sphincteric action at the papilla. He invoked "the law of contrary innervation" to explain the physiological coaptation of contracting musculature and relaxing sphincter. He then suggested testing, by means of the duodenal tube in jaundice and in biliary colic by the local application of a 25 per cent solution of magnesium sulphate, and stated, "It may relax the sphincter of the common duct and permit the ejection of bile, and perhaps even permit the removal of a calculus of moderate size wedged in the duct in front of the papilla of Vater." Lyon[2] adopted this means as a diagnostic test for diseases of the gall-bladder (basing this upon the study of the amount, color, character, cytology and bacteriology of the contents obtained) and advanced the procedure as a means of treating biliary conditions. Since Lyon's articles appeared many have employed this means of diagnosis and treatment, and it now seems timely to present the facts we obtained from a dispassionate study of the method.

Lyon[3] presents five reasons for believing that the darker bile, obtained after a few minutes of aspiration, is obtained from the gall-bladder. These with our experience are offered as follows:

"1. Because I believe that Meltzer's law of contrary innervation as applied to the biliary apparatus is a correct one, and is based upon a sensible interpretation of the most probable mechanism of the physiological storage and discharge of bile." (Lyon.)

Four operative cases were examined with the duodenal tube *in situ*. The abdomens being opened the installation of magnesium sulphate solution was made. None of these were instances of gall-bladder disease. Care was taken not to touch or cause any pressure on the gall-bladder or the ducts. Since vermicular movements of the intestines stop when exposed to air, and they are only active when in contact with the peritoneum, care was taken to keep the upper abdomen closed to air and the normal contact of the parts preserved. At intervals, with as much care as possible, visual examination of the gall-bladder was made, and in no instance was it possible to prove any vermicular action on the part of the gall-bladder or any visible reason to suggest that any contraction took place or that the characteristic dark-colored bile when obtained was from the gall-bladder. For the latter purpose it was sometimes necessary to keep the abdomen open up to one-half hour, which from many aspirations of bile with the method is about the time when the characteristic "B" bile could be depended upon to be secured from a single instillation of magnesium sulphate solution.

Independently, one of us (W. H. L.) carried out investigations on operative material to prove or disprove "Meltzer's law of contrary innervation," these being offered in the following cases:

² Jour. Am. Med. Assn., 1919, lxxiii, 980-982.
³ Am. Jour. Med. Sc., 1920, clx, 515.

CASE 1.—Appendicitis. The duodenal tube was passed one and three-quarter hours before operation. Right rectus incision. Appendix removed. Upon palpation the tube was found to be in the duodenum, with the tip about opposite the papilla of the common duct. The gall-bladder was palpated and was found full and slightly tense. Fifty cc of a 25 per cent solution of magnesium sulphate were injected into the duodenum. The gall-bladder was gently held in the hand of the operator for eight minutes. It did not contract nor diminish in size. The tension was apparently the same as before injection. Two separate aspirations were now made of the duodenal contents. The gall-bladder was not affected, but was now compressed and easily emptied. Another aspiration obtained very much darker bile than the last specimen.

CASE 2.—Appendicitis. The tube was passed one- and one-quarter hours before operation. Right rectus incision. Appendix removed. Upon palpation the duodenal tube was found in the duodenum with the tip about opposite the opening of the common duct. The gall-bladder was palpated and was found apparently normal. Slightly flaccid. Fifty cc of a 25 per cent magnesium sulphate solution were injected through the tube into the duodenum. The gall-bladder was gently grasped and held for five minutes in the hand of the operator. It did not contract. Two aspirations were now made. The gall-bladder did not change apparently. The gall-bladder was now gently compressed, easily emptied and much darker fluid was obtained upon aspiration.

Not being satisfied with palpating the gall-bladder, I determined to try out the test on the first clean case of cholelithiasis, where we could actually visualize the actions of the gall-bladder.

CASE 3.—Cholelithiasis. The tube was swallowed one- and one-quarter hours previous to the operation. The gall-bladder was exposed through the right rectus incision. The tip of the duodenal tube was found in the pyloric portion of the stomach by the operator and passed through into the duodenum, extreme care being taken not to touch the gall-bladder. That I had stones to deal with I was sure, as determined by roentgen-ray findings, and upon exposing the gall-bladder the stones were plainly visible. Fortunately, the patient was a thin little woman with a concave abdomen, so that I could observe the gall-bladder without having to wall off any loops of intestines by foreign material, as lap pads, etc. The edges of the wound were gently retracted and lifted upward, and I was enabled to observe the gall-bladder without manipulation and without in any way interfering with its physiology. The question having arisen as to how much the manipulations in the previous tests did interfere with the natural action of the gall-bladder, we demonstrated in this case the peristaltic wave going through several

exposed loops of intestine that were visible to all present. The gall-bladder was sliding up and down with the liver in as natural a condition as possible under the circumstances. Fifty c c of a 25 per cent magnesium sulphate solution were injected into the duodenum and the gall-bladder was directly observed for five minutes. It did not decrease in size, no change apparently taking place. It was the opinion of some of the observers that it had slightly increased in size. First aspiration, light fluid; second aspiration, darker; third aspiration, the same. The gall-bladder was then palpated, compressed and was found to contain numerous stones. The fourth aspiration after compression obtained darker bile-stained fluid.

CASE 4.—Appendicitis. Tube swallowed one and a half hours before operation. Right rectus incision. Appendix removed. Stomach palpated. Tube found not to be in the duodenum, but coiled in the stomach with the loop passing across the pyloric end and tip at the cardiac end of the stomach. The tube was passed into the duodenum by manipulation of the operator. The gall-bladder was palpated and was found quite tense and hard. Fifty c c of a magnesium sulphate solution were injected and the gall-bladder held in the hand for eight minutes. It underwent no observable change. Two aspirations—one light and one dark. The gall-bladder was then compressed and emptied, requiring considerable pressure. At the third aspiration much darker fluid was obtained.

CASE 5.—Exploratory laparotomy for definite pains in the upper right hypochondriac. Roentgen-ray findings were negative. The patient never complained of pains in or about the appendix. A duodenal tube was passed one hour and thirty-five minutes before the operation. Right rectus incision. A tightly contracted pylorus was observed; the bulb of the duodenal tube was at but not through the pylorus. The gall-bladder was normal. The appendix was a white fibrous rod and was removed. Upon section no lumen was disclosed.

Diagnosis. Fibroid obliterating appendicitis, causing pylorospasm. Pylorus was with difficulty dilated large enough to admit a finger. Invaginated through the anterior gastric wall. A duodenal tube was passed through into the duodenum by the operator. Sixty c c of a magnesium sulphate solution were injected into the duodenum and the gall-bladder was observed, as in Case 3 by direct vision, for fifteen minutes. Absolutely no visible change took place during this time. Two aspirations—light and dark fluid. The third aspiration, after compressing and emptying the gall-bladder, was slightly darker.

In two of these cases the duodenal tube was found by the operator not to be in the duodenum, although distinctly bile-stained fluid was escaping from the outer end of the tube before anesthesia was

commenced. It was suggested that perhaps the tip had been in the duodenum and was afterward regurgitated into the stomach. In the last case, however, although bile was escaping from the tube, the bulb had stopped at the pylorus and we do not think that it was possible for it to have passed through the pylorus at all on account of the pylorospasm present, nor can I account for the bile getting through the same pylorospasm into the stomach.

CASE 6.—Appendicitis. Tube swallowed one and a half hours before operation. Right rectus incision. Appendix removed. The gall-bladder and the duodenum were palpated. Tube was found in the duodenum. The gall-bladder was of moderate tension. Fifty c c of a 25 per cent solution of magnesium sulphate were injected. The gall-bladder was held for eight minutes. Four aspirations of duodenal contents were obtained—from clear to dark. The gall-bladder after the last aspiration was thought to have become less tense. The gall-bladder was compressed, easily emptied and much darker fluid obtained on the fifth aspiration. (W. H. L.)

It is a well-known fact that with the identical technic in the same individual, various findings as to different colored bile are obtained at different times. If a relaxation of the muscle of Odii could be obtained at one time with corresponding contraction of the gall-bladder there is no reason that it should not be accomplished at all times that the procedure is practised. The evidence is daily, and always in the same individual even, that the error is beyond what variability of physiological phenomena could account for. It is far more logical to believe that Lyon was overenthusiastic in his acceptance of Meltzer's suggestion as a proved fact. Also, Lyon draws his simile in the action of the gall-bladder with the urinary bladder. It must be remembered that the control in the urinary bladder is entirely voluntary, while that in the gall-bladder is involuntary.

It is a well-known fact that cholectomized pigeons die in a few days from acute pancreatitis, due to the entrance of bile into the pancreatic substance. This danger exists only to a very limited degree in the human, as is proved in acute obstruction of the common bile duct (stone impacted in the common duct). There is a protective equation in bile not being able to gain the general circulation and also in its intense concentration in the biliary channels. In these instances marked distention of the gall-bladder and ducts is met with. It is our belief that in the interval of active bile secretion the pressure within the biliary channels is not as great as during active secretion. We are rather of the belief that the gall-bladder acts as a buffer or pressure-valve to relieve acute distention and protect the pancreatic tissue rather than that its primary function is that of a reservoir of bile for intestinal digestion. This belief is also fortified in that while the human may live without a gall-bladder, Nature dilates the ducts after its removal to compensate for this function of the

channel system, and until this takes place bile flows more steadily into the duodenum. We therefore believe that there is no evidence to substantiate the belief that installation of a 25 or a 33 per cent. solution of magnesium sulphate into the duodenum causes relaxation of the Odii sphincter or that any contraction of the gall-bladder or emptying (even partially) takes place, and therefore the assumption of Meltzer's and Lyon's reasoning seems to be vitiated.

"2. My second reason lies in the fact that the color and viscosity of this second bile indicates a higher concentration, and strongly suggests it as coming from its storage chamber within the gall-bladder." This is further fortified by the observation that bile is found thick and sometimes tarry in diseased gall-bladders containing mucopurulent flakes, pus cells, inflammatory debris, bacteria, etc., and that such are also met with in "B" bile. (Lyon.)

This is a very difficult matter to prove in "B" biles, the specific gravity of which is so changed (elevated) by the magnesium sulphate content that specific-gravity estimations are quite worthless. We believe that the specific-gravity practically corresponds to the salt content present in the specimen, and, further, that in gall-bladder biles not obtained by this method the specific gravity is not much elevated from hepatic bile, at least to no practical degree by the addition of the mucin it gets in the gall-bladder. This seems difficult to believe, but it is, nevertheless, true. More than that, it is not possible to differentiate mucopurulent flakes, pus cells and inflammatory debris, particularly bacteria, as to what part of the biliary tract they come. They are commonly as largely met with in the first bile (A) and not uncommonly in C and D. When we assume that such findings are from the gall-bladder when there is so much liability of admixture from the duodenum or stomach contents which have been poured into the duodenum, and there is no positive proof in the examination of specimens to sustain it, the liability of clinical error is too great for this statement to go unchallenged. Mucopurulent flakes are far more often from the duodenal mucosa than from the biliary tract, and the same is true of bacteria. On the other hand it is not uncommon that the bile stream at the end of the test (bottle C and D), "liver drippings," has a larger bacterial content than that obtained in the B bottle. The bacteria here are probably from infections of the ducts and perhaps even of the liver substance itself. From these cytological findings we feel that reasoning No. 2 is too liable to error to be conclusive in any way. More than that, the color change to the "B" bile is so irregular, often so illy defined and so slowly transitional, that it is not possible clinically to draw definite deductions that the "characteristic bile in bottle B" is from the gall-bladder.

It is evidently assumed by the advocates of this method of diagnosis and treatment that the old physiological belief—namely,

that the gall-bladder is a reservoir containing a ready-at-hand supply of bile for quick ejection into the duodenum for the initiation of intestinal digestion—must be true, although it never has been proved and still remains an assumption from anatomy. On the entrance of food into the duodenum it takes but a very few minutes for bile to start running; in fact, it begins running actively when food is still in the stomach. This is accomplished so quickly on the ingestion of food that it is believed by us to occur sooner than a harmonic action from the duodenal mucosa could bring about. If it is due to secretin the secretin must come from the stomach, because it occurs before resorption and stimulation of the hepatic and pancreatic functions could take place after the first entrance of food into the duodenum. It may, on the other hand, be due to some reflex action because it occurs within a few moments after food is in the stomach and promptly when many substances are instilled into the duodenum.

Finally, it is agreed upon by all that the bile contained in the gall-bladder is deeper in color than that which flows directly from the liver substance, and it is assumed by-many that this change in color is due to concentration, although the specific gravity estimations do not sustain it distinctly. It more probably is due to oxidation of the biliary coloring matter, the oxygen being derived from the epithelium of the gall-bladder, or, as seems more probable, the first bile secreted by the liver in the process of active digestion contains a large content of oxydase (which is a heavy content in liver substance, particularly in the first bile after a meal). Such a bile then could and would be darker in color without having resided in the gall-bladder. This finding is confirmed in the cholectomized individuals, which cases commonly show characteristic " B " bile shortly after operation (one to three weeks) before there has been time for the ducts to dilate, as well as in those cases which have been cholectomized some time before and in whom perfect " B " biles are obtained, even if Lyon states to the contrary. From our observations and experiments, then, it is suggested to us that the change of color is due to an oxidation process in which ferments or constituents contained in the bile cause the conversion of color, this dark bile coming directly from the liver substance as well as being caused by residence in the ducts or gall-bladder when ordinary bile low in oxydase naturally would deepen in color.*

" 3. My third reason for believing that this second bile is derived largely from the gall-bladder lies in the fact that unless we account

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* Dunn and Connell: Jour. Am. Med. Assn., October 1, 1921, present conclusive evidence in a case of hepatoduodenostomy which was carefully studied by them, that the *A. B. C.* bile sequence can be obtained in the absence of the gall-bladder and the common ducts; that these sequences can be repeatedly observed by successive instillations of magnesium sulphate solutions and that the various colored biles are secreted directly by the liver by magnesium sulphate carried to the liver by the portal circulation.   These observations confirm those made by us, our article being submitted for publication in June, 1921, and the experimental work was carried out through the winter of 1920 and 1921.

for it as gall-bladder bile we must account for the presence of from
one to (in certain cases) nearly six ounces of this darker colored and
more concentrated bile as coming from somewhere between the
common duct sphincter and the secreting cells of the liver.'' (Lyon.)

This is partially answered in the above in the quick response of
bile secretion on the injection of food into the stomach and its ready
flow when anything like food is sent into the duodenum. The above
reasoning presupposes that when food is present in the duodenum
only such bile as has been formed and is residential in the gall-
bladder and ducts is available for use. Einhorn[4] shows that various
inorganic salt (sodium sulphate, sodium phosphate, magnesium
citrate) solutions stimulate a quick response of bile secretion into
the duodenum. Stepp recommended that Witte's peptone in 5
per cent. solution be used for the same purpose for which Lyon uses
the magnesium sulphate. Our experience with fibrinated and
defibrinated pig's blood, with or without biliary salts, or a solution
of biliary salts, accomplished the same thing in the way of a quick
secretion of bile with the characteristic color changes that Lyon
describes with the magnesium sulphate solution. With the use of
any of a number of substances the characteristic A, B and C biles,
and mainly the so-called "B" bile, is obtained quite as readily as
with the solution of magnesium sulphate. There is therefore no
specific point in the use of the magnesium sulphate solution when so
many other substances accomplish the same end. Our experience
has been that if there is any point in obtaining a large quantity
of bile in an aspiration there is no better stimulant than a weak
solution of hydrochloric acid corresponding to the affinity of gastric
juice. Instillation of 50 cc at a time, or 10 cc quantities (which
will not give the characteristic changes until three or four instilla-
tions have been made), will produce a far larger quantity of bile
than any other method. We have obtained as much as 620
cc of bile fluid return after the use of a $\frac{1}{2}$ per cent solution of hydro-
chloric acid, which in acid affinity corresponds to about one-third
the acidity of normal gastric juice.[5] In not a few instances where
we have not been able to get the characteristic "B" bile we have
used hydrochloric acid solution instead of magnesium sulphate,
and obtained it far more readily. In fact our experience lately has
been that for uniformly obtaining the characteristic "B" bile the
instillation of from 5 to 50 cc of a $\frac{1}{2}$ per cent solution of hydro-
chloric acid is a far better procedure than the use of the magnesium
sulphate solution. These facts therefore refute the specific action
of magnesium sulphate relaxing the sphincter at the papilla of Vater

[4] New York Med. Jour., February 19, 1921.

[5] It has been our experience that the amount and rapidity of secretion of bile
correspond to the concentration of hydrochloric acid. However, in using concen-
trations over 0.5 per cent of the C. P. (31.9 per cent) hydrochloric acid, patients often
complain of burning sensations in the epigastrium and "cramps." On the other
hand, no ill effects accompany the use of the 0.5 per cent solution, even using quanti-
ties up to 100 cc and higher, which give very satisfactory results, as described above.

or influencing favorably the innervation of the gall-bladder, because it stands as irrefutable reasoning that if any one of a number of substances produces the same result as quickly and sometimes more abundantly than magnesium sulphate, Lyon's third reasoning fails to be convincing. It disproves the belief of Lyon that "six ounces" as a large quantity must come from the biliary channel as erroneous. If, on the instillation of magnesium sulphate, six ounces of bile, including the characteristic "B" bile, rushed suddenly into the duodenum there might then be some reason to it, but with the magnesium sulphate the flow is slow and the characteristic "B" bile does not occur until some minutes, often as long as thirty. In the same individual the characteristic "B" bile may be obtained much quicker with the use of a weak solution of hydrochloric acid, and perhaps in varying lengths of time with solutions of other characters. It is true that with the instillation of a weak solution of hydrochloric acid the specific gravity is low, and no doubt there is a considerable content of succus entericus; but, nevertheless, as judged from the color of the material obtained, larger quantity than six ounces is secured directly from the biliary channel. We therefore believe that if the obtaining of bile in quantities is an important point in a therapeutic way, and this bile possesses all the characteristics of that obtained from an instillation of magnesium sulphate solution, the use of a weak solution of hydrochloric acid is a far better means to obtain a large quantity than magnesium sulphate.

"4. My fourth reason, and I feel it is the strongest, for believing that this second type of darker yellow and more viscid bile is actually coming in large part from the gall-bladder, lies in this (I think) convincing fact—namely, that in the cholecystectomized patients that I have studied postoperatively, some ten or more cases, I find (a) that I never recover the second type of dark bile but pass immediately from the light golden yellow or relatively more concentrated common-duct bile to the light lemon yellow and limpid bile that I believe is freshly secreted liver bile and collectable for long periods as rapidly as it is secreted, and (b) I find that (in this cholecystectomized group) in the larger number of instances, bile is continuously entering the duodenum in the fasting stomach and duodenal state, indicating that the duct sphincter is in a state of inhibited tonus, probably permanently so, since the antagonistic or contrary innervation has been cut when the gall-bladder was removed." (Lyon)

This has already been answered. Characteristic "B" biles are are not only obtained from the vast majority of cholectomized individuals but also from those not yet out of bed from the operation before the ducts have had a chance to dilate to take up a gall-bladder function. It is true that in an occasional one the characteristic "B" bile is not obtained with the magnesium sulphate solution, whereas it might readily be with a weak solution of hydrochloric acid or other stimulant, and as one has experience through

many people without gall-bladders, here and there, one is met with in which it is not obtained with any stimulant. But this is not proof that "B" bile is from the gall-bladder because there is practically as large a portion of people having gall-bladders in which no stimulant causes the "B" bile to occur. If one studies this method in true achylia gastrica cases (atrophic gastritis) it will be found that magnesium sulphate solution but rarely secures a "B" bile, while with the weak hydrochloric acid solution it can often be obtained. It is true that in cholectomized individuals the flow of bile is seemingly more steady into the duodenum, but the "B" bile is present just the same, and in many the whole phenomenon from the instillations is quite as in normal individuals. This reason does not hold true to our clinical experience.

"5. I might add a fifth reason, to the effect that in my post-operative group of cholecystectomized patients upon whom this non-surgical method has been practised (because the length of time over which surgical drainage could be maintained has not been sufficient to allay the catarrhal inflammation or to arrest the infection), that is in this group, together with a group of non-operated patients with cholecystitis or with gall-bladder biliary stasis, I have seen this second-type bile, easily demonstrable as pathological, gradually clear up and return to a more normal appearance under biweekly drainage by this method." (Lyon.)

This, it occurs to us, is entirely a happy assumption and will remain so until it is proved that the so-called "B" bile is derived from the gall-bladder, which in our belief has not been done. It has not been proved on observations with the abdomen opened, and Crohn, Reiss and Radin,[6] in a recent article, experimenting upon dogs in which he (R.) injected a small quantity of methylene blue in physiological salt solution into the gall-bladder and watching the flow of bile from the papilla into the duodenum, noticed that the flow of bile was almost continuous after a meal, and that this bile consisted entirely of liver bile, the blue discolored gall-bladder bile not appearing at all except when manually expressed. More than that, we have taken quite a few definite cases of gall-bladder pathology and have seen no lasting improvement. There are many who do fairly well, but our belief today is that the less the pathology the more the benefit. Apparently there is benefit to be obtained in the simple catarrhal conditions mainly when this is in the ducts (cholangitis). No benefit can be obtained by the method alone in cholelithiasis, with or without biliary colic, and especially in the latter, excepting such as comes from moral effect on the patient of seeing dark bile being aspirated and assuming that it must do some good. There is often a symptomatic benefit in the true gall-bladder case, but it is difficult to decide that this is actual because these cases often have distinct remissions of

[6] Jour. Am. Med. Assn., 1921. (Not published when this Ms. was submitted.)

symptoms and feel quite well without any treatment. Our pur-
pose here is not to dilate on this part of the subject, because we
have had enough material and experience to present this more fully
later on. We desire only to draw attention to the fact in *bona fide*
pathology of the gall-bladder that the method has no comparison in
results with proper surgery.

Pharmacology has taught us that in the ingestion of salines,
mainly those of a purgative nature, these are not resorbed into
the portal stream and excreted by the liver. Our experience has
refuted this in the sense that in all biles obtained by the magnesium
sulphate method, magnesium sulphate is present in the bile. This
content of magnesium sulphate continues up to two hours and more.
It was our belief at one time that the magnesium sulphate content
was probably derived from the duodenum either by the magnesium
sulphate solution being residual in the duodenum or regurgitated
back into the first part. The physiology of the duodenum proves
distinctly that anything that enters into it is rapidly discharged
into the jejunum. Regurgitation from the jejunum into the duo-
denum does not take place except in the instance of distal stenosis,
interfering with the onward flow of intestinal content into the small
intestine. More than this is the fact that in the instillation of a
weak solution of hydrochloric acid such returns as are obtained
show the presence of hydrochloric acid for only a few minutes after
its instillation. The same is probably true of any substance of a
fluid nature that is injected into the duodenum.

Smithies[7] states: "Gall-bladder bile fractions of more than 100
cc with specific gravity higher than 1020 are abnormal. They
indicate bile stasis." Our belief is that the specific gravity estima-
tion of the aspired bile by this method either in the way of proving
that " *B* " bile is from the gall-bladder or for any diagnostic reason is
open to too much fallacy to be practically worth the while. We
believe that the specific gravity of the various types of bile obtained
is due largely if not entirely to the magnesium sulphate content of
the bile that comes from the liver.

Fig. 1 shows the various content of magnesium sulphate in *A*, *B*
and *C* bile. It will be noted in the right-hand figure of the " *B* " bile
that the magnesium sulphate is distinctly more than in *A* or *C* bile.
It is our claim that this increment of inorganic salts markedly
increases the specific gravity of the specimens obtained. The pre-
sumption of higher specific gravity having practical significance can-
not be sustained in fact.

The left-hand tubes *A*, *B* and *C* in Fig. 1 are a test using barium
chloride, and were found by us to be erroneous. The right-hand figures
of *A*, *B* and *C* represent a simple test for comparing the quantities of
magnesium sulphate in aspirated bile specimens. It was made as
follows: To 2 cc of the specimen were added 2 cc each of a 10 per

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cent ammonium chloride solution, concentrated ammonium hydroxide and 10 per cent sodium phosphate solution. A white crystalline precipitate of magnesium-ammonium-phosphate settles out. This is shown by the chemical equation:

$$MgSO_4 + 2NH_4Cl + NH_4OH + Na_2HPO_4 = MgNH_4PO_4 + 2NaCl + (NH_4)_2SO_4 + H_2O.$$
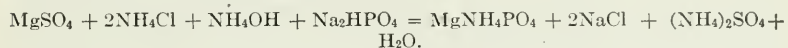
The amount of the reagents indicated are usually sufficient to precipitate all the magnesium in the 2 cc of the specimen. After the precipitate has settled a little a few drops of the reagent are added. If more precipitate forms the precipitation is not complete and more reagent is necessary. The tubes are then allowed to stand overnight and the sediments compared the following morning. The amount of precipitate formed and the specific gravity have consistently been directly proportional. Since the tests were tried we have found that a more accurate comparison may be made by using graduated centrifuge tubes and centrifuging for two minutes at 1500 revolutions. One cc of a 25 per cent magnesium sulphate

Fig. 1

30 cc	60 cc	25 cc
Colorless	Pea-green	Yellow-green
Sp. gr. 1.005	Sp. gr. 1.027	1.004
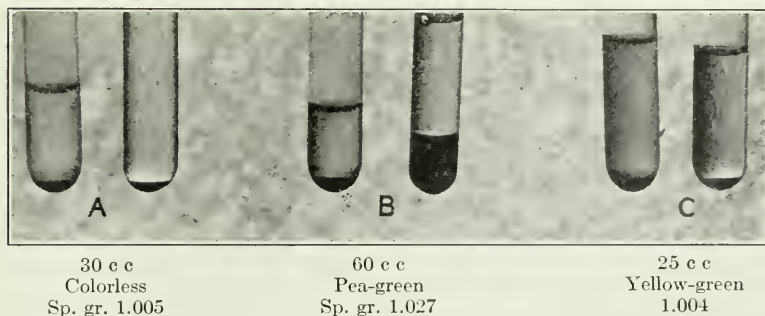
solution gives approximately 0.5 cc of precipitate. In this way the amount of precipitate and concentration of magnesium sulphate in a given specimen may be roughly gauged. Two cc of the specimen to be examined is a convenient amount to work with. A mixture of equal parts of ammonium chloride and 10 per cent sodium phosphate solutions are added to the 10 cc mark and concentrated ammonium hydroxide solution added to the 14 cc mark. This amount of reagent has been found sufficient to completely precipitate the magnesium in 2 cc of a 25 per cent magnesium sulphate solution.

Fig. 2 shows a graduation in specific gravity according to the content of magnesium sulphate. This observation was made on the same case as Fig. 1 above, and shows the variability in this method, which is one of the most prominent factors of it. Here for some reason we have a large content of magnesium sulphate in the A bile and gradually decreasing through B, C and D, having such a slight increase in the specific gravity of the D bile that it may be

considered negligible. It may be stated, parenthetically, that the color of the bile is independent of its specific gravity in the presence of magnesium sulphate. Our observation has been that, with the use of the weak solution of hydrochloric acid that we recommend, changes in color correspond more accurately to changes in specific gravity than is true when magnesium sulphate is present in the bile.

FIG. 2
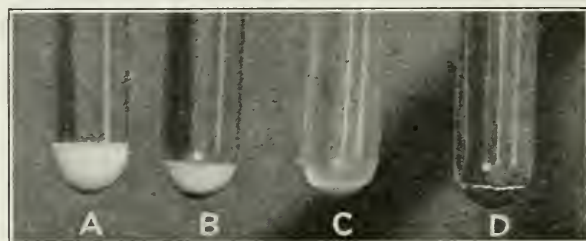
50 cc	30 cc	40 cc	35 cc
Golden-yellow	Pea-green	Light-yellow	Golden-yellow
1.028	1.016	1.010	1.012

As a result of our observations we feel the following conclusions are warranted:

1. The assumption by Meltzer of "the law of contrary innervation" is not proved, and this throws into doubt any specific effect of relaxation of the sphincter of Odii and contraction of the gall-bladder induced by a magnesium sulphate solution.

2. Any one of many substances taken into the stomach or injected into the duodenum will cause a ready flow of bile, of which a solution of hydrochloric acid in about one-third the acidity of normal gastric juice is the most potent for discharge of bile in large quantities and obtaining characteristic "B" bile.

3. That the deeper color of "B" bile is due to oxidation and not concentration from retention in the gall-bladder, this bile most often coming directly from the liver as a phenomenon of bile secretion.

4. That the viscosity of bile does not elevate its specific gravity to any practical extent.

5. That the margin of error in deducting from the presence of mucopurulent flakes, pus cells, inflammatory debris, bacteria and cells in the aspirated bile as positively coming from the gall-bladder is too great for clinical deduction.

6. That the physiology of the gall-bladder should not be deduced from anatomy and relationship alone—that its most important function seems to be to relieve pressure within the biliary system to protect the pancreas rather than acting as a reservoir for bile in a digestive sense, and that the physiology of bile secretion and gall-bladder function should be studied more thoroughly.

7. That cholectomized individuals show the characteristic "*B*" bile even shortly after operation before the ducts have had a chance to dilate. This occurs so commonly that "*B*" biles cannot always be from the gall-bladder.

8. The increase in specific gravity in aspirated bile by this method is due to the content of magnesium sulphate, which appears to be resorbed into the portal circulation and is excreted by the liver substance in the bile. It is erroneous to deduce clinically in both amount of biles obtained of any gradation (*A*, *B*, *C*, *D*) or by specific gravity estimations as to whether bile stasis exists or not.

9. That where true pathology exists in the gall-bladder the method is a poor substitute for proper surgery. It may be employed in suitable cases as a temporizing means, but it should not be depended upon to correct or definitely benefit pathologically diseased gall-bladders or when gall-stones exist.

ACUTE PANCREATIC NECROSIS.[1]

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It is generally recognized that the cause of acute pancreatic necrosis is related to disease of the biliary system, but just what this relationship is and the various factors which enter into the etiology and pathology of the disease are as yet far from being generally known. Therefore the treatment cannot be based on the soundest surgical principles. It is accepted since the work of Claude Bernard, in 1856, that in animals the injection of certain substances into the pancreatic duct will cause death from or various degrees of the lesion of acute pancreatic necrosis. Bernard used a mixture of bile and olive oil. Since that time these experiments have been repeated, and gastric juice, duodenal contents, solution of acids, alkalies, formalin, bile and bile salts were found to have the same effect, while less irritating substances had little or none.

The work of Opie in 1901, in which he produced acute pancreatic necrosis in animals by the injection of bile into the duct, and his publication of an autopsy finding, in which a small gall-stone obstructed the ampulla of Vater in a patient dying of acute pancreatic necrosis, linked up much of this experimental work with the findings of the disease in human beings. Five years later Flexner proved that the essential constituent of the bile necessary to cause pancreatic necrosis was the bile salts, of which the taurocholate

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[1] Read before the Hospital Graduates' Club, New York, March 25, 1920.

was the more active. He also showed that the mixture of mucin, due to its action as a colloid, with the injected material rendered it less active.

Other clinical and experimental observations have been responsible for various theories. It was found that experimental obstruction to the ampulla alone did not cause acute pancreatic necrosis and that small quantities of bile frequently entered the duct without causing any lesion in the pancreas. However, the injection of a bacterial culture into the gall-bladder under the same experimental conditions caused pancreatic necrosis. The observation that after the passage of a gall-stone through the common duct there resulted a dilatation or paralysis of the opening in the papilla was responsible for the theory advanced by Hess, and by Williams and Buck that acute pancreatic necrosis was caused by a damming back of the duodenal contents into the pancreatic duct. It has been shown, however, by experiment that after producing low obstruction of the duodenum it was impossible under normal conditions to force back the duodenal contents into the common or the pancreatic duct. This theory will be further considered later.

There is also the theory, strongly supported by Deaver, on which he has written extensively, of the retrograde infection through the lymphatics from an infection of the gall-bladder. In an article on acute pancreatitis published in 1917, he writes: "The work of Bartels, Arnsperger, Franke, Deaver and Pfeiffer, and Sweet has seemingly established the fact that such extension commonly occurs by way of the lymphatics, which form a rich anastomizing network in the retroperitoneal tissues about the pancreas." He also states that such infection may occur from a duodenal ulcer, appendicular infection or colitis. In an article published in 1919 he repeats this theory, stating: "Inflammation of the gall-bladder is followed by enlargement of the cystic lymph glands, periductal lymphangitis, enlargement of the glands at the head and at the margin of the pancreas and often of the regional lymph channels at the head of the pancreas." While it is true that this lymphadenitis does occur, there must also be considered the facts that infection does not usually occur against the lymph stream, especially after the passage through several chains of lymph nodes; and particularly the fact that the pancreatic lesion is not primarily an infection but a necrosis, with infection not occurring at all, or if it does occur, it is a secondary process. Also, even when an abscess of the pancreas results, it is frequently sterile. Therefore, in view of the known experimental facts, the enlarged peripancreatic lymph nodes may better be explained as secondary to the pancreatitis rather than the etiological factor.

The experimental work of Archibald has done much to explain an important factor in the production of the lesion of acute pancreatic necrosis. By his experiments on cats he found that the

small sphincter at the common duct orifice, first described by Oddie in 1887, furnished this link. Oddie had demonstrated that irritation of the duodenal or even the stomach mucosa, either mechanically or with dilute hydrochloric acid or stimulation of the vagus, would cause spasm of the sphincter and that the sphincter in dogs would resist a pressure of 50 mm. of mercury. Archibald, by the introduction of infected bile under just sufficient pressure not to overcome this sphincteric action, was able to cause the death of a cat from acute pancreatic necrosis in twenty minutes.

These experimental observations then would explain the various factors in the etiology of the disease. They have been stated by Archibald as: "First a change in bile composition increasing the proportion of bile salts: second, undue resistance, perhaps often amounting to spasm of the common duct sphincter; and third, abnormal rise of pressure in the biliary system behind, either in the gall-bladder or common duct." The necessity of the presence of all of these factors makes easier to understand several things previously explained with difficulty.

It must also be recognized that the disease is primarily a necrosis caused by the introduction of the changed bile into the duct. The other pathological changes which occur are secondary. Hemorrhage is a result of destruction of the vessel walls in the gland, due probably to the cytolytic action of the altered bile with later digestive ferment action. Suppuration is always secondary. Therefore the terms suppurative or hemorrhage pancreatitis or the old term pancreatic apoplexy are misleading and the term pancreatitis, usually used, itself is a misnomer, the primary lesion not being an inflammation, but a necrosis. The factor of the infection of the bile as a cause is primarily due to change of the proportion of bile salts causing necrosis and not to its action as an infective agent. It is also possible that infection precipitates the mucin from the bile, thus removing an element which renders it less destructive. A stone in the cystic duct might have the same effect by preventing the mucin from the gall-bladder mixing with the bile. Herein also lies the explanation of the relative frequency of the presence of gall-stones in cases of acute pancreatic necrosis and also explains the disease when gall-stones are absent, because while infection is an etiological factor in gall-stone formation, cholecystitis frequently exists without cholelithiasis.

The early experiments of Oddie, showing that various forms of irritation of the duodenum or even the gastric mucosa by acids, etc., causes spasm of the sphincter at the ampulla of Vater, explains why hyperacidity, duodenal ulcer or alcoholism and similar conditions causing duodenal irritation, in the presence of the other two required factors, furnishes the remaining element in the etiology of an attack of pancreatic necrosis. It is also well known that the secretion and flow of bile is stimulated by its need in the process

of digestion, and therein lies the third necessary element, an increased pressure, and explains why the acute attack frequently follows a heavy meal.

Variations in these three factors result in lesions of different severity. This was demonstrated by the experiments of Archibald. He was able to produce lesions varying from a necrosis which was fatal in twenty minutes to such small areas of focal necrosis in the pancreas that they were not demonstrable without the aid of microscopic examination and which in some instances were and in others were not accompanied by fat necrosis. Archibald has suggested as a result of his experiments the existence of attacks occurring in general practice, characterized by upper abdominal pain which are due to an undiagnosed moderate degree of pancreatic necrosis which does not proceed to the degree of sequestration, and which may even be accompanied by fat necrosis, but the lesion being aseptic is ultimately replaced by a fibrosis.

Three of my own patients exhibited conditions with a close bearing on this subject. An autopsy on a man who died after I had performed an operation for acute pancreatic necrosis revealed, besides the acute necrosis and hemorrhage for which the operation was performed, several areas in the pancreas of fibrosis, surrounding masses of creamy material which had obviously been the result of a previous attack from which he had recovered. His history showed that this attack had occurred one year earlier and had been diagnosed as a gall-stone attack. Another man developed an acute pancreatic necrosis while in the ward of Bellevue Hospital, convalescing from an operation for a urethral stricture. He refused operation, subsequently developed a large mass in the area of the pancreas, had later an elevation of temperature, a Cammidge reaction, which has since proved to be of less value than it was thought at that time, and had fatty diarrhea. This made the diagnosis of a pancreatic lesion obvious, but while he still persisted in his refusal to allow an operation, in the course of time the mass disappeared, he made a complete recovery and left the hospital free of symptoms. His subsequent history is unknown. In a third patient, a colored woman, the symptoms complained of were all referable to the pelvis, and at operation for a salpingitis which was present I noticed areas of fat necrosis in the omentum. After a salpingectomy an incision over the pancreas showed it very hard and indurated with hemorrhagic and greenish gangrenous appearing areas throughout the body of the organ. She made an uneventful recovery.

The first two cases then demonstrate the possibility of recovery from severe attacks and the third case the possibility of a marked lesion without anything pointing definitely to the fact that the pancreas was involved, as Archibald has demonstrated experimentally the possibility of mild attacks occurring with recovery ensuing.

The pathological lesion in the pancreas appears to be due to the

direct cytolytic effect of the changed bile permeating the gland, and Archibald believes that the ultimate extent of the lesion depends on this primary destruction. It is known that the secretion obtained directly from the pancreas has no digestive power until the ferments have been activated. This may occur pathologically by calcium from the blood or bile, inflammatory exudate, the product of an aseptic necrosis, or as it occurs normally in the intestine, by entero-kinase, the duodenal secretion; and the trypsinogen thus activated probably carries on some of the destruction previously originated. It is interesting to note, however, that in gastric resections or operations in which an adherent ulcer or carcinoma of the posterior stomach wall necessitates an injury or even a shaving off of pancreatic tissue, neither protein digestion of neighboring tissue nor fat necrosis occurs.

Even if we accept, however, the experimental and clinical facts which prove that the injection of changed bile into the pancreatic duct causes pancreatic necrosis, and explain the variations of the lesions by the different factors, contributing to the degree of the necrosis, it cannot be recognized as the cause of all cases of pancreatic necrosis. Opie in his book on *Diseases of the Pancreas* quotes various case reports in which the reflux of bile could not have been a factor. In one case reported by Eliot the duct of Santorini was the larger and entered the duodenum about 1.5 cm. above the papilla, through which emptied the smaller duct of Wirsung and the common bile duct. The necrosis in this case was most marked in the portion of the gland drained by the larger duct of Santorini. Johnstone reported 2 cases of pancreatic necrosis in which the pancreatic duct opened into the duodenum 1 or 2 cm. above the common bile duct opening. Basset reports 1 case in which the necrosis involved the area drained by a small duct of Santorini which entered the duodenum through a small diverticulum above the papilla.

The theory that duodenal contents might be forced back into the pancreatic duct and thus cause pancreatic necrosis has been already mention in this article, together with the work of Hess and of Williams and Buck, who observed a paralytic dilatation of the opening of the common duct after the passage of a stone, and assumed that this allowed the reflux of duodenal contents. Archibald writes: "This theory still remains theory." The anatomical conditions reported by Eliot, Bassett and Johnstone demonstrate, however, the impossibility of biliary reflux into the pancreas being the etiological factor in their cases, and as it is known that duodenal contents injected into the duct will cause pancreatic necrosis (Polya), it seems fair to assume that this was the cause of the pancreatic necrosis in the cases mentioned; for while, as has also been previously mentioned "under normal circumstances, it has been found impossible by experiment, such as complete obstruction, to force back the duodenal contents into the common duct," in the cases quoted by

Opie these were not normal circumstances, as the duct in relation to the area of necrosis entered the duodenum by an independent orifice. It is assumed that the reflux from the duodenum is prevented by the sphincter of Oddie. Whether in the presence of an independent opening of the duct of Santorini a sphincter is also present I do not know and can find nothing written on the subject. If there is no sphincter this might explain the occurrence of a pancreatic necrosis due to duodenal reflux along the course of this duct. This is also the only theory which remains to be proved or disproved by anatomical examinations of specimens when this less usual arrangement of the ducts is found.

Fat necrosis is an interesting phenomenon resulting from the pancreatic lesion. Apparently the basement membrane of the acini, as well as the connective tissue binding the lobules of the glands, is sufficiently destroyed to allow the escape of a certain amount of lipase, the fat-splitting ferment, and this attacking the fat in small areas, splits the fat globule into a fatty acid and glycerin, and the fatty acid combining with calcium salts forms an insoluble soap which appears in the omentum, mesentery and subserous fat and on the surface of and about the pancreas as small white opaque spots. In an autopsy on a patient who died after an operation for acute pancreatic necrosis these areas of fat necroses were found extending down retroperitoneally as far as the pelvis. This fact seems to me to have a bearing on the treatment, as I shall mention later. It is easy to understand this direct extension of the pancreatic ferments, but I am unable to discover any adequate explanation of why these small isolated areas of fat necrosis so diagnostic of pancreatic involvement occur at a considerable distance from the gland or how the lipase is carried to these areas. Turner has reported two cases of acute pancreatic necrosis in which he made the observation that one presented an area of discoloration and edema of the skin about the umbilicus, the other a similar condition in both loins, due to subcutaneous fat necrosis by direct extension.

Considered from the foregoing viewpoint of the etiology and pathology of the disease, as being essentially a primary necrosis and not an inflammatory process, its symptomatology is more readily understandable. The primary attack with its extreme pain, excessive prostration, subnormal temperature, shock and vomiting and resemblance to an acute intestinal obstruction, may be understood by the consideration of certain factors. The extreme pain is due to the immediate swelling of the gland and the pressure resulting therefrom. The absence of infection and of consequent irritation of the peritoneum explains the absence of early rigidity so characteristic of a perforation of a stomach or duodenal ulcer or perforated gall-bladder from which it is usually necessary to differentiate the acute fulminating attack. The vomiting, shock and extreme prostration, subnormal temperature and absolute constipation which resemble so

clearly the symptoms of an intestinal obstruction, while partly explained by shock or reflex action, is further explained by the biochemical similarity in the toxin produced in both processes. As shown by Whipple, the cause of death in cases of high intestine obstruction is a split-proteid product of the nature of a peptone developed in the mucous membrane of the intestine. It is reasonable to suppose that the pancreatic necrosis followed by the digestive action of the activated trypsinogen results in a similar toxic product. This again is a factor which must be considered in determining treatment. In the acute fulminating cases this is probably the cause of death. Dobrauer has transplanted necrotic pancreatic tissue into the peritoneum of dogs with resultant death. In those cases in which the primary damage to the pancreas is less extensive the similarity to a low intestinal obstruction is more marked. In a patient on whom I recently operated the bowels could not be moved by enemata for forty-eight hours and a mass in the epigastric region suggested a carcinoma in the transverse colon, there being no temperature elevation. The roentgen ray demonstrated, however, that a barium enema easily filled the large intestine, making the diagnosis of pancreatic involvement practically certain.

In view of the foregoing conception of the etiology and pathology of this disease it would appear that we should question the accepted treatment of this lesion. Based on the theory of an acute infection, the treatment of an infection of any part of the body being always drainage and removal of the infection when this is possible, the treatment advocated has been and still is drainage of the pancreas either by gauze, tubes or rubber dam down to or into the organ by cutting the capsule or boring into it by a blunt instrument.

In the discussion of a paper on "The Treatment of Acute Pancreatitis" before a surgical society, in which seven members of the society took part, the discussion being published in the *Annals of Surgery* in 1917, mention of drainage of the biliary ducts or gallbladder was made in only one case, the discussion being confined to the best manner of drainage of the pancreas itself.

If, however, the lesion in its primary aspect is a necrosis and the cause of death in the acute fulminating cases, poisoning by a split protein product, can this necrosis be drained and does not the injury caused by the attempts at drainage cause more damage to the organ? Also the experiments of Whipple and Goldpasture showed that the exudate about the pancreas had a protective action against the liberated ferments. As to drainage of the gall-bladder or common duct, which would seem to be indicated by the foregoing theory of the etiology and which I have practised in these few cases on which I have operated during the past five years, if Archibald's idea that the amount of the primary lesion is determined by the amount and virulence of the bile entering the duct then the amount of that damage cannot be lessened by biliary drainage, but we do not know

whether or not this reflux of bile may be repeated. Those cases which after a period of improvement suddenly get worse would suggest that this happens unless an elevation of temperature and other signs of infection ensue. I have recently seen a patient operated on for acute pancreatic necrosis by Dr. M. K. Smith in St. Luke's Hospital, New York. A cholecystostomy had been done and the patient was convalescent, up and out of bed on the twenty-first day, when she had a recurrence of symptoms similar to the primary attack. The biliary drainage had ceased, but after reëstablishing the discharge of bile the symptoms cleared up.

It has been suggested by Balfour that cholecystectomy would cure chronic pancreatitis, the gradual dilatation of the common and other bile ducts finally overcoming the action of the sphincter of Oddie, but it would seem that in the meantime the pressure in the ducts would be increased and the danger of reflux greater. One of my patients on whom I had performed a cholecystectomy died from a hemorrhage from the wound following an operation for acute pancreatic necrosis occurring two years later.

The suggestion has also been made that cutting of the sphincter of Oddie through an opening in the duodenum be done to prevent its closure and back-flow into the duct. The objection to this would be the difficulty of doing so in a very sick patient, as it might be very hard to accomplish in the presence of an acutely swollen enlarged pancreas, surrounded with exudate and areas of fat necrosis, and there would also be the possibility of a fistula resulting or stricture occurring later.

It must be recognized that either with or without any operative treatment certain of the acute fulminating cases will die unless some means be discovered of combating the protein poisoning which appears to be the cause of death. Of the milder cases many will recover without operation, and it is difficult to determine the correct course to follow in the presence of an acute case. Those patients who appear most desperately ill in the first twenty-four hours would surely have a poorer chance of recovery if a prolonged anesthetization and operation were superimposed on their primary toxemia, but it is not always possible to rule out an acute inflammatory disease of other origin in the upper abdomen which would positively indicate operation.

That it is impossible to drain a necrotic process until the sloughs have separated has been pointed out, but this does not mean that drainage is not indicated. It is of frequent occurrence that if the patient survives the primary necrosis this is followed by a breaking down of areas in the pancreas with the formation of an abscess or cyst, and frequently there is a sequestration of areas of the pancreas which come away in large sloughs. When an acute process is present and the pancreas has been exposed, either through the gastro-colic or gastro-hepatic omentum, if a superficial incision is made along

its anterior surface, parallel with its long axis, this might relieve some of the tension and direct the discharge of subsequently broken-down material. If there is already a broken-down area this may be opened down to with a blunt instrument. It has been my practice to lead down to this a large gauze pack, protected from the peritoneal contents above and below, as well as the skin, by a rubber dam. This for the purpose of allowing later discharge of broken-down material and protecting as a cofferdam the rest of the cavity. I am opposed to the use of rubber-tube drainage, as usually recommended, for two reasons: First, there is nothing to drain out of the tube in the early cases, and second, because of the tendency of the tube to cause pressure necrosis of neighboring vessels or even the intestine. I have had 2 patients die, 1 after three days and 1 fourteen days, after operation for pancreatic abscess, due to profuse hemorrhage from the wound, evidently from one of the large blood-vessels in the vicinity of the pancreas.

Unless an abscess or broken-down, softened area is present I do not see any special advantage to be gained by following the usually advised method of boring into the gland with a blunt instrument, such as a clamp or scissors, and it seems to me to have very obvious disadvantages, such as damage to tissue which has not already become necrotic and the condition found at the autopsy which I have previously mentioned, in which the fat necrosis had followed the retroperitoneal tissue planes, made me feel that I had been somewhat responsible for this portion of the after-results in my efforts to drain the pancreas.

Finally, in respect to the question of the advisability of biliary drainage, even though it be accepted that the maximum damage is accomplished with the primary reflux of bile, as we do not know whether this reflux may be repeated, it would appear that biliary drainage should be established if its accomplishment would not by prolongation of the operation jeopardize the recovery of the patient. The number of cases in which the unusual termination of the ducts exclude the possibility of biliary reflux as an etiological factor must form too small a group to indicate the omission of this step in the operative procedure, as even in these cases, if rapidly done, it can do no harm. In a case in which no stones are present in the gall-bladder it is usually easy in a few minutes to establish a cholecystostomy through a stab wound in the right hypochondrium, the tube being sutured into the gall-bladder through the primary incision and then led out through the stab wound. Whether in the presence of cholelithiasis, with or without a small contracted gall-bladder, cholecystectomy should be done and the common duct drained would become a matter of judgment, depending on the individual case and condition of the patient for determination.

IMMUNE BODIES IN A TYPE I LOBAR PNEUMONIA.

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THE study of the development of immune bodies in the serum of patients recovering from lobar pneumonia has at all times been of interest because of the close association found by all investigators between the crisis and the appearance of these bodies. Occasionally discordant results had been obtained in such tests by observers who did not use strains of pneumococci homologous with those infecting the patient. In recent years the question has been fully studied particularly by Dochez,[1] Clough[2] and Chickering.[3] Dochez found the serum after the crisis to contain large amounts of protective substances in a study of cases before the biological classification of the pneumococci was recognized. Clough also found ample evidence of immunity in the form of protective bodies and also that the serum taken during recovery was capable of stimulating phagocytosis of homologous pneumococci. The investigations of Chickering were mainly upon cases of Type I pneumonia, some of which had received Type I antiserum. He stated that agglutinins developed just before or just after the crisis and he thought that the use of immune serum had little influence in the development of these bodies. The occurrence of large amounts of agglutinins and protective bodies in a case of Type I pneumonia treated with Type I antiserum has seemed to us interesting enough to record, especially since it is our impression that the clinical improvement and the presence of these immune bodies were related to the administration of the serum.

The patient, C. D., male, aged twenty years, was admitted October 15, 1920, with a temperature of 102° to 103° F., and with atypical pulmonary signs suggesting influenza. In several days consolidation was manifest in the lower lobes of both lungs. The leukocyte count was 24,800. A Type I pneumococcus was found in the sputum. The other laboratory and clinical data of importance were as follows: Urine: specific gravity from 1030 to 1023; a heavy

[1] Jour. Exper. Med., 1912, xvi, 665.
[2] Bull. Johns Hopkins Hospital, 1913, xxiv, 295; Ibid., 1919, xxx, 167.
[3] Jour. Exper. Med., 1914, xx, 599.

cloud of albumin; a number of granular casts. The red blood cells were 3,920,000; hemoglobin, 80 per cent. Blood Wassermann was negative; blood-pressure ranged about 130 systolic and 60 diastolic. Examination of the heart revealed a double aortic lesion and a mitral regurgitation of rheumatic origin and apparently well compensated.

On the sixth day of illness 100 cc of Type I antipneumococcus serum were given intravenously after appropriate desensitization. Eight hours later 50 cc of serum were given. Sufficient improvement was evident by the next morning and no more serum was injected. The temperature fell in a step-like fashion from 101.4° F. to normal in three days after injection of the serum. Six days after the introduction of the serum, serum sickness appeared with a typical urticarial eruption and edema of the face and arms particularly. This was preceded by a marked fall in the specific gravity of the urine to 1005, approximately a day before the onset of symptoms of serum sickness. During the second day of the serum sickness the urine showed 2.11 gm. of total chlorides in twenty-four hours. No particular stress is placed upon these figures since preliminary observations with a standard diet had not been made. However, we were reminded of the studies of Rackemann, Longcope and Peters,[4] who demonstrated a marked retention of chlorides with low chloride output in the urine during serum sickness.

Serum for testing the presence of agglutinins and protective substances was procured from blood removed four days after injection of the immune serum. Agglutinin tests were conducted by the macroscopic method by mixing in small test-tubes 0.5 cc of a twenty-four-hour broth culture of pneumococcus Type I and 0.5 cc of the patient's serum in various dilutions, the final dilution being, of course, double that of the strength of serum used. The test-tubes were then incubated at 37.5° C. for one hour, placed in the refrigerator for twenty to twenty-four hours and read for clumping. By this method the patient's serum showed definite power of agglutination in dilutions up to 1 to 10 (final dilution).

In performing the protective tests it was first necessary to establish a minimal lethal dose. Mice were given intraperitoneal injections of broth cultures in doses ranging from 0.000002 cc to 0.01 cc. All dilutions were made in bouillon to avoid autolysis of the organisms. It was found that the culture was sufficiently virulent to cause death in forty-eight hours, using 0.000002 cc (1 cc of 1 to 500,000) of a twenty-four-hour broth culture.

Mice were then given intraperitoneal injections of various dilutions of the culture, as outlined in the table, together with 0.5 cc of the patient's serum, the dosage being so arranged that the total bulk of fluid did not exceed 1 cc per 20 gm. of weight. Controls

[4] Arch. Int. Med., 1916, xviii, 496.

received 0.5 cc of serum from a normal individual and also culture alone. Observations were made on the basis of ninety-six hours, though, as a matter of fact, those animals surviving this time survived indefinitely. The heart's blood of the dead animals were examined for pneumococci except in those instances in which the body had been mutilated by the survivors.

The results as outlined in tabular form indicate that there were sufficient immune bodies in 0.5 cc of the patient's serum to protect against 500 times a lethal dose of Type I pneumococci. Controls of normal serum did not protect against the lowest dose.

PROTECTIVE VALUE OF PATIENT'S SERUM AGAINST TYPE I PNEUMO-
COCCUS CULTURE.

Mouse No.	Culture, c c.	Patient's serum, c c.	Control serum, c c.	Result in days.			
				1	2	3	4
1	0.000002	..	..	S	D		
2	0.000002	..	0.5	S	D		
3	0.00001	..	..	S	D		
4	0.00001	..	0.5	S	D		
5	0.00001	0.5	..	S	S	S	S
6	0.00002	0.5	..	S	S	S	S
7	0.0001	0.5	..	S	S	S	S
8	0.0002	0.5	..	S	S	S	S
9	0.001	0.5	..	S	S	S	S

S = survived　　　D = died.

STUDIES ON THE CHEMISTRY OF THE BODY IN DISEASES OF THE SKIN.

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THE changes that may be noted in the blood in conditions of disease of the skin must be viewed very critically before deductions can be drawn that the change in the composition of the blood was due to the pathological state of the skin or that the skin lesion was

the result of the patho-chemistry of the blood. The appreciation of cause and effect is a difficult matter in such studies, for the deviation in the composition of the blood may be due to altogether other factors than the skin pathology and the skin lesion may be not at all the effect of the causative factor of the blood changes, but may be due to some totally different cause.

It may be that a patient suffering from nephritis, for example, may have a coincident eczema. Now, one cannot ascribe the marked disturbances in the blood chemistry to the eczema nor can one state with any shadow of definite evidence that the eczema was due to the blood changes observed. It is therefore necessary to scrutinize results and to be conservative in drawing conclusions in such researches.

We have endeavored in this preliminary attempt to observe if any change is constant in any dermatological affection. In most of the patients we examined the blood for its carbon-dioxide combining power according to the method of Van Slyke; for non-protein nitrogen according to Greenwald's technic; for urea nitrogen according to the urease method of Van Slyke and Cullen; for creatinin by the method of Folin; for glucose according to the method of Lewis and Benedict. In certain cases we also examined the blood for uric acid by the method of Folin and Denis and for cholesterol by the process of Autenrieth and Funk. The accompanying tables record the figures obtained in this series of experiments.

Discussion. Barber and Semon, studying the relation of seborrhea to body chemical changes, classified seborrheic individuals into two groups: (1) Those who have an exudate diathesis and are congenitally predisposed or acquire the tendency in infancy, and (2) those in whom the condition is of sudden onset and give no history of an exudative diathesis. They however remark that both of these types are characterized by an acidosis, as is evidenced by the hyperacidity of the urine and the reaction to treatment by alkalies. They somewhat confuse the subject by comparing the condition to diabetic ketosis, though they point out that there is no resemblance in degree between the two conditions. It seems to us that the acidosis of seborrhea is, if anything, of the true increased hydrogen ion concentration type, whereas the acidosis of diabetes is due to the ketonic substances generated by the improper decomposition of fats due to the maloxidation of carbohydrates. Whereas the true acidosis will clearly be helped by the administration of alkalies, the ketosis of diabetes will not be relieved by that medication. The authors attempted to indicate a similarity in the two conditions of diabetic ketosis and seborrheic acidosis, implying a supposition that the basic disturbance may be similar, whereas the acidosis in seborrhea is, if anything, the underlying cause of the skin condition, the ketosis of diabetes is the resultant of carbohydrate-fat maloxidation. According to the experiments of Barber and Semon the condition

of acidosis has no relation to and should not be contrasted with (in our opinion) diabetic acidosis.

BLOOD CHEMISTRY; MISCELLANEOUS SKIN DISEASES.

No.	Diagnosis.	CO_2	Urea N.	NPN.	Creat- inin.	Uric acid.	Glucose.	Cholesterol.
1	Urticaria	52	9	22	1.5			
2	Urticaria	..	12	34	....	....	0.12	
3	Urticaria	48	28	38	2.8	....	0.09	
4	Angioneurotic edema	48	18	26	2.1	4.2	0.14	147
5	Purpura	36	26	38	2.6	2.5		
6	Purpura	56	9	..	....	....	0.11	
7	Erythema	58	17	30	1.2	....	0.56	
8	Erythema	40	10	16	0.7	....	0.11	
9	Erythema	46	11	24	2.0			
10	Erythema mul- tiforme	30	12	25	....	....	0.13	
11	Erythema mul- tiforme	59	13	20	1.47	....	0.12	
12	Erythema nodo- sum	54	9	26	1.2			
13	Dermatitis her- petiformis	50						
14	Gangrene	..	....	..	....	....	0.17	
15	Gangrene	..	....	..	....	....	0.18	
16	Gangrene	30	9	..	....	....	0.24	
17	Gangrene	..	....	..	....	....	0.16	
18	Perforating ulcer	..	....	..	....	....	0.19	
19	Thrombo-angeitis obliterans	42	24	35	2.3	4.75	0.18	
20	Rosacea	52	10	26	0.8	....	0.09	
21	Lupus erythem- atosus	76	10	38	1.0			
22	Scleroderma	62	18	25	1.8	....	0.165	
23	Scleroderma	42	11	24	3.4	3.2	0.09	167
24	Pruritus	64	....	..	....	....	0.078	
25	Folliculitis	46	21	27	....	....	0.18	
26	Carbuncle	36	....	..	....	....	0.36	
27	Carbuncle	28	12	23	2.0	....	0.32	
28	Carbuncle	..	....	..	....	....	0.1	
29	Gumma (lues)	46	19	37	2.4	....	0.11	
30	Lichen planus	48	13	30	0.6			
31	Pompholyx	64	10	21	1.7	....	0.1	
32	Xanthoma	..	....	..	....	....	0.13	210
33	Erythema ·	58	16.5	21	2.8	....	0.11	
34	Chloasma	50	12	23	....	....	0.09	
35	Hyperidrosis	52	17	24	1.9	....	0.95	
36	von Reckling- hausen's dis- ease	60	8.3	36	1.2	....	0.07	
37	Pityriasis rubra pilaris	74	....	..	....	....	0.07	
38	Hodgkin's dis- ease	60	8	12	1.9	....	0.22	
39	Moeller's glossi- tis	63	12	23	1.5			

Schwartz, Levin and Mahnken studied the carbon-dioxide combining power of the blood plasma in 139 cases of skin lesions. They concluded that a lowering of the alkali reserve of the blood has been

found sufficiently frequently in acne, psoriasis, urticaria, furunculosis and eczema—particularly seborrheic eczema—to warrant further investigation.

We have examined the state of acidosis in a large number of eczema and other skin diseased patients and we shall discuss our results under several headings.

Eczema. The acidosis in this condition was investigated by several methods, although not all of the methods were applied to all the cases. A certain number of patients were examined by all the methods. The urine was examined for total acidity by the Folin method; the formalin titration coefficient was determined by the method of Henriques-Sorensen; the blood was examined for its carbon-dioxide combining power by the method of Van Slyke and the alveolar carbon-dioxide was determined by the method of Fridreicia. The results in 17 cases of eczema thus investigated were as follows:

ACIDOSIS STATE IN ECZEMA.

No.		Total acid urine 24 hours.	HCHO coefficient.	CO_2 blood.	CO_2 alveolar air.
1		514	0.54	62	
2		570	0.55	58	
3		620	0.72	52	
4		600	0.84	56	5.2
5		610	0.93	56	
6		595	0.73	..	5.6
7		480	0.56		
8		570	0.48	..	5.5
9		630	0.92	64	
10		722	1.75	..	6.2
11		882	0.87	58	5.9
12		665	0.75	55	5.8
13		549	0.63		
14	Diabetes	755	1.42	42	4.4
15	"	828	1.98	38	4.2
16	"	970	2.08	36	4.0
17	"	850	2.27	40	

In all 42 cases of mild eczema have been studied. Of these, 4 were diabetics, 1 had furunculosis and 1 had Hodgkin's disease. Acidosis was present in these cases. Of the others only 4 showed a mild degree of acidosis as measured by the carbon-dioxide combining power of the blood. These were Cases 11, 17, 19 and 25. The total acid of the urine, the amino-acid as measured by the formol titration method and the alveolar carbon-dioxide were absolutely normal in those patients in whom investigations were made.

So far as the blood chemistry of patients suffering from mild eczema was concerned nothing unusual was discovered. Of course, in the patients with diabetes the abnormalities that were found were due to the underlying metabolic derangement and were not reported here because they have no concern with the subject under discussion. The figures for urea nitrogen, non-protein nitrogen, creatinin and glucose as well as for cholesterol and uric acid (in

those instances in which they were determined) were altogether normal.

CHEMISTRY OF THE BLOOD IN ECZEMA.

No.	CO_2	Urea N.	NPN.	Creatinin.	Uric acid.	Glucose.	Choles-terol.
1	60	10	22	0.85	...	0.1	
2	57	17	21	1.0			
3	52	11	26	0.6	...	0.09	
4	54	11	20	1.1	...	0.075	
5	..	10	35	....	...	0.09	
6	62	10	26	1.7	...	0.085	
7	58	10	25	1.0	...	0.07	
8	58	20	28	1.8	3.8	0.09	
9	42	14	30	1.2	...		
10[1]	36	....	..	....	...	0.14	
11	50						
12[2]	40	....	..	....	...	0.11	
13	61	18	22	1.5			
14	62	20	30	2.2	...	0.1	
15	58	17	27	2.0	...	0.09	
16	..	9	28	1.4	...	0.074	
17	48	17	..	1.1	...	0.13	
18	52	15	..	1.0	...	0.08	
19	45						
20	58	16.5	21	2.8	...	0.11	
21	52	17	28	2.6	...	0.18	
22	58	14	28	1.6			
23	..	17	27	2.6	...	0.14	
24	28	26	39	2.8	4.1	0.11	197
25	46	9	19	1.2	...	0.08	
26	50	13	28	2.2	...	0.09	

In instances of diffuse eczema in which the sulphur partition was made on the urine we found a marked increase in the ethereal sulphate fractions, seeming to point to some state of intestinal putrefaction. In these cases there seemed to exist a mild degree of acidosis as evidenced by the various tests. The blood chemistry, in general, however, was apparently normal.

Case.	Total S.	Inorganic $SO_4\%S.$	Eth. $SO_4S.$	Neutral $S.\%S.$
1	1.25	62.5	29.2	8.3
2	0.94	56.8	32.8	10.4
3	0.92	63.4	26.9	9.7
4	0.86	65.7	26.5	7.8

Case.	CO_2 per cent.	Urea N. mg.	NPN. mg.	Creatinin. mg.	Glucose. per cent.	Uric acid, mg.	Cholesterin, mg.
1	42	14	20	2.2	0.09	3.2	152
2	40	17	25	2.4	0.09	2.7	147
3	52	12	27	1.8	0.11	2.8	140
4	55	16	25	2.0	0.08	3.4	159

Case.	Urine acidity.	Amino-acid.	CO_2 alveolar air.
1	620	1.8	4.7
2	790	2.2	4.4
3	680	1.85	5.0
4	785	2.35	4.9

[1] and furunculosis.   [2] and Hodgkin's disease.

The sulphur metabolism studies previously reported are those by Géber and by Hammerli in psoriasis, by Stuve in pemphigus vegetans and by Rosenbloom and Cameron in urticaria. Géber's results of an increased excretion of sulphur in psoriasis were not corroborated by Hammerli. Stuve found the sulphur metabolism normal in pemphigus and Rosenbloom and Cameron found but slight variations from the normal in their metabolic investigations in a case of chronic urticaria.

We have found no increase in the non-protein sulphur of the blood in eczema.

The calcium content of the blood was determined in several cases of eczema, but normal figures were obtained.[1]

Acne Vulgaris. It has been reported by Schwartz, Heimann and Mahnken that there is an increase in blood sugar in cases of acne. In 15 cases of acne vulgaris that we have examined 6 gave figures of blood sugar above 0.1 per cent. All the others showed normal blood-sugar content. In 4 cases not necessarily associated with the high glycemia there was reduced carbon-dioxide absorption power of the blood plasma. In general the blood chemistry showed no marked deviation. The non-protein sulphur content was normal.

CaO IN BLOOD IN ACNE VULGARIS.

Case.	Mg. CaO in 100 c c.
1	8.5
2	9.0
3	9.7
4	11.2
5	8.7
6	8.5
7	7.4

NORMAL FIGURES.

Carbon-dioxide combining power of the blood	60 per cent.
Urea nitrogen	16 mgm. per 100 c c blood
Non-protein nitrogen	25 mgm.
Creatinin	1 mgm.
Uric acid	2.5 mgm.
Cholesterol	140 mgm.
Glucose	0.1 per cent.
Calcium oxide	10 mgm.
Carbon-dioxide alveolar air (Fridericia)	6 per cent.
Total acid urine	600
Formol coefficient	0.75
Inorganic sulphate sulphur (urine), per cent of total sulphur	70 per cent.
Ethereal sulphate sulphur, per cent of total sulphur	15 "
Neutral sulphur, per cent of total sulphur	15 "

The calcium content of the blood in acne deserves special discussion. Thro and Ehn have recently reported that in acne vulgaris

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[1] In a more detailed article complete description of methods and results obtained will be given.

the calcium content of the blood (in 12 cases) showed a marked increase, the figures they obtained being from 13.6 to 25.7 mgm. per 100 cc of blood. They attempt to deduce some relationship between the condition of acne and this calcium increase in the blood. In cases of furunculosis the calcium was reduced in amount. They say: "The pathological lesion of acne is in the sebaceous glands of the hair follicles while in furunculosis the sweat glands become infected. It is of interest to note then that in one patient with folliculitis barbæ in which the hair follicle is involved the amount of calcium in the blood was increased."

Independently of Thro and Ehn we examined the blood from a number of patients with acne and other skin conditions for calcium by the method of Halverson and Bergeim. Our results did not show any increase in the calcium content of the blood in acne vulgaris.

Psoriasis. In a number of cases of psoriasis investigated no change in the blood chemistry so far as the nitrogen distribution goes was observed. A number of the patients showed a state of mild acidosis. A remarkable increase was observed in the non-protein sulphur of the blood. We shall reserve for a future communication the discussion of this subject.

No.	CO_2.	Urea N.	NPN.	Creatinin.	Glucose.
1 . . .	44	10	22	0.85	0.1
2 . . .	62	. .	17	1.1	0.11
3 . . .	66	15	25	1.7	0.1
4 . . .	52	20	33	1.25	0.09
5 . . .	38	11	27	1.1	0.1
6 . . .	44	10	22	0.85	0.1
7 . . .	38	12	29	1.5	0.22
8 . . .	53	. .	. .	. . . .	0.074
9 . . .	44	12	24	1.0	0.1

Conclusions. 1. In mild cases of eczema no disturbances were observed in the chemical composition of the blood nor in the condition of the hydrogen-ion concentration of the body fluids. In eczema accompanied by other metabolic derangement the deviation of the blood chemistry was due to the metabolic diseases, as, for example, diabetes. In the latter case conditions of acidosis were noticed. In severe diffuse eczema we observed a state of acidosis, an increased ethereal sulphate fraction in the urine, indicative, perhaps, of intestinal putrefaction, but otherwise a normal blood chemistry.

2. No marked deviation in the blood chemistry aside from hyperglycemia was observed in cases of acne vulgaris.

3. In cases of psoriasis the non-protein sulphur of the blood seemed to show larger figures than usual.

4. In one case of xanthoma a marked increase of the blood cholesterol was observed.

5. A mild acidosis seemed to accompany some of our cases of seborrheic eczema, psoriasis, acne vulgaris and urticaria.

ACUTE SUPPURATIVE APPENDICITIS (GANGRENE OF THE APPENDIX) EXPERIMENTALLY PRODUCED.

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Acute appendicitis is usually held to be caused by some foreign body which may be a hard particle of food irritating or injuring the mucosa, so that bacteria pass through into the submucous layer and induce an inflammation. The inflammation results in swelling, which interferes with the circulation of the blood in the muscular wall. Continuation of this results in a decrease of nutrition of the wall and consequent death of the tissue. (De Forest.) This is the usual explanation of the cause of appendicitis.

However, if irritation alone is the cause of the inflammation—

1. Why does not inflammation of a similar character occur in the intestine, where the same irritation, but greatly magnified, is present? It is usually answered that the anatomical structure of the appendix is different from that of the bowel, in that it contains much lymphoid tissue. At least such an explanation has been made.

2. An enterolith or rough food particle may be present in the appendix for years without producing inflammation, and this foreign body must in the time of its residence produce numerous abrasions and traumata to the mucosa of the appendix.

If the two preceding statements are correct there must be other causative factors which are more or at least equal in potency to the enteroliths or foreign bodies as a cause of appendicitis. Additional factors are:

1. A fixed or abnormal position of the appendix in relation to the cecum and parietal wall, with associated bands or adhesions binding the appendix to surrounding structures, namely, the lateral abdominal wall, the psoas muscle, the cecum, the ileum and the colon.

2. A disturbed blood supply, due to kinking or obstruction of the bloodvessels.

3. Dislocation of the cecum with distention of the cecal lumen and consequent traction on an adherent appendix.

4. Obstruction of the lumen of the appendix. This seems from our experiments on rabbits to be the most potent factor in causing acute suppurative appendicitis (gangrenous appendicitis.) These experiments were incidental to other experiments on the production of intraperitoneal adhesions. The results of the latter experiments were reported in the American Journal of Medical Sciences, September, 1920.

In the first experiment an attempt was made to determine whether perforation or injury of the mucosa is an active cause of acute appendicular inflammation. A rabbit was operated on February 4, 1917. The abdomen was opened, the appendix was isolated and a subserous suture of linen was introduced circumferentially around the appendix and was tied. A hypodermic needle of large lumen was then introduced into the distal end of the appendix and an attempt was made to remove some of the contents. There did not seem to be any free fluid in this terminal portion of the appendix. After the needle was removed it was possible to express a small amount of the fecal matter from the appendix through the needle opening. This was collected and dissolved in a tube of salt solution and a culture made. The culture was sterile.

On reoperation February 12, 1917, the appendix was inflamed and very red. There were adhesions at the extreme tip to two adjacent segments of the bowel. These adhesions were very firm and were separated with difficulty. They extended, however, only for a short distance and corresponded to the area at which the fecal material had been expressed on to the surface of the appendix. The rest of the appendix was free. The appendix was removed and opened. The lumen of the distal portion was free and showed no abnormality, not being different in any way from the proximal portion. Opposite to the portion where the circular ligature had been applied there was a line in the mucosa which indicated that the circular occluding ligature had at this point cut completely through the muscularis, the submucous and the mucous layers of the walls. It was found in the wall of the appendix. There was not the slightest obstruction. The circular defect in the mucosa must have persisted for a few days, so that there was sufficient time for infection to spread through the mucosa into the submucous tissue and to give rise to an appendicitis. This had not occurred.

Confirmative of this is the result obtained in a rabbit operated on September 18, 1917, in whom a subserous ligature had been placed around the appendix. On tying it tightly it cut through the muscularis and mucosa. The rabbit was killed on October 13, 1917.

The appendix was found to be normal. The mucosa was intact except at one place, where there was subserous thickening. No adhesions were present. The ligature apparently had pulled through the mucosa, but had produced no obstruction. The defect in the mucosa, the submucosa and the muscularis had not resulted in inflammation of the appendix.

A further confirmation of the conclusion that injury of the mucosa will not cause acute appendicitis in the rabbit is the operation performed September 19, 1917. Here a subserous ligature was placed around the appendix. It was of very fine linen. On tying, the feeling was present that the suture had pulled through the wall into the lumen. On operation October 12 it was found

that the terminal portion of the appendix was not dilated. On November 10 the abdomen was reopened. The appendix was firmly adherent to the adjacent intestines. The intestines were separated by sharp dissection and the appendix was freed. The appendix was removed. No special change, except the surrounding adhesions, was noted in the appendix. Cultures from the lumen of this appendix were sterile.

To definitely determine whether, in the presence of active bacteria (streptococci and colon bacilli), an injury to the mucosa would lead to an acute inflammation, the following experiment was performed late in November, 1917.

The appendix was denuded and a culture of living streptococci and colon bacilli was injected into it. The denudation of the serosa was about one inch away from the area of the injection and was of such a degree that bleeding ensued.

On December 4, that is, about three weeks after this experiment, the abdomen was opened. There was great difficulty in finding the appendix. It was finally located high up on the right side and apparently firmly attached by adhesions at its base to the posterior wall, so that it could only with difficulty be delivered into the wound. It was found that the serosa was normal in appearance, except at the place where it had been adherent. This adhesion was at the place where the serosa had been denuded. The injection into the lumen of the appendix of active growth of streptococci and colon bacilli may also have had some influence in causing an active inflammatory reaction and the formation of adhesions at the point of denudation. There was no change in the mucosa.

In this case there was a defect in the mucosa at the point where the injection needle had perforated it; still, acute suppurative appendicitis had not resulted.

Even incomplete stasis, in which there is a *partial blocking off of the appendicular lumen, does not in rabbit experiments cause appendicitis* even though fecal material collects in the part distal to the partial obstruction.

This is verified by the experiment of January 9, 1918: A culture was taken from the lumen of this appendix and was found to be sterile. The lumen was then blocked by means of a circular subserous suture. After tying the suture the lumen was not entirely obliterated, so a second suture was applied above the first, about one and a half inches from the distal end of the appendix. On February 10, 1918, the rabbit was reoperated. The appendix was found to be very large. There were a few adhesions to the adjacent bowel at the mesenteric attachment of the appendix. Inspection of the appendix showed a slight constriction at the point of previous ligation. The serous surface of the appendix was smooth and glistening. The appendix was removed. On being opened the appendix, distal to the partially obstructing ligature, was filled

with dark material. The portion of the appendix proximal to the obstruction was free of this material.

The obstruction was not of great moment. It seemed to act as a partial valve, so that material passed through from the bowel to the distal end, but did not easily pass in the opposite direction. The mucosa was not injured.

In this case an *injury to the mucosa of the appendix and a partial obstruction of the lumen had not resulted in appendicitis. If, however, an obstruction totally blocks the lumen and affects the mucosa alone, the submucous area and the muscularis being free, lymph-like fluid collects in the submucous space and increases to such a degree that it will dissect free the mucosa,* as is illustrated in an experiment on a rabbit operated January 20, 1918.

The appendix was occluded by a purse string suture halfway between the tip and the base. The suture was inserted subserosally. Some weeks later the rabbit died.

On opening the abdomen few adhesions were found. There was no free fluid. The abdominal skin wound was infected. The appendix had become enlarged into a mass about 10 cm. x 5 cm. x 5 cm. It was rather tense. The small intestines had spread over it and become adherent in various places. These adhesions were mostly between the mesentery and the surface of the appendix. The place on the appendix where the purse string occluding suture had been inserted was surrounded by rather dense adhesions. The appendicular mass was opened and proved to be a large cyst with very thick walls. The cavity was filled with a thick, whitish material with no odor. On the inner surface was a whitish membrane, very friable. Beneath this membrane was a smooth surface, the muscularis. Attached to the place where the purse string suture had been placed, *i. e.,* at the point where the appendix was occluded, a mass of tissue was hanging free in the cavity. This was regarded to be the mucosa, which had evidently been undermined and loosened from the subjacent tissues by the fluid which had collected in the submucous space. Communication between the proximal (normal) appendicular lumen and the occluded distal lumen was obliterated. (Unfortunately cultures made from this material as well as the fluid itself were lost, so that a complete determination of its character could not be made.)

In the above case the muscularis was not included in the obstructing ligature. If it had been severe, inflammatory reaction likely would have followed. This occurred in an experiment on November 6, 1917, when a circular suture of linen was placed around the appendix subserosally and drawn snug enough to make a marked constriction. The meso-appendix was not touched. In two days the rabbit died. The appendix was found to be very thick and infiltrated, especially in one place where it had rested on the mesentery and on an adjacent segment of bowel. The infiltration and inflammation

were only present in the segment distal to the point at which the circular suture had been placed. From the surface colon bacilli were cultured. On opening the appendix the lumen was greatly dilated in the segment beyond the point of constriction and was filled apparently with pus or a material which resembled pus. The mucosa and muscularis beyond the point of obstruction were destroyed. There seemed to be a complete blocking of the lumen at the point of obstruction. Proximal to the obstruction the mucosa and muscularis were apparently normal. The reaction in this case was not quite as severe as in the following case, where the appendix was occluded by a double subserosal ligature of linen. This resulted in gangrene of the appendix and death the next evening.

This rabbit was operated on October 11, 1917. The proximal part of the appendix was occluded by a ligature passing around the appendix beneath the serosa. This ligature was of linen and was doubled. After the operation the rabbit did not seem to be especially ill, but he died in about twenty-four hours after the operation.

Autopsy showed that the contents of the lower portion of the abdominal cavity were firmly attached to the peritoneal covering of the abdomen. In many places in the lower abdomen, quantities of fibrinous exudate were present. The entire lower portion of the abdomen was filled with a mass of inflamed intestines. In the right lower quadrant there was a considerable quantity of free fluid, serofibrinous in character. The appendix was adherent to the adjacent intestine. It was withdrawn from the abdominal cavity and was found to be gangrenous. The gangrene was most marked at the distal extremity beyond the point at which the circular ligature had been placed at the time of operation.

The gangrene was indicated by a dark discoloration. There was a distinct line of demarcation. It had extended up underneath the serosa for about one inch proximal to the point where the ligature had been applied. The meso-appendix also was very red and inflamed and rather dark in color. On dissecting the meso-appendix the two layers were found to be separated by a thick bloody exudate. This exudate extended back beyond the junction of the mesoappendix with the mesocolon and also beyond the point of the juncture of the appendix with the cecum. The lumen of the appendix was not opened. The appearance of the appendix indicated that there had first been a destruction of the tissues of the appendix lying distal to the ligature. Then that this destruction had induced infection of the supplying bloodvessels (sufficient to cause thrombosis) with gradually progressing necrosis and associated gangrene of the appendix, which (in this instance) extended toward the base.

The serosa of the appendix distal to the ligature was intimately involved in the inflammatory reaction, while the serosa of the appendix proximal to the ligature did not seem to be involved.

*Acute suppurative appendicitis (gangrene) in this case was appar-
ently caused by strangulation of the mucosa, submucosa and muscularis.*

On December 22, 1917, a circular ligature was inserted around the
appendix of a rabbit so that it blocked the lumen. It was tied
tight. Some bleeding occurred at the point of ligation.

In this rabbit, which died two days later, the appendix showed some
necrotic areas of the mucosa. On the external surface of the
appendix there was a considerable deposit of fibrin-like material.
This deposit was between the bowel and the appendix. The appen-
dix was gangrenous. This is a further confirmation.

In order to determine what effect, if any, blocking of the circula-
tion of a restricted portion of the appendix may have on the por-
tion of the appendix supplied by the obstructed vessels, an experi-
ment was performed in which the circulation to the appendix was
partly restricted, with a kink of the appendix resulting, with no struct-
ural changes in the appendix. In this experiment the abdomen was
opened and the appendix was found and brought out of the peritoneal
cavity. About one inch from the distal end of the appendix the sup-
plying vessels in the meso-appendix were surrounded by a ligature in
a direction parallel to the meso-appendicular border of the appendix.
The long vessels which run parallel to this border were also caught
in the ligature. The ligature was now tied, entirely blocking this
portion of the circulation. A second ligature was then placed farther
up toward the mesocecal junction, so that at least one-half inch
or three-fourths of an inch of the meso-appendix near to the place
where it joins to the mesocolon was included to the ligature. The
appendix was now replaced in the peritoneal cavity. This rabbit
seemed to be perfectly well until two weeks after the operation,
when it would not eat and seemed to be apathetic. Finally it died.

On autopsy few adhesions were present in the abdominal cavity.
The appendix showed no special inflammation. There was a rather
well-marked kink present where the vessels had been tied, but this
did not seem to produce any stricture or other change in the appen-
dix at this point. The appendix was removed. The above experi-
ment was repeated several times with the same result.

The absence of structural change in the appendix is interesting,
showing in this experiment that in the rabbit *partial destruction of the
circulation in the meso-appendix is not necessarily conducive to inflam-
mation or to any great change in the appendix itself.* Apparently
the adjacent collateral circulation in the meso-appendix, or the
circulation in the wall of the appendix is able to carry on nutri-
tion, so that necrosis does not occur. It may be that the nutrition
of the appendix is carried to a great extent through the vessels
which are in the muscular or subserous layer of the appendix.
Otherwise it would be difficult to explain why gangrene should
take place when the muscular, the subserous and the mucous coats
are strangulated, while no apparent change results when the cir-

culation is blocked. Gangrene is usually thought to be due to bloodvessel obliteration.

If the disturbance of the blood supply in the meso-appendix does cause gangrene of the appendix the only supposition for the origin of the gangrene in the appendix is, that the gangrene is due to a rapidly extending inflammatory process in the appendicular lumen, involving the muscular, mucous and submucous coats and quickly spreading into the veins thus producing thrombosis and gangrene of the ascending type, moist in character.

RÉSUMÉ. From our experiments on rabbits it was noted that the only time acute inflammatory reactive changes in the appendix occurred was when the lumen of the appendix was entirely obstructed, with strangulation of the mucous, the submucous layer and the muscularis.

Obstruction to the lumen alone apparently resulted only in a collection of fluid between the mucosa and the muscularis in the submucous space, so that a cyst of the appendix was formed. However, when the obstruction extended beyond the mucosa and included the submucosa and muscularis a very marked reactive inflammation resulted, and gangrene of the appendix with sepsis and death of the rabbit took place.

The presence of bacteria in the lumen of the appendix is not, in the rabbit, a necessary prelude to inflammation. Gangrene of the appendix may occur even when previous cultures from the lumen of the appendix showed no bacterial growth; however, when inflammation had already taken place and the surface of the appendix was inflamed, cultures from the surface of the appendix gave growths of colon bacilli. This inflammation in our experiments apparently did not primarily result from thrombotic changes in the blood vessels of the meso-appendix. The blood vessels of the meso-appendix may be partially blocked and no pathological change occur in the appendix. The pathological variation or change evidently took place both in the lumen and in the coats of the appendix and led to deadly inflammatory reaction in the walls of the appendix. This reaction was always distal to the obstruction which we had erected.

How closely the above processes may simulate those which occur in the human is problematical. The appendix of the rabbit is longer, larger and has a slightly different arrangement of blood supply than has the human appendix. However, clinical observation seems to confirm, at least to a degree, that the above observations may also be applied to man.

Obstruction of the appendix may result clinically when a foreign body is present in the appendix and obstructs the lumen at some point where there has been a constriction. Gradual swelling of the mucosa may be sufficient to produce a strangulation of the submucous and the muscularis layers the same as occurs when a ligature or clamp is applied. When this stage is reached gangrene supervenes.

AN AUSCULTATORY SIGN OBSERVED IN ACUTE ABDOMINAL DISEASES.

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The methods employed in examination of the abdomen are commonly limited to inspection, palpation and percussion. Cabot says: "Our methods are crude and inexact compared to those applied to the chest. Auscultation is of practically no use." Gerhardt speaks of a single sound and at times a systolic murmur heard over the abdominal aorta. He describes friction sounds heard over the liver, the spleen, or tumors, and over the intestines in case of peritonitis. He mentions the rare finding of signs due to sacculations of air and fluid, as in subphrenic pyopneumothorax. No additional data are found in the works of Sahli or of Brugsch and Schittenhelm.

Believing that some information might be obtained by examining with the stethoscope, auscultation was applied to the abdomen in acute cases. Most of these were cases of appendicitis.

In some patients examined in this way it was found that the heart sounds and the inspiratory murmur were audible over three or four of the quadrants. The heart sounds were somewhat distant and reminded one of the fetal heart sounds familiar to the obstetrician. The inspiratory murmur was audible at times with quiet respiration, at other times only when the patient was requested to breathe more deeply. When the abdomen was opened the peritoneal cavity of patients presenting these auscultatory signs was found to contain free pus, seropurulent fluid or blood (as in a case of ruptured tubal pregnancy). After a number of such experiences it became apparent that the physical sign had some significance and the keeping of data on this point was begun. The unreliability of shifting dulness as a sign of free fluid in the acute abdomen is well known. If this auscultatory sign should prove significant of free fluid it would be of clinical value.

It was suggested by a colleague that cases of ascites ought to present the sign, but it was deduced that it would not be present for the following reason: Ascites is a gradual accumulation of fluid causing stretching of the parietes, whereas the sign appears with a sudden accumulation of fluid under tension. The physical conditions are different. Several cases of ascites in the medical services were examined with negative auscultatory findings in every instance.

Many patients in the surgical wards without abdominal disease were examined and in no instance was the sign described encountered.

Occasionally the heart sounds were audible in the epigastrium or a systolic tone was heard over the abdominal aorta.

Analysis of Case Records. 1. Cases with positive auscultatory sign and positive findings at operation, 17.[1]

Of these 17 cases the heart sounds and inspiratory murmur were heard in all four quadrants in 10, in three quadrants (right and left upper and right lower) in 3, in two quadrants (right and left lower) in 3, in two quadrants (right upper and lower) in 1 case. The patients' ages ranged from one to fifty-five years. Shifting dulness was made out in only 2 cases. In 7 cases the usual symptoms and signs of peritonitis (facies, general abdominal rigidity, rebound tenderness) were present. In 8 cases the presence of peritonitis was not considered or seemed very doubtful.

In 2 cases (both infants) aspiration of the abdomen with needle and syringe yielded pus. (For the use of this procedure I am indebted to Dr. Howard Lilienthal.) Both of these were operated upon because smears of the pus excluded a primary pneumococcus peritonitis.

The findings at operation in these 17 cases were as follows: In every one of this group free pus or seropurulent fluid was found in the peritoneal cavity. In 15 cases this was due to an acute appendicitis with perforation in 7. In 1 it was due to an acute postabortive metritis. (Examined through the courtesy of Dr. Hiram N. Vineberg.) In another the underlying condition was a purulent cholangitis due to common duct stones. The gall-bladder itself showed only chronic inflammatory changes, the peritonitis apparently resulting from extension through the duct walls.

2. Cases with negative auscultatory sign and negative findings at operation, 12.

In 3 cases of marked abdominal distention in acutely ill patients the absence of the auscultatory sign was of interest, as the possibility of the production of the sign by distention had come up for discussion. The cases were: (1) Incarcerated femoral hernia, (2) obstructing carcinoma of splenic flexure, (3) acute gangrenous appendicitis with reflex ileus.

In 4 cases of acute gangrenous appendicitis and 1 of acute pancreatitis the general symptoms, the widespread abdominal rigidity or marked rebound tenderness strongly suggested active peritonitis. In none was the auscultatory sign present and in none was fluid found in the peritoneal cavity at operation. In a case of penetrating bullet wound in the right hypochondrium with marked rigidity of the upper abdomen the sign was absent and the subsequent course excluded intraperitoneal hemorrhage or perforation

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[1] An additional case was recently examined on the pediatric service of Dr. Henry Heiman. It was a case of pneumococcus peritonitis in a child of three years. The auscultatory sign was present and the diagnosis proved by aspiration and culture of the pus obtained from the abdominal cavity.

of a viscus. In the case of a child run over by an automobile the physical findings strongly suggested intraperitoneal injury. The auscultatory sign was absent and subsequent course and operation proved the injury to be confined to the right kidney with production of an "extrarenal hydronephrosis."

In a case of perirenal hematoma of unknown origin and in a case of suspected tubal pregnancy, in both of which the sign was absent, operation proved the peritoneal cavity to be free of blood or fluid.

3. Cases in which heart sounds were heard in one or both upper quadrants only, 4.

Transmission of heart sounds to one or both upper quadrants was regarded as of doubtful significance because of the following cases: In one case of transmission to both upper quadrants a small amount of seropurulent fluid was found in the pelvis. In another case with similar signs no free fluid was found. In a case with heart sounds audible in the left upper quadrant only an acutely inflamed retro-cecal appendix was found with no free fluid. In a case showing transmission of heart sounds and inspiratory murmur to the upper quadrants only a small amount of clear serum caused by a twisted Meckel diverticulum was encountered.

4. Cases with negative auscultatory sign and positive findings at operation, 3.

In 2 cases with negative auscultatory findings a small amount of serum was present in the pelvis. In neither case could a peritonitis really be said to exist. In a child of seven years brought to the hospital *in extremis*, with a small, rapid and at times imperceptible pulse with shallow respirations, forty to fifty per minute, auscultation was negative. Operation revealed a diffuse purulent peritonitis. The heart sounds were barely audible over the precordium, and this in itself precluded transmission to the abdomen.

5. Cases with positive auscultatory sign and negative findings at operation, 2.

One of these was a woman, aged fifty-two years, with a markedly distended colon and an empyema of the appendix without free fluid in the abdomen. The second was a boy, aged ten years, with an acute gangrenous appendicitis, considerable distention of the small bowel, but no free fluid.

These 2 cases prove that the sign is not an infallible one and may be occasionally caused by distention of the bowel.

Conclusion. Auscultation of the abdomen in acute conditions accompanied by seropurulent or purulent exudation into the peritoneal cavity reveals a physical sign which is present in a high percentage of cases. Of 20 such cases the sign was positive in 18, doubtful in 1, and negative in 1. The last was an infant *in extremis*. In only 2 of the cases was shifting dulness demonstrable. In 8 cases the symptoms and usual physical examination did not suggest the presence of peritonitis.

In 2 cases presenting the sign and not showing the expected peritonitis marked intestinal distention was present. In 3 other cases of distention without peritonitis the sign was not present. Further observations will be necessary to determine how much this factor vitiates the value of the sign.

Only 1 case of intraperitoneal hemorrhage, a ruptured tubal pregnancy, was observed, and it showed the sign. Observations on traumatic conditions of the abdomen will be of interest in this connection.

A CONTRIBUTION TO THE STUDY OF LETHARGIC ENCEPHALITIS IN ITS RELATION TO POLIOMYELITIS.[1]

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Since lethargic encephalitis, so called, has appeared in pandemic form it has been most intensively studied by pathologists and clinicians the world over. As a result of these studies it has not been possible to arrive at a definite conclusion whether it is a distinct disease entity or another phase of epidemic poliomyelitis. The problem uppermost in the minds of investigators now is how close is the relation between lethargic encephalitis and poliomyelitis? In this connection we have taken up the study of the effect of serum of patients recovered from lethargic encephalitis upon the virus of poliomyelitis *in vitro*.

It is a well-established fact, as was shown by Flexner and Lewis, Netter and Levaditi, Roemer, and Anderson and Frost, that serum of patients recovered from poliomyelitis neutralizes virus of poliomyelitis *in vitro* and also protects monkeys from the disease when injected with such a mixture. It is also known that normal human serum does not, as a rule, neutralize the virus.

Following are the protocols of our experiments:

Experiment 1. March 6, 1920, Macacus A was injected intracerebrally with 0.5 c.c. of a mixture of poliomyelitis virus and serum of patient Miriam S., aged sixteen years, three months after recovery from lethargic encephalitis, prepared in the following manner:

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[1] Read before the Association for Research in Nervous and Mental Diseases, December 29, 1920, New York City.

COMPARATIVE RESULTS OF NEUTRALIZATION EXPERIMENTS WITH
POLIOMYELITIS VIRUS AND SERA OF PATIENTS CONVALESCENT
FROM POLIOMYELITIS AND LETHARGIC ENCEPHALITIS

Investigators.	Monkeys. Virus and serum mixtures.	Result.
Flexner and Lewis	5 polio virus + human convalescent polio serum	4 protected. 1 paralyzed, living.
	3 polio virus + human suspected polio serum	1 protected. 2 paralyzed and died.
	7 with nine injections of polio virus + normal human serum of adults and children	3 paralyzed and died. 5 protected. 1 died; no paralysis; no polio lesions.
Netter and Levaditi	4 polio virus + human convalescent polio serum	4 protected.
	1 control polio virus + normal salt solution	1 paralyzed and died.
	3 polio virus + human convalescent polio serum	3 protected.
	1 control, polio virus + normal human serum	1 paralyzed and died.
Roemer	3 polio virus + human convalescent polio serum	3 protected.
	1 control, polio virus + normal salt solution	1 paralyzed and died.
	3 polio virus + human convalescent polio serum	3 protected.
	1 control, polio virus + normal newborn infant serum intracerebrally and 5 c.c. pure virus intraperitoneal.	1 paralyzed and died.
	2 controls, polio virus + normal newborn infant serum	1 slightly paretic; recovered 1 paralyzed and died.
Anderson and Frost	1 polio virus + human convalescent polio serum	1 protected.
	10 polio virus + human suspected polio serum	7 protected. 1 paralyzed and died. 2 paralyzed; survived.
	2 controls, polio virus + normal human adult serum	2 paralyzed.
	5 polio virus + normal human adult serum	3 protected. 2 paralyzed and died.
	3 polio virus + normal human adult serum	3 paralyzed.
Authors' cases	5 polio virus + human convalescent Leth. encephalitis serum	5 protected.
	4 controls, polio virus + human normal adult serum	1 paralyzed and dying. 1 paralyzed; survived. 2 paretic, recovered.
	1 control, polio virus + normal salt solution	1 paralyzed and dying.

0.125 c.c. of a 5 per cent suspension of brain and cord of a monkey
that died of poliomyelitis—obtained through the courtesy of Dr.
Amoss from the Rockefeller Institute—were mixed with 1.25 serum

of the above patient and incubated at 37° for two hours and kept in the refrigerator for twenty hours.

Result. The animal remained well without any visible ill-effects until April 21, when it was found dead. The autopsy showed that the cause of death was tuberculosis.

Control. Macacus B was injected in the same manner with 0.5 c.c. of a mixture of the same virus and in the same proportion with normal adult serum prepared as above.

Result. The animal became paralyzed on the eighth day in the right upper and lower extremities, but survived until October, when it was anesthetized and autopsied.

EXPERIMENT 2. May 18, 1920, Macacus E was injected intracerebrally with 1 c.c. of a mixture of equal parts of a 5 per cent suspension of Rockefeller Institute poliomyelitis virus and serum of patient, Dave J., aged thirty years, recovered from lethargic encephalitis since February 20, 1920. This mixture was incubated at 37° for one hour and twenty minutes and kept on ice for nineteen and a half hours.

Result. The animal never suffered any ill-effects and remained perfectly well until August 25.

Control. Macacus D was injected in the same manner with 1 c.c. of a mixture of equal parts of the above virus and normal adult serum prepared as above.

Result. May 24 the animal was found ill sitting in a corner of the cage. May 25 the animal was paralyzed in all four extremities and muscles of the neck with shallow respiration. Anesthetized and autopsied. Macroscopic changes were characteristic of poliomyelitis.

EXPERIMENT 3. June 22, 1920, Macacus F was injected intraspinally with 4 c.c. of a mixture of equal parts of a 2.5 per cent suspension of virus of monkey D and serum of Dr. G., aged fifty-five years, suspected of having had lethargic encephalitis and was left with a paralysis of facial nerve, with complete reaction of degeneration. This mixture was incubated at 37° for two hours and kept on ice for twenty-two hours.

Result. The animal suffered no ill-effects and remained well up to November 5.

Control. Macacus G was injected as above with 4 c.c. of the same virus mixed with equal parts of normal NaCl solution and incubated as above.

Result. June 28 the animal was ill and refused food.

June 29 paralyzed in all four extremities and muscles of the neck. Anesthetized and autopsied. Macroscopic and microscopic changes were typical.

EXPERIMENT 4. October 8, 1920, Macacus K was injected intracerebrally with 1.5 c.c. of a mixture of equal parts of an 8 per cent suspension of poliomyelitis virus of M. E. and serum of patient

M., of Dr. Foster Kennedy's service in Bellevue Hospital, six months after recovery from lethargic encephalitis, incubated for two hours at 37° and kept in the refrigerator for twenty-two hours.

Result. The animal suffered no ill-effects and is well today.

Control. Macacus L was injected the same way with 1.5 c.c. of a mixture of equal parts of the above virus suspension and serum of a normal adult, prepared as above.

Result. October 14 the animal was very ill; the left upper extremity was paretic. October 16 both hind limbs were paretic. October 19 the animal recovered from pareses and is well today.

EXPERIMENT 5. October 28, 1920, Macacus M was injected intracerebrally with 1.5 c.c. of a mixture of equal parts of a 10 per cent suspension of poliomyelitis virus of M. E. and serum of Mary S., aged sixteen years, a patient of Dr. Foster Kennedy, from the service of Bellevue Hospital, and originally observed by Dr. Tilney and described by him as Case IV in his book on *Lethargic Encephalitis*. The patient is at present in the neurological service of the City Hospital. This mixture was incubated at 37° for two hours and kept on ice for twenty-two hours.

Result. The animal remained well without having suffered any ill-effects at any time.

Control. Macacus N was injected in the same manner with 1.5 c.c. of a mixture of the above virus suspension and equal parts of serum of an eighteen-year-old laboratory helper in the laboratory for clinical pathology of Cornell Medical School, who claims that he was never ill. This mixture was prepared in the same manner as the one above.

Result. November 2 the animal was ill and paretic in the right upper extremity and showed also a slight hypotonia in the right lower extremity. The same condition still prevails today.

EXPERIMENT 6. In order to establish whether some of the animals that were protected by the convalescent encephalitis serum, were refractory Macacus E was injected intracerebrally with 1 c.c. of a 5 per cent suspension of brain and cord of Macacus G on August 25, about three months after the initial injection.

Result. August 31 the animal was found paralyzed in all extremities and dying. Macroscopic and microscopic changes were characteristic of poliomyelitis.

EXPERIMENT 7. Monkey M was injected intraspinally, January 3, 1921, with 2 c.c. of a 5 per cent suspension of poliomyelitis virus.

Result. January 11 the animal became paralyzed in all the extremities and died that night. Macroscopic and microscopic findings were characteristic.

It should be noted here that all sera used proved Wassermann negative; that for each control serum of a different person was used.

Since we have mentioned above the reports of Flexner and Lewis, Netter and Levaditi, Roemer, and Anderson and Frost on neutrali-

zation experiments with mixtures of poliomyelitis virus and serum of frank and suspected cases of poliomyelitis, it may not be out of place to compare their results with ours.

Flexner and Lewis[2] by their experiments show that out of 5 monkeys injected with a mixture of poliomyelitis virus and serum of convalescent poliomyelitis patients in proportion of 1 c.c. serum and 0.4 and 0.3 c.c. virus respectively, 4 were completely protected and 1 became paralyzed, but survived, retaining the paralysis.

Of 3 monkeys injected with virus and serum of suspected cases of poliomyelitis, 2 developed typical paralyses and died, and 1 was completely protected.

Of 7 animals with nine injections of virus with normal human serum of adults and children, 3 died with the typical picture of poliomyelitis, 3 were completely protected and 1 died twenty-seven days after the injection without any paralyses, and no changes in the cord or brain characteristic of poliomyelitis were found.

Netter and Levaditi[3] report that in their first series 4 monkeys were injected with 0.25 c.c. of a mixture of equal parts of virus and serum of recovered poliomyelitis patients. The 4 animals were protected. One control was used for this series and injected with virus in normal solution. This animal became paralyzed on the seventeenth day. In the second series they injected 3 monkeys with virus and serum of recovered poliomyelitis patient and all 3 animals were protected. In this experiment they have also used one control, but this time the virus was mixed with normal adult human serum. The control became paralyzed on the seventeenth day.

Roemer[4] reports a series of experiments in one of which he used one control for 3 virus-immune-serum injected monkeys. The 3 monkeys were protected. The control was injected with virus in normal salt solution and this animal became paralyzed and died in thirteen days. In the second series 3 monkeys were injected with virus and immune serum and all 3 animals were protected. Of the 3 controls in this series 1 was injected with virus and normal new-born infant serum intracerebrally, and in addition 5 c.c. pure virus intraperitoneally, and this control animal became paralyzed on the thirteenth day and died on the twenty-third day. The 2 other controls were injected with virus and normal newborn infant serum only. Of these 2 controls 1 became paralyzed and died on the fourteenth day and the other was paretic in the right upper extremity on the seventh day, but soon recovered and remained well. In two further suspected cases the virus and serum animals as well as the controls never showed any ill-effects.

Anderson and Frost[5] have in their series of experiments injected

[2] Flexner and Lewis: Quoted by Peabody, Draper and Douchez, Monograph 1, Rockefeller Institute, 1912, p 16.

[3] Netter and Levaditi: Société de Biologie, 1910, pp. 617–885.

[4] Roemer: Die epidemische Kinderlaehmung, Berlin, 1911.

[5] Anderson and Frost: Jour. Am. Med., Assn., 1911, lvi, 663.

the monkeys with 1.1 c.c. of a mixture of 0.5 c.c. of each serum and 5 per cent suspension of virus and 0.1 c.c. fresh normal serum. One monkey received an injection of virus and serum of a convalescent adult poliomyelitis patient. This animal was protected. Ten monkeys were injected with virus and serum of suspected cases of poliomyelitis. Of these 7 were protected, 1 became paralyzed and died and 2 became paralyzed and survived. As a control to this series of 11 monkeys 2 were injected with virus and normal human adult serum. Both animals became completely paralyzed. Two additional series of monkeys were injected on December 24, 1910, one month and eleven days after the first series of injections, and again on January 12, 1911, nineteen days after the second series. Whether one could properly speak of the two series as controls to the first series injected November 13, 1910, or not the results were as follows: In the December 24 series 5 monkeys were injected with virus and normal serum. Of these 3 were protected and 2 became paralyzed and died. In the January 12 series 3 monkeys were reinjected with virus and normal human serum of the cases that were not protected in the earlier series. All the 3 animals became paralyzed.

To summarize we would say that 5 monkeys were completely protected from poliomyelitis by sera of patients convalescent from 4 undoubted cases of lethargic encephalitis and one suspected case, and secondly, that our results compare favorably with the results of other investigators in the neutralization experiments of poliomyelitis virus and convalescent human poliomyelitis sera.

We wish to thank Dr. William C. Thro, Miss Matilda W. Harms and Dr. Foster Kennedy for their assistance and encouragement, and Dr. Amoss for his kindness in providing us with poliomyelitis virus.

MERALGIA PARESTHETICA (ROTH'S OR BERNHARDT'S DISEASE): WITH THE REPORT OF FIVE CASES; THREE CASES OCCURRING IN THE SAME FAMILY.

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Most of the literature on the subject of meralgia paresthetica, (Parästhesie der Hautnerven am Oberschenkel, paresthesie de Bernhardt, meralgie de Roth, Bernhardt's Sensibilitätsstörung) has been written during the past twenty years. A number of cases were reported during 1895 and 1900 in America, France and Germany.

At the February (1900) meeting of the New York Neurological

Society, Dr. Philip Meirowitz showed two cases, one in a man, forty-eight years, a presser of coats, the condition was probably due to the long-continued pressure against the thigh, standing at a table in ironing coats for twenty years, thus affecting the external cutaneous branch of the femoral nerve. There was anesthesia, tactile hyperesthesia, and at the lower part of the affected area the touch of the finger was painful.

The other case was a man, aged forty-seven years. The paper by the late Dr. Musser and Dr. Sailer is very complete. They were able to collect 90 references on the subject, and report 10 of their own cases in the AMERICAN JOURNAL OF THE MEDICAL SCIENCES for January, 1900. Dr. Edwin Bramwell exhibited a case of Bernhardt's Sensibilitätsstörung, or meralgia paresthetica, March 5, 1902, before the Medico-Chirurgical Society of Edinburgh. The patient was a a miner, aged forty-three years; for eighteen months he had suffered from pain over the right hip and over the lower part of the right thigh anteriorly, also from a feeling of coldness on the outer side of the right thigh. The pain was greatly increased on walking and incapacitated him from work. He had not had rheumatism nor syphilis. The condition was attributed to sleeping on hard boards in damp clothes. A relative cutaneous anesthesia was present on the outer side of the right thigh, while there was marked tenderness on pressure over a point an inch and a half below and just external to the right anterior-superior iliac spine. The patient's symptoms were obviously referable to the right external cutaneous nerve. No improvement resulted from rest in bed and faradism. Thomson cut down on the nerve at the level of Poupart's ligament and excised three inches. The nerve and its relations appeared to be normal. The pain immediately disappeared. No degenerated fibers were found in sections stained by the methods of Busch and Weigert. He considers meralgia paresthetica a distinct clinical entity. The pathology is obscure. It may be a neuralgia or a neuritis. Roth has recorded 15 cases. The condition is not generally recognized, and it is important to remember this entity in making a differential diagnosis.

In Miller's case, corset-pressure appeared to be the causative factor, and cutting out a section of the corset cured the patient. Some of the reported cases have been improved with faradism. Resection of the nerve is to be done as a last resort in severe cases. There seems to be no definite causative factor of the disease. It appears to be much more common in men than in women. Influenza, gout, syphilis, corset-pressure, table-pressure, hernial truss or belt, alcoholism, constipation, pregnancy, traumatism, long-standing, typhoid fever, rheumatism, diabetes, obesity and hereditary influence have all been mentioned as possible or probable factors in the causation of this disease. In one case with autopsy there was found

a spindle-form swelling in each nerve at the point where it crossed the crests of the ilia. In these regions there was evidence of neuritis and perineuritis. The spinal cord in this case showed slight sclerosis in the posterior columns.

Warda found a swollen tender nerve on palpation in one of his cases. There is probably some lesion of the external cutaneous branch of the femoral nerve in these cases.

The late William Osler read a paper on this subject before the Philadelphia Neurological Society in 1897 and reported 3 cases of monocrural paresthesia which he believed to be exaggerated forms of this disease.

Roth, who wrote a short monograph on this disease, reported 14 cases (1895). Roth states that in all of his patients the area of pain has been the same—that is, in the distribution of the external cutaneous nerve. A burning sensation may extend at times over the whole thigh. In 5 of his 14 cases the condition was bilateral. Roth believes there may be some compression of the nerve either in its passage under the psoas muscle or where it runs close to the anterior-superior spine of the ilium.

Musser and Sailer were able to collect from the literature 89 cases, and they think it is not a very common disease.

Sabrazes and Cabannes collected 62 cases. Finally, Musser and Sailer's definition for this condition is "a disturbance of sensation on the external surfaces of the thigh, characterized by various forms of paresthesia, associated with dissociation and more or less diminution of sensation." In the 99 cases found (including their own 10 cases) 75 were in men and 21 in women; in 3 the sex was not stated. Ten of the patients were physicians.

Mary Damon reported an interesting case in a school-teacher, aged thirty-eight years. She was rather overfat. She had an attack of epidemic grippe in December, 1900.

There was excessive sensitiveness just below the anterior-superior spine and over an area 8 cm. long over the anterior crural region. There was hyperalgesia throughout. At individual spots in the regions supplied by the ilio-inguinal, iliohypogastric, external cutaneous and middle cutaneous nerves, a single touch sent pain flashing long distances through other branches of the plexus.

Roth was, I believe, the first writer to report this condition as an independent clinical entity and called it meralgia paresthetica.

Pieraccini, Bernhardt, and Musser and Sailer observed several cases previously but did not report them as distinct clinical entities.

Goldflam reported a number of cases who were arteriosclerotics past middle life. In Musser and Sailer's collection 57 cases occurred between the ages of thirty and sixty years. They include a complete bibliography up to 1900 on the subject. I will therefore add a few additional references from 1900 to 1920.

CASE I.—Mrs. Elizabeth K. W., married woman. Has charge of a busy café and restaurant. Aged forty-four years. Had two children, one living and well. One died of membranous croup. Last normal period six months ago. Not pregnant. Had a very free flow; excessive bleeding for nine consecutive periods prior to the last period. Has "hot flashes" and thinks she was badly frightened and shocked when she heard revolver shots close by on New Year's eve, when she began to bleed, the flow from the uterus continued for four hours then stopped. Always well, except for soreness, and numbness and a painful spot low down near the groin, and hip and side of the thigh (left). Complains of poor appetite. Stands on her feet at her work the greater part of the day.

General examination is negative. She has some symptoms of the climacteric.

Blood-pressure. Systolic, 130–140 (auscultatory), diastolic, 90 to 95. An area with the anterior-superior spine of the ilium as the center, the size of the hand, is exquisitely tender to the slightest touch, particularly an area extending about $2\frac{1}{2}$ inches posteriorly and $2\frac{1}{2}$ or 3 inches anteriorly to the superior spine and downward toward the groin and across to the side of the thigh. This sharply defined area, which is an irregular triangle, is surrounded by another area of analgesia and hyperesthesia. This area is not nearly so well defined as the painful tender, "tingling or stabbing" area.

Blood Wassermann is 4 plus.

I advised that a section of the corset extending down to the thigh be cut out, or if possible for her to do without the corset for a while. I also ordered lutein tablets with ovarian residue to be taken one three times a day, and a digestant three times a day. Massage was suggested, if not too painful or annoying, and she was advised not to press or stand against the table or counter in the restaurant and to avoid standing up or excessive walking. Of course, antiluetic treatment is indicated. She was married four times; she is now living with her fourth husband. The four factors to be considered here are (1) her occupation, (2) climacteric, (3) lues, (4) corset or counter-pressure. Neurosyphilis and posterior root involvement must be considered and excluded.

Roth has emphasized several points along the line of the nerve (external cutaneous) where trauma of this character may occur— *i. e.,* mechanical factors are believed by some to be the most important, because the peculiar curve of the nerve and its relation to surrounding structures render it especially liable to compression when the thigh is extended.

Very distressing at times is the extreme hypersensitiveness of the skin over the affected area, so that, as in my case, the slightest touch and pressure even of the clothing is annoying and painful. Souques reports a case in which the pain was so intense that during a spasm morphine was necessary.

Roth's points are (1) just after the exit of the nerve where it passes beneath the psoas muscle; (2) where it curves around below the anterior-superior spine and finally the fibrous canal in the fascia lata. Among the mechanical factors responsible there have been mentioned the pregnant uterus, pelvic tumors, varices, tight bands, direct trauma and flat-foot. Pressure on the nerve by the lower edge of Poupart's ligament was found in one case and the symptoms disappeared after partial section of the ligament. Hereditary influences may play a role.

Miller's case was a young woman, aged twenty-three years. Family history negative. She did office work, standing most of the day. Two years before she noticed a peculiar sense of numbness over the upper and outer side of thigh when standing or walking. Several weeks later she suffered from occasional attacks of burning or stabbing pain in this region. These attacks increased and she stopped work; standing would excite an attack. Pain disappeared on sitting down or lying down. At times the slighest irritation over the affected area would cause her to scream.

Examination. A circumscribed area of tenderness located below and slightly outward from the anterior-superior spine of the ilium. Surrounding this was an ill-defined area of hyperesthesia. No analgesia, anesthesia nor thermalgesia. The area of hyperalgesia was triangular in outline, the upper border forming the base about 5 cm. above the iliac bone and extending from the crest of the ilium to 5 cm. medianward from the anterior-superior spine of the ilium. The apex of the triangle was located at the junction of the lower and middle two-thirds of the thigh. General examination of patient negative.

Lower edge of the corset hooked over the anterior superior spine, pressing into the thigh so that when standing erect it was forced in. Miller advised the patient to cut out a portion of the corset over this region, and the relief in a few days was marked. The attacks of pain entirely disappeared. After a lapse of ten days she complained only of slight numbness occasionally.

S. Sherwell, of Brooklyn, in 1910, reported his own case. For about the last ten years of his life he complained of symptoms of meralgia in the area supplied by the external cutaneous nerve, particularly in the outer and lower two-thirds of his left thigh after exertion—walking, riding and cycling. He felt better on lying down and was made worse on resumption of exertion. Sherwell was sixty years old when making his report. He believes that the condition comes from a constriction or pinching of the nerve as it passes through the tough fasciæ of a muscular individual, giving rise to a "temporary non-essential zoster as it were." He thought a rheumatic tendency would have an aggravating effect on the condition.

W. J. Rutherford reports a dozen cases of this disease that he has

seen in the last ten years. The condition, as he found it, is characterized by mononeuritis of the external cutaneous nerve of the thigh. The special feature of this neuritis which, as the external cutaneous nerve is purely sensory, is unattended by motor disturbance, is dissociated sensation, the deep or protopathic sensibility, through afferent fibers contained within the motor nerve bundles, supplying the muscles being unimpaired. Sensation over the area of distribution of the affected nerve, which, as a rule, can be strictly delimited, is lost, so far as finer sensibility is concerned for slight touch, for perception of points, for heat and cold, and to a certain extent for pain, while deep pressure can be perceived, and a touch on the bare skin is felt as though a layer of clothing intervened or as one might feel a touch on the back of a gloved hand. In old standing cases a distinct cutaneous thickening may be made out locally if a fold of skin is pinched up between the finger and thumb and the skin of the affected area (in some cases at least) begins to grow bald from atrophy of the hair follicles; while, either in association with this, or as a result of the analgesia, the phenomenon of the cutis anserina is lost locally, so that if the patient is examined in a cold room there is no goose-skin or on an area in the upper and outer aspect of his thigh, even though the other parts show this distinctly, with erection of the hairs over the rest of the limb.

Not only is there this anesthesia or rather analgesia, but perverted sensations are present in the affected area. These take the form of shooting pains, of a sensation as though an invisible hand had grasped the thigh, and was screwing around a handful of the flesh, and of a sensation as though scalding water were being poured down the outside of the limb. These sensations are usually of short duration and are of variable onset; they may occur for months on end, or even for years in old standing cases, but are liable to recur again and again on little or no provocation. The etiology of the condition seems to be unknown. Treatment is of little use. Tonics, massage, electric treatment have all been tried and have all failed. The attacks of pain tend to wear off and to become less frequent with the lapse of time.

Cumston (June, 1919), in a brief note on the subject, states that Lenoir has published the results of his studies in 39 cases while Sabrazes and Cabannes have reported 62 cases, making a total of 101 case reports of this interesting affection. Of these 65 occurred in men and 29 in women, the others not stated. In all these 101 cases paresthesia occupied the antero-lateral (external) aspect of the thigh, 38 in the left and 36 in the right. He does not report any cases. No mention is made of Musser and Sailer's excellent review on this subject nor of the more recent reports on this interesting clinical entity.

Comment. In Nartowski's case pain increased during sleep.

The symptoms are very variable. There may be tingling, pain;

this pain is usually worse on standing or walking. There may be numbness or cold or damp feeling. Exquisite tenderness may be elicited at times, as in my case.

V. Lutzenberger, in his own case, thought there was hyperalgesia with anesthesia to cold, later analgesia with anesthesia to heat. This is not as found in some of the other cases reported.

Diagnosis. The diagnosis must be made from neurosyphilis, ordinary neuralgia or neuritis; akinesia algera or apraxia algera; intermittent claudication, hysteria, bone disease, etc., must be excluded.

Prognosis. The course of the disease is variable and very indefinite. It is trivial in nature although very annoying. It does not affect the general health of the patient as a rule.

Treatment. Treatment is not satisfactory. It depends entirely on the cause. Various methods of treatment have been tried without much benefit. Rest, massage, counterirritation, antirheumatics, sedatives, electricity, ultraviolet rays, high frequency, etc., may be tried.

Case II.—Mr. Samuel T., aged forty-five years, white adult male. Patient was a dealer in bottled goods (soda water, seltzer, beer and whisky), delivering box and case goods to customers from a wagon, for several years. Complains of peculiar (paresthetic) sensations over the outer side of the left thigh. This "numbness" or "loss of feeling," as if the side of the limb is "dead" and "does not belong to him," is present over the front and external aspect of the thigh from the iliac crest to just above the knee. The condition comes on after walking or standing a while. When he sits or lies down "it eases up and goes away." At the time he has this peculiar feeling he does not feel any pinch or stick along this area of the left thigh—there is apparent anesthesia and some disturbance of thermal sense. He attributes his condition to bathing in the ocean at Atlantic City in the summer of 1919, because he first felt this trouble the next morning after an ocean dip. He has not gone into the ocean since that day. On standing erect five to ten minutes this "dead numb" sensation appears; pinching and sticking in the area over the upper and outer two-thirds of the thigh is not felt by the patient; there is evidently loss of tactile and pain sense for some minutes. On lying down for a while these pinching and sticking tests become somewhat more sensitive, and he begins to notice them.

He has attacks of slight faintness and feeling of weight and discomfort over the heart. He thinks his "heart is weak" and complains of constipation and belching. Sometimes during these spells he thinks he is going to die and "is scared." The vague dull, aching sensation over the heart comes and goes for the past five years. It comes on especially after some exertion. He informs me that several years ago he was told he had "heart strain" and that the roentgen

ray showed the heart to be enlarged. Sometimes he has pain in the right temporal region.

Examination. Heart: Slightly enlarged; no cardiac murmurs; heart sounds somewhat weak, muffled and slow. Heart-beat, 60. No pulse deficit. No pulsus alternans. Myocardial disease. On hopping across the floor there is a slight increase of the heart-beat to 76 or 80 for a minute or two.

Blood-pressure, 118–115 S. (second visit); 72 D. auscultatory. (First visit: S. 125–130, D–85.)

Lungs: No rales.

Blood Wassermann: Negative on two occasions. *Gums and teeth* need dental attention (pyorrhea).

Urine: Moderate amount of indican present; clear; acid; specific gravity, 1.021; urea, 1.6 per cent, 8 gr. in fluidounce; no albumin; no sugar; no casts; few pavement form epithelia; few leukocytes; no red blood cells, little mucus.

Phthalein renal function test (intramuscular): Thirty per cent at first hour and 20 per cent at second hour, total 50 per cent for two hours. Some distention of abdomen and some fulness of descending colon. Liver apparently not enlarged. Spleen not palpable.

He has always been pretty well except for constipation, the "heart and stomach trouble" and this condition of peculiar "dead numb" feeling of the left thigh. There has never been a true attack of angina pectoris with the typical pain over the heart up to the neck and down the left arm. There have been attacks of pseudo-angina (?) or angina pectoris sine dolore (?). His wife never had any miscarriages.

This case in some respects resembles the case reported by Alfred Gordon (Philadelphia, 1900). In Gordon's case the whole external cutaneous nerve, with both its branches and the cutaneous branches of the crural nerve was affected.

The external cutaneous nerve ordinarily arises from the anterior divisions of the second and third lumbar nerves. Then it crosses the outer border of the psoas muscle, cuts perpendicularly the iliacus muscle, to which it is attached by the aponeurosis, leaves the pelvis through the notch beneath the anterior-superior spine of the ilium, is placed in the double layer of the fascia lata, and at 2 cm. below the spinous process divides into two branches: one, the posterior, passes through the fascia lata and divides into branches to supply the skin of the buttocks; the anterior branch becomes superficial below Poupart's ligament and innervates the skin of the antero-external surface of the thigh from the greater trochanter as far down as the external condyle of the femur. This nerve is therefore (according to Gordon) placed in a muscle indispensable to standing and walking (psoas muscle) and in the fascia lata, the contraction of which in walking presses upon it and stretches it. The musculo-

aponeurotic relation and the superficial position of the nerve expose it to traumatic injuries, especially in individuals predisposed to painful paresthesia. Gordon further states that a slight neuritis, that perhaps would remain latent in any other territory of the nervous system, is marked in the sphere of the anterior branch of the external cutaneous nerve. It is to be remembered that even without any inflammatory condition of the nerve, any infection such as acute rheumatic fever, typhoid fever, streptococcic tonsillitis, etc., may of itself be capable of giving rise to neuralgia in a predisposed individual. The sensation over the external part of the thigh in my patient was similar to that of Gordon's patient, in that he feels at each contact the sensation similar to that of rubber or leather, and as stated, the tactile sensation over this area is very much diminished.

CASE III.—Herbert B., white schoolboy, aged eleven years. Has a "burning feeling" over the outer side of the right thigh and in the region of the anterior-superior iliac spine. He has worn a belt for two years. For a short period he had a small area, about 5 x 3 inches on the outer side of the left thigh, in which there was some paresthesia, "burning and stinging." This has now disappeared. A younger brother complains slightly of a similar condition; he also wears a belt all the time.

Seven or eight years ago the boy had measles, influenza and a discharging ear. He also had several attacks of tonsillitis and rheumatism and was dropsical on one or two occasions, due to cardiac decompensation. His adenoids, tonsils and several bad teeth were removed in the fall of 1920. He had an attack of acute articular rheumatism (rheumatic fever) with acute endocarditis in April, 1920.

Examination. April 20, 1920. Mitral regurgitation.

Fluoroscopic and Roentgen-ray examination (by Dr. Roberts) showed the heart to be enlarged a little to the right and to the left.

Lungs: Negative.

Blood: Red blood cells, 3,690,000. White blood cells, 15,800.

Polynuclears 73 per cent; small mononuclears 22; large mononuclears 2; transitionals 2; eosinophils 1.

Blood Culture: Sterile at the end of seven days; at the end of the tenth day there developed a slow-growing pneumostreptococcus. This may have been a contamination.

Throat Culture: Streptococcus viridans.

Urine: No albumin; no casts; total solids, 23.3 gm. per liter; urea, 8 per cent, ammonium urates present. Specific gravity, 1.010. Some squamous cells; few renal cells.

Another urine specimen showed no albumin; no sugar; no acetone; no diacetic acid; some bladder epithelial cells; some cylindroids; few amorphous urates; few white blood cells; acid; specific gravity, 1.025.

Another throat culture showed Streptococcus viridans predominating and a few pneumococci and Micrococci catarrhales.

Blood-pressure: S. 90; D. 68 auscultatory (April 27, 1920). Since the removal of the tonsils and adenoids by Dr. Husik the boy has been in much better health, although he still complains of this burning and stinging sensation in the region of the great trochanter, anterior-superior spine of the ilium and along the outer side of the middle and upper third of the right thigh.

Donley's (1904) patient, a primipara, was a white married woman, aged forty-three years. Complained of disability in the left thigh. Gave birth to one child nineteen years ago. About a year ago had an attack of "neurasthenia" for six weeks. She is a woman of high-strung temperament and heavy build. No history of syphilis or alcoholism. Constipation. Climacteric, with flushings, dizziness and palpitation. She injured her right foot by dropping a flat-iron on it twelve weeks ago. Eight weeks later she began to notice a peculiar ill-defined feeling of tingling and numbness accompanied by a sense of constriction on the outer side of the left thigh. Because of the severe injury to the right foot she was compelled to throw as much weight as possible upon the left leg. This sensation was usually absent during rest and appeared shortly after she began to walk or stand, followed by considerable pain compelling her to sit down. At times she also complained of an intense heat, or cold, and damp ("wet cloth") feeling, at other times only the pain, numbness and tingling. She had anesthesia on the outer side of the left side of the left thigh from the great trochanter to the head of the fibula. Pain, temperature, tactile pressure and hair sensations were greatly diminished, particularly those of pain and temperature. Strychnine, massage and galvanism rapidly improved her symptoms, and in three weeks they had completely disappeared. In the cases of Féré and Moller the affection involved the anterior crural nerve and the external popliteal nerve was affected in Sollier's case. In Claisse's case it followed malaria. In one of Musser and Sailer's patients the pressure of a heavy army belt caused the symptoms in both thighs. In my case (No. III) of the little boy the factors to be considered were the streptococcic tonsillitis, articular rheumatism (acute rheumatic fever) and the endocarditis (Streptococcus viridans infection) or the pressure of the belt which he was wearing for two years. He was complaining of the "burning feeling and stinging" for a little while a year or so ago on the opposite (left) thigh, but at present most of this trouble is limited to the outer side of the right thigh. In my case (No. II) of the man the occupation of climbing and jumping from the delivery wagon and carrying the boxes (against the front and side of the thighs), gastro-intestinal intoxication from chronic constipation and the cold sea-water bathing are factors to be considered. In the little boy's case the local

application with friction of methyl-salicylate in an oily iodine vehicle and rest, together with moderate doses of salol, strontium or sodium salicylate or cincophen and fractional doses of calomel with sodium bicarbonate seemed to relieve the condition.

Devic employed salicylic acid in ointment form locally. In Donley's case iodine seemed to be harmful, the iodine causing a painful dermatitis—however, this patient may have been hypersensitive to iodine, iodoform and other such drugs, and this one case does not prove that "counterirritation is harmful in these cases," as is stated by Donley. In three of my cases mild local applications and counterirritation seemed to do good.

Osler's first case occurred in a healthy, vigorous man, aged sixty years. The second case was in a healthy looking man, aged thirty-two years, who for a month complained of numbness and queer feelings in the left leg. Osler thought his first case, in the early stage, suggested akinesia algera (Moebius), in which painful sensations in the muscles follow the slightest movement, in consequence of which the patients may be bedridden and helpless. Osler says he "has never seen a typical case of paresthetic meralgia," and then goes on to report the "three remarkable instances of monocrural paresthesia, which are possibly exaggerated forms of this trouble" (March, 1897). Osler's third case occurred in a southern college professor aged thirty-seven years. He was a very nervous man and had worked hard. He complained of a sensation of numbness, burning and lifelessness over the hollow of the right foot; later this sensation extended up the leg almost to the knee. Sitting down and resting lessened the uneasy and numb sensations. He felt worse in cold weather. Walking would cause the sensation of numbness and burning over the leg and thigh. Physical examination was negative.

Walsh states (October, 1900) over 100 cases of meralgia paresthesia have been reported by various observers in the past six years.

Walsh's patient was a neurotic and "neurasthenic" man aged forty-five years, a cabinetmaker, who complained of painful, at times hot, feelings on the outer part of his right thigh. An oval patch of the cutaneous surface 5 x 3 inches was almost anesthetic when pricked with a pin-point. In a corresponding area on the other (left) leg there was a patch of slight hyperesthesia. He felt worse just before a rainstorm. At his work (as a cabinetmaker) he was on his feet all day. His right thigh was constantly rubbed during his work (used a plane a good deal) against the side of the work-bench. He always felt better when he sat down, and was entirely relieved upon lying down. In Walsh's case chloroform and iodine locally made him worse, salicylates did no good, rubbing with simple soap liniment did relieve him. He suffered from this condition for several years. Walsh thought it was due to a functional disorder (neurosis) of a localized part of the central nervous system.

Shaw reports (February 13, 1897) 4 cases of this affection: (1) A man, aged fifty years, in whom both thighs were involved, complaining of a feeling of numbness and a burning sensation, and on standing had a painful, stinging sensation on the lower and outer side of the right thigh for ten years. On the left thigh there is some paresthesia in an area 3 x 2 inches but is never painful. (2) A large powerful man, aged fifty years. He had lues twenty-seven years ago. Eats a great deal; bowels are irregular. Complains of a burning sensation in his left leg "like fire" or as if a lot of bees had "stung him." Antiluetic treatment did not seem to relieve him. A year and a half ago he began to have headache in the left temporal region and over the eye, which was constant and made him miserable. The pain in the leg was much increased on walking. His pulse was below fifty and labored. No valvular lesion; the heart appears weak and embarrassed; the sounds are not sharp. Abdomen negative and no gaseous distention of the intestines is present. (3) A female, aged thirty-six years, was treated six years ago for "neurasthenia," from which she recovered entirely. She has one child, eight months old. Complains of a burning sensation about the middle of the outer side of the left thigh. (4) Female, aged sixty years. Also complains of a burning sensation on the left thigh. Shaw thought that "toxemic states" are probably a cause of this condition. He suggests the Turkish bath, electric brush and outdoor exercise.

CASE IV.—The little brother (Arthur B.) aged eight years, of my Case III, Herbert B., has had his tonsils and adenoids removed by Dr. D. N. Husik, of Philadelphia about three months ago. He, too, now feels much better. Ten badly decayed teeth were removed at the time of the tonsil operation by Dr. D. E. Cooper, of Camden. No other treatment has been given this boy except to suggest the putting aside of the belt and the performance of the above-mentioned operations.

CASE V.—The father, George B., aged thirty-five years, had some "vague pains," but these I attributed to a large direct (right side) inguinal hernia, which was operated upon by Dr. Alfred C. Wood, a short time ago, at the Howard Hospital, Philadelphia. The patient had previously been operated upon for this hernia on two occasions. Pressure of the truss belt was probably the causative factor in this Case V.

Dr. Spiller, of Philadelphia, reported a case of meralgia paresthetica in a middle-aged man complaining of distinct burning and drawing sensation, attended with severe pain in the distribution of the external cutaneous nerve of the right thigh. When in bed, or sitting in a chair, or immediately after standing upon his feet, no unpleasant symptom was noted, but after standing for a short time, or walking, a

distinct burning with drawing pain was experienced. The condition of the muscles and sensation otherwise were normal. The affection had existed one year and was getting worse. Spiller states that stretching or even cutting the external cutaneous nerve might be advisable if other measures fail. The nerve could be easily reached at the anterior-superior spine of the ilium.

F. Savary Pearce saw the same condition in a woman who had sepsis and had been subjected to operation upon the bladder and womb. In his case the middle cutaneous nerve of the thigh appeared to be alone involved.

Sailer has made the diagnosis in 2 other cases since his report on the subject.

Wharton Sinkler saw 2 cases of this disease. One patient was a woman who recovered several months later. The second case was a patient who suffered injury in a railroad collision. Intense burning pain was experienced in the distribution of the nerve.

McCarthy's case was a man, aged forty-eight years, who suffered for several years with an uncomfortable creeping sensation over the anterior and external surface of the right thigh. The left thigh also became affected. For nine years he had worn a heavy truss to control a bilateral inguinal hernia. There was anesthesia to the strongest faradic current and changes in temperature and touch sensation, and there were vague, uncomfortable paresthetic sensations over the antero-external surfaces of the thighs, extending to a few inches above the patella. F. X. Dercum believes that these cases are not uncommon and that the condition is a neuralgia of the external cutaneous nerve of the thigh.

Chipault has operated on 3 cases with great improvement of the symptoms. As this nerve is only sensory, resection would only cause loss of sensation in the part supplied by it. Mauclaire and Wondsbeck also obtained excellent results from resection of the nerve.

Gordon (1900) in his report states about 100 cases have been reported since Roth's and Bernhardt's papers in 1895. Gordon's patient was a neurasthenic man, aged forty-five years, who had typhoid fever four years previously. He began to suffer intense pain in the region of the fourth sternocostal articulation during convalescence. At the same time pain appeared in the antero-external and posterior surface of the left thigh. The pain was present for two years. He complains of a burning sensation over the antero-external surface of the upper two-thirds of the thigh from the anterior-superior spine of the ilium down and over the posterior surface of the upper third, from the crest of the ilium down, covering the external surface of the buttock. The tactile sensation is much diminished. When he walks the burning sensation is associated with pain, the pain appearing after he has walked for a few minutes. Pinching and rubbing are extremely painful. The thermic sensa-

tions are normal. In Gordon's case intermittent lameness (Charcot-Goldflam) was present; this is usually due to some constriction or obliteration of the arteries of the affected limb when it occurs in aged people. Several nerves, including the posterior branch, as well as the anterior branch of the external cutaneous nerve, and the cutaneous branches of the crural nerve were involved in Gordon's case. He concludes with a discussion of the atypical features of his case and a consideration of the etiological factors. Potassium iodide and massage seemed to help, although he insists that excision of the external cutaneous nerve is the only treatment for a case of genuine meralgia paresthetica.

Price's case (1909) occurred in a white married woman, aged thirty-one years. Her symptoms began when she was two months pregnant. She complained of sharp or cramp-like pain occasionally on the outer surface of the thigh, with paresthesias over the same area, particularly "numbness." There was some tenderness on pressure. The pain was made worse by walking and at times the pressure from the clothing caused discomfort. There was loss of pain sense and diminution of tactile and temperature sense. He treated her with hot fomentations locally, aspirin internally, rest, galvanism—resulting in prompt improvement. When she again became pregnant the trouble returned. At four months she miscarried and the paresthetic symptoms again disappeared under treatment. She had several miscarriages, but Price does not mention whether syphilis was present or not.

White's (1906) patient was a man, aged fifty-five years. He complained of tingling of the outer lower two-thirds of the right thigh; there was a dull, deep pain or ache at times. These sensations ceased on sitting or lying down. The middle cutaneous nerve was not involved in his case.

H. C. Baum and H. Goldenberg, physicians, suffered from this disease. Baum (1906) said he personally suffered from this condition for eleven years. He had seen 2 other cases exactly like his. He complained of a perverted sensation; sometimes there was formication, or prickling, or a sensation of heat or intense cold; there was no anesthesia. He always felt worse when fatigued or ill of any concurrence.

Hyde thought hypertrophy of the prostate might be a factor in some cases.

Hirsch's (1896) case was a man, aged fifty years, who had had syphilis eighteen years ago, and indulged in alcohol liberally. This man was exposed after a shipwreck and a considerable weight had been borne by one leg for about an hour. The man complained of a "burning cold." He was free of these sensations at night or while reclining or sitting. There was no change in the electrical reaction and some diminution of thermal sense was present.

Conclusions. 1. Six cases of Roth's or Bernhardt's meralgia paresthetica are reported in this paper—two woman, two men, and two young boys.

2. There are probably 135 cases of this interesting affection recorded in the entire literature.

3. The etiology is not settled. Infection, strain and persistent continued slight trauma have some bearing and influence on the appearance of this condition.

4. Treatment depends on the cause, if that can be discovered. Rest and avoidance of the usual occupation that traumatizes the front and side of the thighs, excessive walking, jumping or continued standing should be avoided.

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CHRONIC TUBERCULOSIS OF THE KIDNEY.[1]

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This subject was selected for my paper of the evening because it seemed to me that it would make an appeal to a general audience. I welcomed the opportunity to present a review of this subject to you, as my experience has shown me that the profession does not fully appreciate the clinical picture of renal tuberculosis and the great importance of its earliest recognition, when still localized to one kidney. Before an audience of this character I naturally shall not go in great detail into many of the refinements in diagnosis and treatment that have developed in recent years, and even if I fail to tell you anything particularly new, I feel sure I shall have reawakened your interest in the subject under discussion and perhaps helped you to recognize cases of this disease.

There has been a growing tendency to call experts to make the diagnoses when the patient's symptoms fail to respond to treatment, and ultimate reliance on the expert has undoubtedly interfered with the general practitioner's independent and early recognition of renal tuberculosis. One can readily understand the practitioners' attitude, based as it is on their unwillingness to admit their inability to treat such slight symptoms as most patients present in the early stages of renal tuberculosis. But in fairness to the patients, why do they persist so long in blind treatment of these cases without arriving at a definite diagnosis? In the typical cases the expert should not be required to make the diagnosis, but his work becomes absolutely necessary in deciding which kidney, or whether both are diseased or not.

There is probably no disease which surgery has done more to clarify in every detail than renal tuberculosis. Its pathology, its diagnosis and its treatment have all been placed on a firm foundation by the surgeons; and as it is unfortunately a very frequent renal disease, in fact the most frequent renal disease that requires removal of a kidney, surgery can be proud of its accomplishment. Many of the profession in all lands have contributed to this study. I need mention only such names as Gross, Steinthal, Morris, Guyon, Tuffier, Israel and Brown to emphasize the international coöperation that has helped to clarify our views on chronic renal tuberculosis.

The view that chronic tuberculosis of the kidney usually began as a unilateral affection secondary to some other often inactive focus only gradually gained acceptance. Pathologists who saw the

[1] A Clinical Lecture delivered before the Wayne County Medical Society, Detroit, Mich., January 17, 1921.

end-picture of this disease, with tuberculous deposits in both kidneys, in the ureters, in the bladder, perhaps also deposits in the prostate, vesicles, epididymes, not to mention more distant foci in the lungs, meninges, joints, bones, etc., were slow to accept the new teachings, based on surgical experience and a few small series of autopsies. Now it has become our daily experience that these kidney deposits are the only active disease, and if a nephrectomy is performed the patient is cured and rid of his active tuberculosis. This marvelous change in the conception of the pathology of chronic renal tuberculosis in contradistinction to acute and subacute miliary tuberculosis is based entirely on surgical experience of the last forty years, and more especially on the work of the last twenty years. With this change in the conception of the disease the import- ance of early diagnosis became all the greater, and nowadays, with the aid of the cystoscope and the laboratory, suspicious cases are carefully investigated, so that the surgeon is seeing more and more patients in the early stages of renal tuberculosis than ever before. Still even at this date many patients suffer for months before their condition is realized. In going over a series of well over 100 cases I find that nine to twelve months have elapsed from the beginning of the typical symptom-complex until the real condition was defi- nitely diagnosed.

Though chronic renal tuberculosis occurs at all ages it is most common in the third and fourth decades, that is between the twentieth and the fortieth year. It is much less common before the twentieth and after the fiftieth years, though we have seen a number of cases in young children and at least 10 cases in patients over the fiftieth year. This agrees fairly well with other large series that have been published except in the slightly greater frequency after the fiftieth year.

As far as sex is concerned males have slightly outnumbered females. In this regard American data seem to vary from those of our European colleagues. Braasch finds males $63\frac{1}{2}$ per cent to $36\frac{1}{2}$ per cent females afflicted with this disease, whereas Wildbolz[2] quot- ing the figures of European writers, says males are less frequently affected than females in the ratio 1 to 2. If the autopsy data are taken as criteria, rather than the operative data, it would seem that even in Europe the male is more frequently afflicted than the female. The diagnosis formerly was made more readily in the female, and perhaps that accounts for the contradiction between the published incidence in the two sexes. Of the cases that come to operation the right kidney is more often involved that the left, possibly because of its greater mobility. Unfortunately at least 10 per cent of cases come to us when both kidneys are involved in tuberculous disease and at a stage when no radical procedures are

[2] Chirurgie d. Nieren tuberkulose, 1913.

justifiable. In this our experience agrees fairly well with published reports (11 per cent to 14 per cent).

To grasp the symptomatology of chronic tuberculosis of the kidney it is essential to understand the main pathological features of this disease. Practically all cases are hematogenous in origin, being secondary deposits through the blood stream. Very rarely is the involvement ascending and only (in my experience) secondary to prostatic tuberculosis which has led to involvement of the bladder, dilatation of the ureters, followed by ureteral tuberculosis, tuberculosis of the pelvis and kidney or kidneys, the disease being less advanced in the upper urinary tract than lower down. In a large series of cases occasionally one sees a beautiful demonstration of the hematogenous deposit limited to one pole of a kidney, through an accessory artery to which Israel called attention years ago.

For many years there has been considerable dispute as to the primary renal focus, but gradually as surgeons are recovering specimens of earlier and earlier disease it has become more and more evident that in the majority of cases the first manifestation of the disease is in one of the papillæ of the kidney. Whether it starts near the base of the papilla or near its tip cannot be determined, though it would appear that both are favorite sites for the deposit of the tubercle bacillus. Kuester, Oraison, Rovsing, Wildbolz (Wildbolz, p. 26)[3] as well as we have very rarely seen a tuberculosis of the pelvis as primary deposit (L. Buergers[4] case. L. S.). Twenty years ago this was not accepted by investigators, because at that time more advanced cases, cases with extensive caseation, were being operated upon. As the papillary involvement progresses there is extension both into the cortex and into the calices and main pelvis. The bacilli appear to break into the vascular channels as they produce necrosis and caseation, and are carried toward the cortex producing tubercles, and discrete abscesses which both are often found directly under the capsule or separated therefrom by a thin layer of degenerated parenchyma. These shut off depots in the parenchyma of the kidney which do not communicate with the pelvis, probably rarely give symptoms until they perforate into the pelvis or into the perinephric space, which latter is a rare occurrence.

On the other hand the important extension of the papillary tuberculosis is toward the calices, the pelvis, the ureter and the bladder, and in these cases we get the typical symptoms of the disease. Ulcers and tubercles develop in the calices and the pelvis, as well as in the ureter, especially in its upper and lower ends, and finally the bladder is involved in the tuberculous process. With the inflammatory changes in the pelvis, the ureter and the bladder, thickening of the walls of these organs takes place and not infrequently stricture formation with obstruction to the outlet of the kidney secretion.

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[3] v. ante.   [4] L. Buerger.

Not infrequently one sees reparative processes in these tuberculous kidneys, as evidenced by extensive scar formation in a calyx which has shut off an abscess or a tuberculous cyst either near the base of a papilla or in the cortex of the kidney, after destruction of a papilla.

In other cases the caseation has gone so far that little or no parenchyma is left and only a pultaceous or partly calcified mass, more or less of kidney shape, persists. If the stricture formation in the ureter is marked, pyonephroses develop, occasionally though rarely only a hydronephrosis. If secondary infection is superadded we see all the changes associated with acute or chronic pyelonephritis added to the picture of renal tuberculosis; occasionally even calculi complicate the picture.

As the process in the parenchyma progresses the perinephric tissues almost regularly undergo inflammatory changes, with or without miliary abscess formation and absorption of perinephric fat. At times a massive perinephritis develops which envelops the kidney in a shell of inflammatory tissue of great density and 1 cm. or more in thickness.

It is evident from this superficial sketch of the pathology that two processes appear to be going on side by side, destruction and protective repair, similar to what is seen in tuberculous disease in other organs. Unfortunately, however, the destructive processes regularly gain the upper hand, and though kidneys are occasionally seen in which extensive calcification or hydronephroses with complete parenchymal absorption have resulted, or empty shells of kidneys which may have discharged their caseated parenchyma through rigid open ureters. these abortive attempts at Nature's cure are so rare that one cannot expect in any given case even such a measure of success from a waiting policy.

As the tuberculous process in the kidney begins usually in the papillary zone the patients generally present a rather uniform symptom-complex which possibly varies with the natural immunity of the patient, expressed in his or her reparative processes as just outlined. No matter what the termination of the disease, whether it end in hydronephrosis, pyonephrosis, stricture of the ureter, perinephritis with abscess, secondary pyelonephritis (non-tuberculous or not), I am under the impression that a careful search of the history will present almost always a rather uniform picture of shorter or longer duration, which is so clear-cut as to be almost diagnostic. When we compare the value of the patient's history of his troubles in gastric or duodenal ulcer with that of the history in the cases under discussion, I am inclined to the opinion that renal tuberculosis gives a more definitely diagnostic train of symptoms than ulcers in the above-mentioned organs.

The striking symptoms of the typical cases are:
1. Frequency (and urgency) of urination.
2. Pain on urination.

3. (*a*) Pyuria (albuminuria).

4. (*b*) Hematuria.   Pain in the lumbar region.

These symptoms usually develop insidiously, gradually increasing in severity.   Occasionally, however, their development is very sudden—out of a clear sky, as it were, (described later on.)

1. Almost all patients complain of frequency of urination shortly after the beginning of the disease, and though there are occasionally periods of remission, the old symptom recurs to annoy the patient. As these cases often excrete an increased amount of urine their frequency is due in a measure to the polyuria in greater measure, however, to the local irritation of the disease.   This annoying frequency may become so marked and the bladder control so impaired that a condition of pseudo-incontinence results.   In fact, several cases that have come to us in the young had been under treatment for long periods as cases of enuresis (both night and day).   This frequency may be so marked (every ten to fifteen minutes) as to prevent sleep, and as it is usually associated with marked urgency and pain the patients may suffer absolute torture.

2. The character of the pain on urination as well as its location seems to vary.   Many patients complain of a burning or pricking sensation either in the deep urethra or near the meatus; others again have localized the pain at the neck of the bladder.   In some the pain may be most marked as the bladder is emptied, when they become excruciating, often bringing tears to the patient's eyes. Anodynes are often required in these cases.

3 (*a*) Pyuria is an early symptom and the freshly voided urine with its finely distributed flocculi of pus cells produces an almost characteristic looking, delicate cloudiness.   Whether absolutely clear, brilliant urine, as has been repeatedly declared, can be recovered in cases with involvement of the papillæ or pelvis I doubt, though it can readily be seen that such specimen might readily be voided when the process is not in free communication with the excretory channels.   It cannot be emphasized too often that it is only when the tuberculous process extends into the excretory channels that the characteristic symptoms develop.   In fact, one often sees extensive renal tuberculosis shut off in the parenchyma which has produced only transient symptoms of bladder irritability, succeeded by apparent perfect health, only to suddenly flare up as a fresh extension into the excretory channels develops with the production of symptoms of violent vesical involvement.   In the literature a remarkable stress has been placed on the presence of a premonitory albuminuria.   Albuminuria is regularly present when there is a pyuria and its significance is far outweighed by the recognition of the pyuria.   Whether a really "premonitory albuminuria exists prior to the pyuria, that is prior to the extension of the disease into the excretory channels, I have not been able to convince myself. Still, it must be admitted that at this stage of the disease such an

albuminuria is easily understandable and all mild persistent and unexplained cases of albuminuria should be regarded with some suspicion.

3 (*b*). Hematuria varies greatly in these cases. There frequently is a slight admixture of blood in the purulent urine and well mixed with the same. Other cases pass a few drops or a small amount of fresh blood at the end of micturition as their bladders contract. Severe renal hematuria, as the first symptom in the disease, is an infrequent occurrence in our cases.

4. Pain in the kidney region, at times radiating along the ureter, has been much less frequently noted in our series than in the earlier published series. Some authors (Wildbolz, etc.) believe that pain in the kidney region antedates the symptoms of cystitis in 43 per cent of cases. In looking over the records of the more intelligent patients it is quite surprising how regularly they failed to refer any of their symptoms to the kidney region at the stage in which the bladder symptoms were their chief complaint.

It is remarkable how regularly case after case of renal tuberculosis complains of these characteristic symptoms and without any extensive questioning describe the above picture of bladder irritation, cloudy urine, perhaps hematuria, perhaps pain in the kidney region. They almost invariably report months of local treatment with no effect, though occasionally slight temporary improvement has been noted, only to relapse into a condition of greater distress than existed before the period of apparent improvement. While these are the typical cases, and while their history should suggest the correct diagnosis, which can be confirmed by the proper urinary examinations, there are numerous atypical cases, most of which undoubtedly commence in the above way and then gradually become quiescent or masked, while others, which is unusual, apparently fail to notice the usual symptoms of bladder irritation or by the time they seek medical aid have forgotten that period of their trouble.

These atypical cases are much more difficult to recognize and often baffle an expert urologist for some time. Some of these cases start as a massive hematuria, with or without ureter colics as the very first symptom, and this may rarely be so severe as to require transfusion and even nephrectomy. On the other hand the severe bleeding may cease and then the regular picture of the typical cases may develop.

In some cases the reparative and thickening processes, especially if they occur in the ureter, exclude the disease from the excretory passages, and after a brief period of vesical irritation all the symptoms cease as either a pyonephrosis or a hydronephrosis develops above the closed-off ureter. If the process becomes closed off by stricture formation at one or more calices a similar cessation of symptoms may ensue, but sooner or later as the disease recrudesces

a rupture or an extension into the pelvis takes place and suddenly all the symptoms of the typical cases are in evidence. In still another type where a mixed infection has developed the symptoms of the superadded infection, whether it be Bacillus coli or not, may so dominate the picture that one does not even suspect the diagnosis of tuberculosis until the kidney has been removed.

The same applies to some of the cases in which stone complicates the chronic tuberculosis. Another, a fourth, atypical development is that associated with perinephritis, especially the hyperplastic and suppurative types of perinephritis. Fortunately these are unusual and the diagnosis may not be made until some of the perinephric tissue is placed under the microscope. In all of these atypical cases except those with massive bleeding as the initial symptom one is more liable to feel a kidney tumor than in the typical cases.

Having the history of a typical case, or of a case that has once had symptoms suggestive of renal tuberculosis, the first step in confirming the diagnosis is the search for tubercle bacilli in the catheterized urine. From our experience there is no doubt that in the majority of cases of pyuria due to tuberculosis the tubercle bacilli can be found, if careful and repeated search of the properly stained sediment is made. In very advanced cases with thick purulent urine the tubercle bacilli may be so few and far between that they cannot be found. The literature abounds in papers dealing with the difficulties offered by the presence of the smegma bacillus, but in our experience we have had no trouble in recognizing the typical grouped tubercle bacilli and have not confounded it with the smegma bacillus, which is so rarely if ever seen in the catheterized bladder specimen. In our experience over 70 per cent of the cases showed the bacillus of Koch, and if repeated search had been made the percentage would have been much higher. With the development of cystoscopic interpretation one often makes a definite diagnosis before the search is completed, and in these cases, the kidney having been removed for tuberculosis, further study of the urinary sediment is of no great value and consequently abandoned. In those cases in which the kidney has been excluded (autonephrectomy), or in which urine is brilliant and clear, the inoculation of a guinea-pig may at times recognize the tuberculous character of the process. It must, however, be remembered that a positive guinea-pig reaction is at times missed in cases of renal tuberculosis, and at other times this test is positive when the patients have a tuberculous lesion in other organs. A careful analysis of the significance of tubercle bacilluria is always necessary [5] On the whole a positive smear is, in our experience, of greater value than a positive guinea-pig test.

[5] Beer, E.: Significance of Ureteral Tubercle Bacilluria. AM. JOUR. MED. SC., August, 1917, vol. cliv.

Another very helpful point in the diagnosis is the culture of the catheterized bladder specimen in cases of pyuria. As the output of tubercle bacilli may vary from specimen to specimen it is always advisable to culture the urine. A sterile pyuria with acid urine is common in renal tuberculosis, whereas in all other conditions, except perhaps in nephrolithiasis, it is rarely seen.

Whereas the above data when positive practically invariably mean urinary kidney tuberculosis in the female, it must not be forgotten that in the male prostatic tuberculosis may rarely produce a picture closely simulating that of typical cases of renal tuberculosis and tubercle bacilli may be present in the urine. Even an expert may find difficulty in interpreting the findings in such a case.

It will surely be conceded that patients whose symptoms suggest the presence of a renal tuberculosis should have their cases studied in this way, and so far by the general practitioner. Having made the diagnosis of tuberculosis in the urinary tract the need of a urologist of experience becomes evident. Some of these cases, in fact too many, are referred without the above studies to the general surgeon who has had no experience in urological diagnosis, a development of the last twenty-five years, and if there is local tenderness and perhaps a palpable mass in the kidney region, such a case is operated upon forthwith, either a nephrectomy or a nephrotomy being done. To operate on any kidney case without attempting to determine the presence of an adequate second kidney prior to the operation is nowadays absolutely unpardonable. All these cases should be studied carefully by the cystoscopist, who must determine, using gas-oxygen anesthesia if necessary where the disease is, and if in one kidney whether the second is healthy and adequate. It is up to the cystoscopist to rule out prostatic tuberculosis as a source of the tubercle bacilluria and it is up to him to diagnose the exact condition of the diseased kidney and to determine that the second organ is not tuberculous.

Fortunately all these things can be done with great accuracy. Experience has proved conclusively that the lesions in the bladder, the edematous ureteral meatus, its more or less rigid walls, the adjacent polypoid (or pseudopapillomatous) edema, its retraction as the ureter becomes thickened, the ulcers and the tubercles about the involved ureter produce a picture which is sufficiently characteristic to make the diagnosis. In 1907 Rovsing[6] made the statement that occasionally the bladder involvement is about the ureter meatus of the healthy kidney. Personally in hundreds of cases examined by me this has never obtained. In view, however, of this publication it is advisable to collect ureteral specimens whenever possible and confirm the presence of pyuria and tubercle bacilli on the side that is chiefly involved in the bladder disease. The use of indigo carmine is invaluable in this work, not only as an aid in

[6] Arch. f. Klin. Chirurg., 1907, lxxxii, 10.

locating the ureters in diseased, contracted bladders, but also as an index of the relative function of the two kidneys; usually the diseased kidney excretes a less concentrated stream of indigo than its healthy fellow. In the strictured ureter cases it may be impossible to collect a specimen on that side and by exclusion of the other kidney whose urine is normal plus the local findings one decides that the tuberculosis is on the strictured side. On many of these cases careful observation will detect a weak little bluish stream trickling out of such a strictured ureter.

Before this audience it is scarcely advisable to go into extensive details concerning the cystoscopic picture in these cases. There is, however, one misconception that should be corrected. It is generally thought that the urine laden with bacilli infects the mucosa of the bladder and produces ulcerations which lead to exudation. This is highly doubtful. It is more likely a lymphatic submucous involvement with production of tubercles, and these gradually break down into ulcers. I have excised such tubercles from the lips of a ureter meatus and weeks later prior to nephrectomy found the excised areas smoothly covered with healthy mucous membrane, which would hardly have happened if the urine infected the mucosal surface as usually thought.

In the typical cases the specialist will be able to clarify the clinical picture and confirm the diagnosis. Rarely he will have to resort to other aids than those already mentioned, such as the roentgen ray of the urinary tract which in advanced cases may show very definitely, irregularly thickened or calcified areas in the kidney region. Pyelography, I believe, is contraindicated and unnecessary in these cases. It is still a moot question whether diagnostic doses of old tuberculin should be used in particularly obscure cases. There is no doubt that indiscriminate use of tuberculin may harm. On my service it is used only as the last resort prior to operation and occasionally has given valuable information both by increasing the output of bacilli, which had not been found prior to the injection of tuberculin, and by producing a focal reaction in the diseased organ accompanied by fever. With the general improvement in cystoscopic and laboratory work the use of tuberculin has become less and less frequent, and in the future it will be used exceptionally.[7]

Despite the most careful preoperative study one occasionally is in doubt as to whether one is dealing with a renal tuberculosis, and as the operative indication in this disease is a nephrectomy, one must confirm the diagnosis on the operating table. Today many of these cases come to the operating table at a stage when the microscopic external appearance of the kidney is that of a normal organ. If the ureter is thickened it is highly suggestive in a case of sterile renal pyuria with negative roentgen ray, that one is dealing with a tuber-

[7] Beer, E.: Use of Tuberculin in the Diagnosis of Obscure Conditions in the Genito-urinary System, New York Med. Record, October 11, 1913.

culous kidney, the history having been typical. Still before removing such an organ it may be necessary to do a nephrotomy and prove the presence of a tuberculous lesion (and exclude a uric acid calculus). Again, in some particularly difficult cases it may be necessary to expose both kidneys and by palpation of the ureter and examination of both kidneys decide which is diseased or whether both are diseased. With experience in cystoscopic work it is becoming less and less necessary to make the diagnosis on the operating table under either one of the above conditions. In recent years careful preoperative study has invariably sufficed to clarify the diagnosis.

Treatment. As renal tuberculosis may be part of a more general tuberculosis, before advising the only treatment that is of avail, namely, nephrectomy, it is essential to make a most thorough examination of the patient. Patients with pulmonary tuberculosis should be operated upon under gas-oxygen. If the disease in the chest is advanced and active operation is inadvisable. The same anesthesia should be used in decrepit or weakened patients. Spinal anesthesia will probably meet the same indications. I have used it successfully in this type of case.

In about 10 per cent of our cases the disease of the ureter has been very extensive producing strictures, in these the aseptic nephro-ureterectomy described recently[8] was rather regularly done. It is very striking to see how all the irritative symptoms cease directly after the operation and how the urine becomes clear at once. In the other 90 per cent we do a typical nephrectomy—remove a few inches of ureter, carbolize the stump, drop it back and close the wound with a tube drain. No great advantage has been seen from filling the wound with saline and closing it completely. In a series of 100 cases in which nephrectomy was done the mortality has been 2 per cent, and but for an error in interpretation it might well have been half of that. Evidently the operative risk is not serious.

Many series of end-results have been published. Braasch's[9] monumental work is the most recent publication of a large series from the Rochester Clinic, and it deserves careful study. His data show complete cure in 60 per cent; recovery 80 per cent; i. e., deaths within five years of operation, 20 per cent. This corresponds fairly well with the experience of others. Patients who can take care of themselves have a better chance than the laboring classes. About 70 per cent of the former seem to be definitely cured and perhaps 50 to 55 per cent of the less fortunately placed. It is more than likely that with earlier recognition of this disease earlier operation will give even better end-results. If we turn to the end-results of non-operated cases as presented to the German Urological Society

[8] Beer, E., and Hyman, A.: Progress in Nephrectomy, Jour. Am. Med. Assn., October 30, 1920, vol. lxxv.

[9] Surgical Renal Tuberculosis: The Prognosis, AM. JOUR. MED. SC., January, 1920. Verhandl. d. Deutschen Gesellschaft f. Urologie, 1912.

by Wildbolz (p. 108) we find that in 316 non-operated cases only 20 per cent lived longer than five years.[10]

Such data teach very definitely that a tuberculous kidney should be removed as soon as the diagnosis is made and while the disease is still unilateral. Today in close to 10 per cent of the cases when first examined the disease involves both kidneys, pus and tubercle bacilli being definitely found in the secretion of each organ. If nephrectomy of the more diseased organ is done I have never seen any real gain to the patient, and it is my belief that the cases in which marked improvement has been reported may not have been bilateral renal tuberculosis. In a paper on the significance of ureteral tubercle bacilluria.[11] I have called attention to some of the factors which may underly a mistaken diagnosis of bilateral tuberculous disease when the disease is unilateral. Moreover, when both organs are definitely diseased it may be difficult to decide which one is causing more trouble and which one is more diseased.

Functional tests will not regularly help in making this distinction. If one organ delivers practically pure pus and little urea, and is, moreover, a useless sac producing disturbance, its removal may benefit the patient even though the second kidney be diseased and its tuberculosis be uninfluenced. Braasch reports 13 deaths within one and a half years following nephrectomy in 16 patients with bilateral disease, and in a series of 62 cases Israel found that about 70 per cent had died shortly after the nephrectomy.

After the removal of the kidney in unilateral involvement the patient unfortunately is not cured and well. There is always some tuberculosis left in the urinary tract which Nature usually takes care of, provided the patient leads a well-regulated existence. The general hygiene of these patients must be supervised and their resistance carefully built up by nutritous diet and fresh air.

Another difficulty which these patients present is the formation of a sinus (in at least 10 per cent of cases) in the lumbar wound which may take months to heal. These sinuses seem to develop in a definite number of cases even though the operation has been absolutely aseptic and no tuberculosis material has been split. These sinuses are usually spoken of as ureter sinuses, but I believe this is a misnomer, as I have seen them repeatedly even when the ureter and kidney have been removed in one piece. At times the whole lumbar wound breaks down with tuberculosis some five or six weeks after the nephrectomy, and then has to be laid wide open. My experience has suggested to me that we are dealing in these slow-healing postoperative wounds with a tuberculosis due to a tubercle bacteremia induced by the operative manipulations. Attempts to pick up the tubercle bacillus in the circulation during the operation have, however, regularly failed despite the use of guinea-pigs. Improved or modified technic will probably be more successful.

[10] Wildbolz: Ibid.   [11] Vide ante.

Another condition that may seriously trouble these patients after nephrectomy is the persistence of bladder symptoms with or without hematuria. Fortunately these symptoms gradually disappear in the majority of cases, but in others they plague the patient and they can see no benefit following the operation. All sorts of remedies have been suggested for these cases from Rovsing's carbolic acid to Marion's lactic acid bacillus milk injections. Personally I have seen the best results when using sandalwood oil and cystoscopic high-frequency cauterization of the usually extensive bladder ulcers.

Before closing this brief and rather superficial review of the most striking features of chronic renal tuberculosis, I must say a word about the complications that develop in other organs in those patients that die either after the operation or unoperated. Experience has shown that after nephrectomy those patients who are destined to die develop complications usually within a year of the operation and die as a result of these complications. Whether the dormant processes in other viscera are activated by the operative procedure or whether the operative trauma produces a bacillemia has not been proved. Both factors probably play a part. The frequency of a subacute miliary tuberculosis following the operation, in the 20 per cent that do not live longer than two years must be borne in mind. We have seen several cases of tuberculous meningitis within a few months of the nephrectomy, but as autopsies were not performed it was not known whether this was part of a miliary tuberculosis or not. Careful studies have shown that pulmonary tuberculosis, tuberculosis of the second kidney often unrecognized at the time of operation and miliary tuberculosis contribute to the death-toll during the first and second years following the nephrectomy. In those cases of renal tuberculosis which for one reason or another did not come to operation, the data at hand suggest that renal insufficiency, general amyloid disease due to chronic suppuration and pulmonary tuberculosis lead to the fatal issue. Miliary tuberculosis seems to play less of a role than in the postoperative cases. This naturally leads to the conclusion that in doing a nephrectomy one should traumatize as little as possible, so as to avoid driving bacilli into the circulation.

If during the next generation the developments in the surgery of renal tuberculosis progress as remarkably as they have during the past twenty years, patients will regularly come to the operating table in the earliest stages of their trouble and their chances of permanent relief will thereby be markedly improved. As we have seen the operative risk is low, and the mortality during the first years after the operation is still much too high. Earlier diagnosis and earlier operation followed by better postoperative care will surely lead to better end-results, and with generous coöperation we look forward to a future accomplishment of which we all shall be proud.

REVIEWS

PRINCIPLES OF BACTERIOLOGY. By A. C. ABBOTT, M.D. Professor of Hygiene and Bacteriology, and Director of the School of Hygiene and Public Health, University of Pennsylvania. Tenth edition, thoroughly revised, with 121 illustrations, 31 of which are colored. Philadelphia and New York: Lea & Febiger, 1921.

A NEW edition of this well known and useful handbook of bacteriology needs but little comment in this journal. But few changes have been made since the ninth edition. Fuller consideration of the hydrogen-ion concentration of media and the Spirochetaceæ are the two chief additions, together with several pleasing pictures of the Pathfinders of Bacteriology.

E. B. K.

DISEASES OF THE SKIN. By OLIVER S. ORMSBY, M.D., Professor and Head of the Department of Skin and Venereal Diseases, Rush Medical College (in affiliation with the University of Chicago); Dermatologist to the Presbyterian, Saint Anthony's and West Suburban Hospitals, and the Home for Destitute Crippled Children; Consulting Dermatologist to the Orphan Asylum of the City of Chicago; Member of the American Dermatological Association and of the Congress of American Physicians and Surgeons; Corresponding Member of the Section of Dermatology of the Royal Society of Medicine, London. Second edition. Pp. 1166; 445 engravings and 4 plates in color and monochrome. Philadelphia and New York: Lea & Febiger, 1921.

DR. ORMSBY has made a thorough and complete revision of his book, *Diseases of the Skin*. Although four hundred pages have been rewritten and fifteen new diseases described, the size of the volume remains the same. This has been accomplished by the elimination of everything superfluous and by concise description. The excellence has been maintained throughout.

The classification has been amplified notwithstanding the number of chapters remains the same. MacKee's dosage and a chart descriptive of his method have been added. Many important references have been included enhancing the value of the work to those desiring research.

Numerous engravings and monochromes have been removed to make room for those more practical and artistic. The present volume contains one hundred and forty-two more engravings than the former.

The advances in syphilis are fully recorded. Among the new diseases described are the following: Keratolysis exfoliativa; folliculitis ulerythematosa reticulata; vaselinomata; chondrodermatitis nodularis chronica helicis; precancerous dermatoses; nocardiosis cutis; Vincent's disease; periadenitis mucosa necrotica recurrens; atrophy of the mucous membrane of the tongue and mouth.

Dr. Ormsby is to be congratulated on the excellence of his work.

F. C. K.

TUBERCULOSIS AND HOW TO COMBAT IT. By FRANCIS M. POTTENGER, A.M., M.D., LL.D., F.A.C.P. Pp. 273. St. Louis: C. V. Mosby Co., 1921.

THIS book is written for the patient, not for the physician. There are few books of worth published for the guidance of the patient save on two subjects—diabetes and tuberculosis. In these essentially chronic conditions the possibility of success in treatment depends upon the patient himself.

Dr. Pottenger's little volume consists of a summary of his talks with his patients. The chapters are brief, each taking up a single proposition or very limited phase of the subject which is discussed without rambling or deviation. The book can thus be read chapter by chapter. The statements are clear and the style concise throughout. The tone is optimistic. The subject of treatment from the standpoint of the patient is thoroughly covered. Whether or not we agree with all of Dr. Potrnger's views as stated in these pages is beside the point. The book is well calculated to stimulate the efforts and encourage the perseverance of the intelligent patient.

R. G. T.

A PHYSICAL INTERPRETATION OF SHOCK, EXHAUSTION, AND RESTORATION. AN EXTENSION OF THE KINETIC THEORY. By GEORGE W. CRILE, M.D., Senior Consultant in Surgical Research, A. E. F., 1917–1918; Professor of Surgery, School of Medicine, Western Reserve University. Edited by Amy F. Rowland, B.S. Pp. 221; 120 illustrations. London: Henry Frowde, Hodder and Stoughton, 1921.

THIS volume presents a summarization of the many researches made by the author and his assistants in their laboratories and clinic at Cleveland, and of the author's observations and research in this subject during the war.

The introduction, in two parts, bears upon the methods of production of shock and exhaustion in the soldier, and upon the coexistence of clinical phenomena and histologic changes in various organs in exhaustion.

The mechanism of shock, exhaustion and restoration as elaborated by the author is dwelt upon in the summaries of the earlier monographs on these subjects, and in addition there are restated the principles upon which shockless operations may be performed.

Further, the author reviews the physical laws upon which he bases his theories, and develops his further researches upon the physico-chemical and electro-chemical considerations and interpretations of the mechanism of shock.

Certain clinical phenomena, as fever, exophthalmic goiter, inhalation anesthesia, tetanus and strychnine poisoning are interpreted theoretically in the light of the author's beliefs.

The practical application of the kinetic theory in treatment is extremely interesting, as to the observations, deductions and suggestions offered which may be put into clinical practice to the benefit of the patient.

The book is an excellent recapitulation of the well-known ideas of the author, and the addition of his observations on the battlefield adds an extra interest to the always intriguing subject of shock.

<div style="text-align: right">P. F. W.</div>

FUNDAMENTALS OF BACTERIOLOGY. By CHARLES BRADFIELD MORREY, Professor of Bacteriology, Ohio State University. Second edition. 171 engravings, 6 plates. Philadelphia and New York: Lea & Febiger, 1921.

In this edition the author supplements the first with the more recent developments in Bacteriology. He includes for discussion the system of classification as adopted by the American Society of Bacteriology, and their key to the genera of bacteria; the hydrogen-ion concentration method of standardization of media; selective action of aniline dyes; the mechanism of invasion of microörganisms into the body; the origin of antibodies; and the nature of antigens, with a table of antigens and antibodies.

The book is well written and clarifies some abstruse points which are ever stumbling blocks for the embryonic bacteriologist. The author's discussion of immunity and hydrogen-ion concentration particularly demonstrate this feature. In a clear and concise manner he has taken up the points just enumerated, and has brought his book as much abreast of the times as a text-book in a growing science can be. Many statements are followed by examples, which may add to their practicability and interest for the student. The discussions are brief, serving only as introduction to the study of

bacteriology. The book is a good primer, but should be followed with more detailed books for the advanced student.

A description of the individual bacteria is not included, constituting a new departure from the usual style of bacteriological text-books; so that in teaching the medical student, at least, it would not quite fill routine requirements. There is no detail in the book, which may favor the instructor by allowing him to expand on any topics which appear of more importance to him. In short, if brevity is the soul of wit, then the author has succeeded in putting before the bacteriologist, a clear, up-to-date text-book in the fundamentals of bacteriology.

L. J.

SURGICAL CLINICS OF NORTH AMERICA. Vol. I, Nos. ii and iii, New York and Boston numbers. Illustrated. Philadelphia and London: W. B. Saunders Company, 1921.

THESE clinic reports are now an established publication and the Nos. i, ii and iii are respectively the work of Philadelphia, New York and Boston writers. Up to the present, at least, these new clinics are adhering to the real type of clinical reports, *i. e.*, with the elimination of all unnecessary routine data in a case report, which data has no bearing at all on the subject. In these numbers there seems but one real dereliction of this type.

The authors are all representative men in their subjects and their presentations are all worth careful scrutiny and study. There are thirty-four contributors in all to the two volumes, giving the reader excellent reading in a small, compact form that can be kept as a reference book.

E. L. E.

ESSAYS ON SURGICAL SUBJECTS. By SIR BERKLEY MOYNIHAN, Leeds, England. Pp 253; illustrated. Philadelphia and London: W. B. Saunders Company, 1921.

THIS book consists of a number of essays or articles that have been written and published at various times during the last few years. They have been altered somewhat and the statistics brought to date. This collection of articles is justified in the eyes of the author in that thereby is presented a consecutive train of thought.

The works of the author need no recommendation. His style and diction are always the best, and one reads his sentences with at once an appreciation of the valuable facts presented as well as the charming style of their expression. It makes most pleasant and instructive reading.

E. L. E.

MANUAL OF OPERATIVE SURGERY. By JOHN FAIRBAIRN BINNIE, M. D., Surgeon to the Christian Church, the Research and the General Hospitals, Kansas City. Eighth edition. Pp. 1311; 1628 illustrations. Philadelphia: P. Blakiston's Son & Company.

THE greatest changes in this new edition will be found in the chapters on Thoracic, Abdominal and Plastic Surgery, all of which have been practically rewritten. The chapter on Orthopedics has been thoroughly revised and most of the article on War Surgery has been omitted. This volume contains more material in a smaller number of pages than does the preceding edition.

The constant endeavor is to give aid and guidance to the surgeon when he is in trouble, putting emphasis on the unusual rather than on the common, as would a text-book. Hence the great space allotted to cardiac surgery, head surgery, retroperitoneal tumors, etc. The book is thoroughly up to date and complete in every respect. E. L. E.

LABORATORY MANUAL OF THE TECHNIC OF BASAL METABOLIC RATE DETERMINATIONS. By WALTER M. BOOTHBY, A.M., M.D., and IRENE SANDIFORD, PH.D., of the Mayo Clinic, Rochester, Minn. Pp. 117; 13 illustrations. Philadelphia: W. B. Saunders Company, 1920.

THE gasometer method of determining basal metabolic rate is herein presented very clearly and concisely. The book is more valuable to the laboratory worker in this line than to the clinician, who customarily uses the less complicated and sufficiently accurate methods based upon oxygen consumption. W. H. S.

TREATISE ON FRACTURES. By JOHN B. ROBERTS, M. D., Emeritus, Professor of Surgery in University of Pennsylvania Graduate School of Medicine, etc., and JAMES A. KELLY, M.D., Associate Professor of Surgery in University of Pennsylvania, Graduate School of Medicine, Surgeon to St. Joseph's, St. Mary's, St. Timothy's and the Misericordia Hospitals. Second edition. Pp. 755; 1081 illustrations. Philadelphia: J. B. Lippincott Company.

THE text of this second edition has been thoroughly revised to meet the needs that we know today govern the results in fractures. As an outcome of the war we have gained enormously in our knowledge of how to handle broken bones. The authors have fully appreciated these advances and show us in this work the latest ideas and the most modern treatment of fractures. A book of this type

is now absolutely essential for any man treating fractures. Workmen's compensation laws and the payment for all hospital accident cases have deepened the responsibility of the one caring for a fracture.

The numerous and excellent illustrations do more to present the subject properly than does the text unaided. The writers drive home the point that there is no fixed and dogmatic rule for fracture treatment unless it be that the surgeon have great adaptability, patience and constant supervision, for responsibility does not cease with the mere reduction of the fragments, for then come the most important features, namely, how to maintain the reduction and return the patient to activity with good function.   E. L. E.

Surgery of the Upper Abdomen. By John B. Deaver, M.D., Professor of Surgery in the University of Pennsylvania; Surgeon-in-Chief to the Lankenau Hospital, and A. P. C. Ashhurst, M.D., Associate in Surgery in the University of Pennsylvania, Surgeon to the Episcopal Hospital. Second edition. Pp. 832; 207 illustrations. Philadelphia: P. Blakiston's Son & Company.

The first edition of the work was published in two volumes and this, the second edition, has followed the same general plan. Many sections have been entirely rewritten, e. g., Gastric Ulcer, Infantile Stenosis of the Pylorus, Causes of Death after Operation on the Stomach and Duodenum, Jejunal Ulcer, etc. New material has been added on Operative Technic, Transgastric Excision of Ulcers, Resection of the Descending Duodenum, Surgery of the Spleen, etc.

A great deal that was obsolete was omitted, as well as extensive bibliographical references and statistical tables have been condensed. Nearly 100 new drawings have been introduced and now in this book of slightly over 800 pages more material is presented than was formerly included in two volumes running almost to 1000 pages.

The work is an excellent one, as would be expected it from these two authors.   E. L. E.

The Diagnosis and Treatment of Intussusception. By Charles P. B. Clubbe, L.R.C.P., M.R.C.S., Consulting Surgeon to the Royal Prince Alfred Hospital, Consulting Surgeon to the Coast Hospital, Sydney. Second edition. Pp. 88. London: Henry Frowde, 1921.

This small clinical review on intussusception, it can hardly be called a monograph, as it is not sufficiently complete, contains the

author's experience with this rather rare condition. It contains first a general description of the condition, followed by a discussion of the anatomy and etiology, succeeded by a description of the various varieties that are likely to occur. The diagnosis is also considered, but the greater part of the text deals with the treatment of the condition. The author, to a certain extent, uses intestinal irrigation and by quoting a few case reports he notes specifically the cure occasionally brought about by irrigation. He has operated upon 253 cases and his operative results seem to be very satisfactory.

<div align="right">J. H. M., Jr.</div>

Aids to Chemistry. By William Partridge, F.I.C., Public Analyist of the County of Dorsit. Lecture in Chemistry, King's College, University of London. Pp. 280. New York: William Wood & Company.

This useful hand-book presents in concise form, many useful facts in inorganic and organic chemistry. There is, however, no practical consideration of the medical aspects of chemistry presented.   E. B. K.

Chemical Pathology. Being a Discussion of General Pathology from the Standpoint of the Chemical Processes Involved. By H. Gideon Wells, Ph.D., M.D., Professor of Pathology in the University of Chicago, and in the Rush Medical College, Chicago. Fourth edition, revised and reset. Pp. 695 Philadelphia and London: W. B. Saunders Company, 1920.

The need of a fourth edition of this book within two years of the third, points to the rapid growth both of scientific knowledge in this domain and of the recognition of its value to clinician and investigator. A new chapter on the "Chemistry of Growth and Repair" has been necessitated by the growing importance of deficiency diseases and a separate chapter on "Anaphylaxis and Allergy" provided. The many excellent features of previous editions, here generously reinforced with new material, require no further commendation in this Journal.   E. B. K.

PROGRESS

OF

MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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Influenza as a Factor in the Activation of Latent Tuberculosis.— The incidence of active tuberculosis of the lungs following influenza and influenza pneumonias has been the subject of a number of papers since the epidermics of 1918–1919, many of these concluding with the observation that influenza had no appreciable effects on pulmonary tuberculosis, or even stating that the tuberculous were less susceptible to acute epidemic influenza than normal individuals. BOISLINIERE (*American Review of Tuberc.*, 1920, iv, 534) as early as December, 1918, encountered active tuberculosis in a number of individuals who had been seized with influenza only a few weeks previously, and who, up to the onset of influenza, had never varied from their usual standard of health. These cases recalled observations made during the pandemics of 1889 and 1890 to the effect that lungs that did not clear up within eight to ten weeks after an attack of "la grippe" were in many cases actively tuberculous. A census of a group of institutions devoted to the case of the tuberculous brought out the facts that from 15 to 20 per cent of the new cases of pulmonary tuberculosis presenting themselves since the onset of the influenza epidemic in 1918 gave no history suggestive of a previous lung lesion, and that they had been caused by the influenza. Further, the census indicated that the incidence of pulmonary tuberculosis has increased to the same extent during that period, and from the same cause. As the pathological basis for increased incidence of tuberculosis of the lungs following influenza, the author cites the acute hyperemia, interstitial edema and serous exudate which

according to him accompany even uncomplicated cases as tending to break down the protective barriers of a dormant tuberculous lesion. He points out that this tendency is much more marked in the instance of influenza and influenzal pneumonias than it is in ordinary lobar and bronchopneumonias. A second factor is that of lowered resistance, based on the negative von Pirquet reaction found during and for some weeks after influenza, a condition likewise obtaining in measles. The author does not mention the possibility of increased susceptibility to primary infection as a factor in postinfluenzal tuberculosis.

Agglutination in Influenza.—Utheim (*Jour. Infect. Dis.*, 1920, xxvii, 460) studied the sera of patients with influenza as to whether the serum of the patient would agglutinate the influenza bacillus obtained from the same patient and whether agglutination would take place with heterologous strains. The antigen consisted of cultures isolated from the nose or throat and suspended in salt solution. After thorough shaking, a homogeneous emulsion was usually obtained, spontaneous clumping occurring in only one instance. Thirty strains were isolated from as many patients and tested with the serum from these patients during different stages of the disease. It was found that 11 gave a positive agglutination with their own bacilli, 6 in a dilution of 1 in 160, 4 in 1 in 60, and 1 in 1 in 20. With the exception of one strain, which gave an agglutination of 1 in 40 with 3 sera of other patients, no cross agglutination was encountered in any serum tested. The blood of 9 patients was examined during different stages of the disease; 8 showed a constantly negative result, while in 1 instance the agglutination became positive in a dilution of 1 in 80 in the convalescent stage. Three strains were isolated from the throat of 1 patient, only 1 of which gave agglutination with the patient's serum. Seven of the 11 which gave agglutination with the homologous strain occurred in uncomplicated influenza and 4 in influenza pneumonia. Of the remaining 19 negative cases, 10 had pneumonia.

THERAPEUTICS

UNDER THE CHARGE OF

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The Use of a High Fat Diet in the Treatment of Diabetes Mellitus. Second Paper: Blood Sugar.—Newburgh and Marsh (*Arch. Int. Med.*, 1921, xxvii, 699) supplement a previous communication (*Arch. Int. Med.*, 1920, xxvi, 625) in which they reported briefly the

results of an investigation of the effects of a diet whose energy came largely from fat, to which was added sufficient protein to maintain nitrogen balance, and the minimal carbohydrate necessitated in making up a diet that a human being can eat over a long period of time. It was shown that with such a diet glycosuria was avoided in severe diabetics and that acidosis was not produced. The present paper presents the blood-sugar determinations in 45 cases treated by this method. All but 5 more or less promptly responded with a reduction of the blood sugar to within normal limits. Of the 5 which did not reach a desirably low percentage 2 were suffering from severe complicating diseases and 1 was suspected of not adhering to his diet.

Dermatitis and Allied Reactions Following the Arsenical Treatment of Syphilis.—A detailed review is given by MOORE and KEIDEL (*Arch. Int. Med.*, 1921, xxvii, 716) of 23 cases of dermatitis and allied reactions following arsenical treatment which have occurred during the last six years in the syphilis department and in the wards of the Johns Hopkins Hospital and in the private practice of the authors. Five of the 23 cases terminated fatally. From the evidence presented it appears that the lesions of syphilis and the duration of the disease exercise no modifying influence upon the dermatitis. Dosage, technic of administration, impurities in the drug and the type of chemotherapeutic arsenic compound can be excluded as etiological factors. Reactions of this group tend to appear early in the course of treatment. The lesions may be classified, on the basis of the constitutional manifestations and their importance, as mild or severe. In the mild group fall urticaria and erythematous and herpetic rashes. In the severe group are macular, maculo-papular and exfoliative rashes, itching and stomatitis. In some cases certain prodromal symptoms may be recognized; itching, mild or fleeting skin eruptions, prolonged fever or marked malaise. The occurrence of any of these during the use of arsenical products should lead to a suspension of treatment and a general survey of the patient. Urticaria is fairly common in association with the nitritoid crisis, is not accompanied by the more severe constitutional manifestations and does not contraindicate continuance of arsenical treatment. The authors call attention to characteristic alterations in the blood picture, which were present in 14 of the 16 cases studied. The changes consist, in general, of leukopenia, decrease in polymorphonuclear neutrophiles, eosinophilia, increase of the large mononuclear-transitional group and the appearance of many fragile cells. The complications of dermatitis exfoliativa, including acute nephritis, polyneuritis, jaundice, skin infection, bronchopneumonia and septicemia, are discussed. In considering the possible etiological factors in reactions of this group the authors cite Auer's recent work and agree that arsphenamine may lower the local threshold for an unknown antigen which in its turn causes an anaphylactic reaction, and thus may cause the deposit of arsenic in the structures where its toxic action is observed, notably in the bone-marrow and in the skin.

Fatal Chronic Nephritis in a Fourteen-year-old Girl with only One Kidney and a History of Scarlet Fever.—PEPPER and LUCKE (*Arch. Int. Med.*, 1921, xxvi, 661) report a careful clinicopathological study

of a fatal case of renal disease in a fourteen-year-old girl. She had pneumonia at the age of two, typhoid fever at the age of three, and mumps at the age of four. At the age of seven she suffered from an attack of scarlet fever, after which she was never strong. There was no history of kidney involvement or edema. She had occasional attacks of belching and vomiting, which were more severe during the past two months. Two months before admission she had an attack of marked blurring of vision and loss of power and sensation in her left arm and both legs, and some difficulty with speech and swallowing. These symptoms disappeared within two weeks. Two weeks before admission she had an attack diagnosed as "grippe." Her menses began at the age of twelve and were exceedingly free, later being associated with bleeding from the nose. The last period commenced nine days before admission and continued with excessive nose-bleed and bleeding from the gums until admission. The positive features of the physical examination included a urinous odor to the breath, evidence of recent bleeding from the nose, the lips and the gums. Blood-pressure 148,132. Urine, 1008; alb. ft. tr.; many red blood cells and white blood cells. Red blood count, 2,270,000. White blood count, 5200. Hemoglobin, 50 per cent. Platelets, 220,800. Blood-urea nitrogen, 210 mg. per 100 cc. Blood plasma, CO_2, 29 vols. per cent. Phenolsulphonephthalein test, -0 in two hours. During the next three days the blood plasma, CO_2, increased to 50 vols. per cent, but the blood-urea nitrogen rose to 228 mg. per 100 cc, and after a steady downward course she died four days after admission. Necropsy revealed early general arteriosclerosis; slight congestion and edema of the lungs; slight fibrosis of the spleen; submucus hemorrhages of the intestines; cloudy swelling of the liver; slight cardiac hypertrophy; aplasia of the left kidney and its ureter. The authors then give a detailed description of the gross and histopathological condition of the small right kidney: a combination of true chronic interstitial nephritis and chronic glomerulonephritis, showing also a remarkable degree of frustrated regeneration. They point out the striking similarity of their photographs to that used by Aschoff to illustrate "genuine" contracted kidney (true chronic interstitial nephritis). In the discussion the authors review the two types of nephritis which occur as complications of scarlatina, acute interstitial and acute glomerulonephritis, and point out the rarity of an opportunity to study the terminal stage of nephritis following scarlatina. They speak of the rarity of true chronic interstitial or glomerular nephritis before the age of twenty. The literature on true agenesis of the kidney is reviewed. The authors reach the tentative conclusion that this unusual picture was the result of the injurious action of scarlatina initiating a nephritis, which because of the inadequate and possibly anomalous kidney present, rapidly resulted in a condition analogous to chronic nephritis of adults.

Comparative Systolic Blood-pressure Readings in the Arm and Leg in Aortic Incompetence.—A careful study of 24 cases of aortic incompetence led Williamson (*British Med. Jour.*, May 21, 1921, p. 734) to doubt the generally accepted statement that a diagnostic sign of aortic insufficiency is the higher systolic arterial pressure in the leg compared to that in the arm when the patient is at rest and in the recumbent

position. The author found that though higher systolic readings in the leg than in the arm appear in the majority of cases of aortic incompetence, there is a large minority (25 per cent) in which they do not obtain. The difference in the readings is due, according to the author, not to aortic insufficiency but to commonly associated conditions of hypertonic contraction or hypertrophy of the muscular walls of the arteries with or without sclerotic changes. In any event the large majority of cases in which the arteries were thickened showed the difference, while in children in whom the arteries were not hypertrophied the phenomenon was relatively rare. The difference in pressures, therefore, is vascular, not cardiac in origin.

The Control of Hemorrhage by the Intramuscular Injection of Calcium Chloride.—GROVE and VINES (*British Med. Jour.*, July 9, 1921, p. 40) recommend the intramuscular injection of calcium chloride for the treatment and prophylaxis of hemorrhage. The dose employed was 100 minims of a 1 per cent solution, and the injection was deep into the gluteal muscles. A subcutaneous injection is painful and is regularly followed by sloughing. It is not possible to state definitely the action of calcium salts in controlling bleeding. It is probable there is a direct constrictor effect on the bloodvessels, and, furthermore, the increased calcium content of the blood may promote combination between calcium and blood lipoids with a consequent acceleration of clotting. The dose may be repeated at the end of twenty-four hours and again a day later.

Further Report on the Treatment of Sleeping Sickness.—The treatment employed by MARSHALL and VASSALLO (*British Med. Jour.*, May 28, 1921) is a combination of intravenous and intrathecal injections of organic arsenical preparations (neo-kharsican). The theory on which this therapy is based is that the trypanosomes having once reached the cerebrospinal canal were, after a certain time, immune to any medication via the blood stream. It is generally agreed that the intravenous injection of an organic arsenical sterilizes the blood stream in a short time. But a relapse soon occurs, probably because the focus of infections in the central nervous system is not acted upon by the drug in the blood. Hence a permanent cure can be effected only by sterilizing both the blood and lymphatic stream and the cerebrospinal cavity. While it may be early to state positively that the present treatment promotes definite cure, the authors feel optimistic in the face of the results obtained. Several of their cases have gone well beyond a year with one dose of treatment, and they have all invariably improved in health and no trypanosomes have been found in the blood or the spinal fluid, although they have been subjected to repeated and careful investigations.

Renal Irritation in Man from High Protein Diet.—SQUIER and NEWBURGH (*Arch. Int. Med.*, 1921, xxviii, 1) present the clinical histories and laboratory findings of 4 cases of hypertension in which urinary evidence of renal disturbance was slight or absent, before and after short periods of forced high protein-feeding. In each case the appearance of red blood corpuscles in the urine resulted, in 3 cases

albumin was found, having been previously absent; in 1 case the amount of albumin in the urine was markedly increased and in 3 cases a definite increase in eye-ground changes was noted following the meat diet. Neither restricted nor forced protein-feeding had any influence on the blood-pressure in any of these cases. A case of recently active nephritis showed similar results after high protein diet, except that the red blood corpuscles which made their appearance in the urine failed to disappear promptly, as in the first 4 cases, on return to normal diet, but persisted for at least five months. Two cases undergoing this test were found to have kidney impairment which had not previously been suspected. Forced meat-feeding for two successive meals was invariably sufficient to cause the appearance of red blood corpuscles in the urine of 5 normal young men. The authors reach the conclusion that high protein diet in man is a renal irritant.

An Atypical Bacillus Paratyphosus B Infection.—MORGAN (*Bull. Johns Hopkins Hosp.*, 1921, xxxii, 195) reports a case of cysto-pyelitis following urethral stricture and urethrotomy, and a detailed account of the cultural and biological characteristics of the causative organism is given. The author reviews the literature and points out that, especially during the World War, there have been many reports of similar organisms which fall, in the classification of Bainbridge between B. paratyphosus B and B. enteritides (Gärtner). These organisms have been variously called "B. paratyphosus C," "Inagglutinable B. paratyphosus B," "Paracolon bac.," etc.; but the author agrees with Schultze that they should be considered as a variant of the B. paratyphosus B originally described by Schottmüller (who also first described the clinical picture of pyelitis caused by this organism), when, as in the case described, the organism shows only slight or moderate serological differences from the accepted B. paratyphosus B.

PEDIATRICS

UNDER THE CHARGE OF

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The Food Requirements of Children. I. Total Caloric Requirements.—HOLT and FALES (*Am. Jour. Dis. Children*, January, 1921) say that in calculating the total caloric requirements of children, there must be considered separately the component parts of which the total is made up. These are the requirements for basal metabolism, for growth, for muscular activity, and the food values lost in the excreta. The basal requirements which have been determined by Benedict and Talbot are highest per kilo at about the ninth month, and steadily fall from this time up to adult life. The food value lost in the excreta normally is a nearly uniform proportion of the intake, about 10 per

cent for all ages after infancy. The requirements for growth are greatest during the period when the growth is most active during the first year of life and during adolescence. They are nearly uniform from the fourth to the tenth or eleventh years. The average for three factors—basal, growth requirements and food values lost in excreta—are nearly uniform for children of the same weight living under the same or similar conditions. The requirement for activity is the only factor which varies widely with different individuals. The great difference in the calculations of different writers, who have estimated theoretical values for total calories per kilo for children, are in part due to the fact that they have not sufficiently considered the different component parts which make up the total. The average caloric requirement of children according to the observations reported in this paper is about 100 calories per kilo at an age of one year or about 9.5 kilos. For boys it falls to about 80 calories at six years or about 20 kilos, and remains practically constant at this value up to the age of fifteen years, the increasing requirements for activity being met by the reduction in the basal requirements per kilo. After an age of about fifteen years or about 50 kilos is reached, the calories per kilo can rapidly be reduced to adult standards of about 48 calories per kilo. The requirements for girls falls to 76 calories per kilo at six years or about 20 kilos, continues at this value until the tenth year, when it rises because the basal requirement is nearly constant while there is an increase in needs for growth and activity. The requirement remains at 80 calories per kilo until growth is complete, and it then falls rapidly to adult standards of about 44 calories per kilo. In these calculations a much higher value for calories per kilo during adolescence has been allowed than that given by others. This seems to be absolutely essential, because of the increased growth needs at this time and the large requirement for muscular activity. According to their allowance the total daily caloric requirement of children of both sexes during adolescence exceeds by nearly 1000 calories the requirements of the adult man or woman of moderate activity. Children who are under weight require more calories per kilo than those who are of average weight for their age. Children who are overweight require fewer calories per kilo than those of average weight.

Calcium in the Blood of Children.—DENIS and TALBOT (*Am. Jour. Dis. Children*, January, 1921) have modified Lyman's method. They employ citrated plasma (0.1 gm. of solid sodium citrate to 100 cc of blood), and they use a variety of standards for the final nephelometric reading. These standards are made up to contain 0.2, 0.15 and 0.1 mg. respectively of calcium. In 119 samples of blood from patients in the children's ward, irrespective of diagnosis, the maximum figure was 13.5 and the minimum 1 mg. per 100 cc of blood plasma. In 22 normal adults the maximum was 12.1 and the minimum was 7.2 mg. and the average was 10 mg. of calcium per 100 cc of plasma. In 28 cases of rickets, 7 in the acute and 21 in the convalescent stage, some gave calcium values distinctly below the normal, but as some of these were suffering other illnesses such as pneumonia, no definite conclusions could be drawn. In tetany the calcium content of the serum was extremely low. The administration of calcium chloride, 25 grains three times a day, in 2 cases gave a marked increase in the blood cal-

cium in 1 case. Associated with this increase was the disappearance of the symptoms and apparent cure. In cases of convulsions not due to tetany the blood calcium was very low. This was especially true in epilepsy. In 25 cases of lobar pneumonia, bronchopneumonia and acute bronchitis the blood calcium was very low. After the crisis it rose somewhat. There was no calcium excretion during the febrile stage, but there was after the crisis.

The Ulcerated Meatus in the Circumcised Child.—BRENNEMANN (*Am. Jour. Dis. Children*, January, 1921) notes that the ammoniacal diaper occurs less frequently and less severely with cream mixtures than with simple whole milk mixtures or even with dried milk mixtures. This would rule out fat alone as a cause of this condition. The writer thinks that in a milk mixture it occurs less frequently if the fat is relatively higher than the protein and the salts as compared with their normal relative representation in whole milk. It occurs more frequently if the normal proportion is maintained or if the fat is relatively lower than the protein and salts. The condition has been observed in which partly fat free milk was used. The protein and salts must also be considered as possible causative factors. The failure of the ammonia to occur except in connection with the wet diaper in place, together with the peculiar behavior of the ammoniacal diaper would suggest a further non-dietetic factor existing in the diaper itself. The ammonium salts are fairly stable. Alkalies in the diapers have been set forth as the factor responsible for the breaking-up of the ammonium salts. The source of this may be strong alkali soap used in washing and not thoroughly rinsed from the diapers or bedding. Alkaline stools may also set about the same breaking-up of ammonium salts. Bacteria have also been suggested as causative factors. While the whole proposition of etiology is not clear, still it is justifiable to believe that there are at least two factors present: First, there is the excessive excretion of ammonium salts due to lack of balance of the diet, and second either alkaline stool or unrinsed soap in the diaper itself or bacteria, which break up the ammonium salts and liberate free ammonium.

Chronic Tuberculous Hilus Pneumonia in Children.—GREENBERG (*Am. Jour. Dis. Children*, January, 1921) reports 2 cases. He says that extensive tuberculous lesions about the hilus may occur in infants and young children and pursue a rather chronic course. Recovery probably takes place in the majority of the cases even in children under two years of age. The onset in this type of pulmonary tuberculosis is more or less gradual, and there may be no lung signs until after the disease has lasted for some time. Irregular fever, sweating, expiratory obstruction, diminished breathing, with impaired resonance, a positive von Pirquet and a characteristic roentgen-ray picture are among the earlier manifestations. Enlargement of the supraclavicular lymph nodes, positive results from the guinea-pig inoculations of material from lung puncture or of sputum, and the presence of tubercle bacilli in the sputum may be found later in the course of the disease. This form of tuberculosis should be suspected in infants or children with prolonged irregular fever and sweating, with a positive von Pirquet.

Blood Volume in Infants Estimated by the Vital Dye Method.— LUCAS and DEARING (*Am. Jour. Dis. Children*, January, 1921) found great variation in blood volume per cent. in newborn infants, ranging from 10.7 to 19.5 per cent of body weight and from 107 to 195 cc per kilogram, and the pigment volume from 304 to 899 cc. The average for these were blood volume per cent, 14.7; blood volume per kilogram, 147 cc; and pigment volume, 521 cc. Another one of the interesting variations was that found between plasma volume and red cell volume. The plasma volume per cent was small as compared with the relatively high red cell percentage. These findings were fairly constant in the newborn during the first ten days. No reason could be given for the wide variation beyond the fact that the blood during the first few days undergoes a definite adjustment to the new surroundings. From studies on blood protein and blood sugars it is known that a similar wide variation occurs during the first few days before the normal averages are established, and the blood volume undoubtedly goes through this same period of adjustment, when the blood-forming organs are first called upon to function independently of any assistance from the maternal circulation. There does not seem to be any constant relation between blood volume and weight, length or age in hours or days up to the fifteenth day. In the infants from fifteen days to one year of age there was a definite uniformity constant for the individuals, and the variations between individuals were much less marked than in the first fifteen days, the extremes being from 9 to 12.6 per cent, and the average 10.9 per cent. There was a fairly definite attempt to stabilize the blood volume during the first few months; and for any given infant over a period of several months, the blood volume remained at a fairly constant level.

A Study of the Spinal Fluid in Fifty-two Cases of Congenital Syphilis. —KINGERY (*Jour. Am. Med. Assn.*, January 1, 1921), in a study of 52 cases, found an unquestionable diagnosis established by the presence of the accepted symptoms and stigmas of prenatal infection, the presence of definitely positive reports or both. The findings reported were those found in the routine puncture without any reference to any indications or group of presenting symptoms. In every case the patient had remained long enough under observation to substantiate any doubtful findings, and to observe any developing symptoms, or the occurrence of former ones not demonstrable at the time of the first examination. The ages varied from three weeks to twenty-one years of age. Of the total of 52 cases, 15, or 28.8 per cent, presented some deviation from the normal, according to the accepted standards of spinal fluid findings. The cases divided themselves into two groups according to the extent or severity of the infection. The first group I, which only slight changes had taken place up to the time of the puncture, consisted of 4 cases. In 3 of these the Wassermann reaction on the cerebrospinal fluid was 1+; in 2, 2+. In addition the cell count revealed a slight pleocytosis. The highest cell count in this group was 15 and was associated with an increase in solids to like degree. The early central nervous system impairment was clinically substantiated by the presence of chorioretinitis, increased reflexes and in 1 case by severe nerve deafness. The second group comprised the

more severe grades of involvement. There were 11 cases each of which gave a definitely positive Wassermann reaction. There was a striking parallelism between strongly positive Wassermann reactions and definite albumin and globulin increase. There was a striking lack of parallelism between the degree of pleocytosis and the other strongly positive findings. The cell count in these cases varied between 6 and 159. In addition to the interesting changes in the cerebrospinal fluid this group presented clinical symptoms of considerable gravity. Four cases presented the clinical picture of juvenile general paresis. The other 7 of this group presented other involvements of the nervous system. Two of these were distinctly retarded mentally. Four suffered from pupillary and deep tendon reflex changes. The other patient of this group had a severe cutaneous involvement without other demonstrable changes.

OBSTETRICS

UNDER THE CHARGE OF

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The Effect of Pregnancy upon the Circulation.—At a meeting of the Obstetrical Society of Vienna, in a discussion upon this subject, WENCKEBACH (*Zentralbl. f. Gynäk.*, 1920, Nr. 38) believes that the most important question in a case of pregnancy complicated by disease of the heart or vessels is whether pregnancy should be interrupted or allowed to go to term. One could base such a decision not only on the condition of the heart, but on the question as to whether it is performing its functions. The consideration of such a case includes many factors. One is the question whether the patient has a living child. If she has not, an additional effort should be made to save the life of the infant. The general health, the condition of nutrition, the hygiene of the patient, all the circumstances of her life must be considered. In studying such a case, one must not fail to include the peripheral vascular system, for the condition of this may prove of the greatest importance. Opinions differ greatly as to the prognosis for a pregnant patient having a lesion of the heart. Some are optimistic and others believe it to be of the gravest import. Each case must be judged upon its merits and reliable grounds for judgment cannot be obtained until a concerted study of the subject is made by pathologists, internists and obstetricians. In continuing the discussion, Thaler would interrupt pregnancy in such a patient only when the compensation was failing. A diseased heart with good compensation and with the patient under favorable circumstances furnishes no indication for the interruption of pregnancy. If, during gestation, the heart begins to fail, medical treatment with rest should first be tried. If the patient improves and compensation is established, interference should be postponed. Under such conditions, if one can

control the patient's environment, a pregnancy can frequently be carried on to its normal termination. There is analogy between these cases and those of nephritis complicating pregnancy. In neither case must the condition be considered hopeless so far as the pregnancy is concerned. When, however, we cannot control the failure of compensation by medical means, when complications such as excessive development of nephritis or goitre develop, then pregnancy must be interrupted. The question will then come up as to whether sterilization shall be practised with the ending of the pregnancy. Where there is acute endocarditis, or where the heart lesion developed recently, the indication for sterilization is not so pressing. The worst cases of heart lesion in pregnancy are mitral stenosis. In some cases, however, if the patient can be tided over one pregnancy, a subsequent one may proceed without complications. Under many circumstances the interruption of pregnancy should be accompanied by sterilization. It is interesting to note how rarely death occurs from cardiac failure in pregnant and parturient women. Among 60,000 patients there occurred but 11 such cases. When these cases are analyzed, there were 7 who had suffered from heart lesions for a considerable time before coming to hospital. Three of these patients had serious lesions in the spinal column. In the remaining 4 there was fatal lack of compensation and in 3 of these the patient had grown very rapidly worse just before labor. In 3 cases autopsy showed a recurrent endocarditis. These patients were admitted to the clinic very shortly before death. One patient had been under observation for some time, and without evidence of a serious cardiac condition. This had rapidly developed just before death. The question arises what method of delivery should be practised at term in a patient suffering from a severe heart lesion? Abdominal Cesarean section is undoubtedly best. When one considers the effect of pregnancy upon the general circulation, we find that the influence of the hormone upon the condition of the blood must be taken into consideration. These substances are produced by the epithelium of the trophoblasts. It is thought that their influence upon the circulation in pregnancy is more potent than the mechanical disarrangements occasioned by pregnancy which have hitherto been considered the essential factors. This is seen especially in the vessels of the peripheral circulation and in early pregnancy when the uterus is too small to influence the circulation by pressure. The development of varicosities may also be ascribed to this source and also certain changes in the heart muscle. The hypertrophy of the heart often seen during pregnancy must, to some extent, be the result of the presence of these substances in the blood. We know that the actual quantity of the blood is not increased during pregnancy and hence, if hypertrophy is to develop, it must be from some other reason than the additional labor of propelling a larger quantity of blood. Kautsky considered mitral stenosis the most important condition of the heart in pregnancy. The form seen in these patients is not that observed after the ordinary rheumatic attack, and there is usually accompanying the stenosis mitral insufficiency. Observations show that the mitral orifice is changed in shape and size during pregnancy, and that this does not resemble the congenital condition sometimes seen in newborn children. This condition is observed in women who have had chorea,

sclerosis and ulcer of the stomach. While a moderate degree of stenosis without insufficiency may do little harm, compensation is so apt to fail that one can understand the high rate of mortality. Where stenosis develops after an infection, especially if insufficiency be present, the prognosis is very bad, even though there may be apparently compensation. When such patients come into labor, they are threatened with acute edema of the lungs or rapid dilatation of the heart. In the puerperal period, they are apt to develop endocarditis, sometimes acute and sometimes developing gradually. With regards to aortic insufficiency, we must distinguish three causes: One is rheumatism, another arteriosclerosis and a third syphilis. The last is especially dangerous because the coronary arteries are often involved and during labor the patient may die from sudden dilatation of the heart. Aneurysm of the aorta may develop during labor and this may produce severe complications even in pregnancy by its gradual development. The least dangerous is the rheumatic form, especially if compensation is maintained. There is probably no greater mistake in diagnosis during pregnancy than the frequent recognition of mitral insufficiency. Systolic murmurs are so often heard at the mitral area and also at the pulmonary area with accentuation of the second pulmonary sound that this mistake is not unreasonable. We have often a rapid pulse and some times a capillary pulse in addition. In these cases dropsy is of considerable importance as a symptom. Mitral insufficiency, unaccompanied by involvement of the kidneys and with good compensation is not a very grave condition. In cases where interference must be practised, the choice should be abdominal Cesarean section, under anesthesia by local injection or into the spinal cord in the region of the sacrum. Such anesthesia disturbs as little as possible the intra-abdominal tension and embarrasses the heart to the least degree. The operation should include the resection of the Fallopian tubes for sterilization.

The Treatment of Antepartum Hemorrhage.—At a conjoint meeting of English Medical Societies, TWEEDY (*Proceedings of the Royal Society of Medicine*, November, 1920) stated his well known views concerning the treatment of antepartum hemorrhage. He does not believe that hemorrhage not arising from placenta previa is accidental, and he is strongly impressed with the inaccuracy of those who deal with these cases in estimating the actual amount of blood loss. In the Rotunda Hospital, antepartum hemorrhage is not considered to be present unless it becomes of considerable severity. So many insignificant hemorrhages are not recorded. In 13,924 deliveries, there were 49 cases of accidental and 45 of unavoidable hemorrhage, and in the out-patient service, in 15,543 cases, there were 47 of so-called accidental bleeding. If all hemorrhages are reported, the percentage becomes much greater, and by this method in 3600 deliveries, there were 44 cases of hemorrhage, most of them of little importance. In another hospital 105 cases of accidental hemorrhage were reported in two years, of which 83 subsided when the membranes were ruptured; 7 died and 15 were treated more radically. From this it would be inferred that there were 22 serious hemorrhages. Among Tweedy's 49 patients, there were 22 in a serious condition treated by packing the vagina; 2 hospital patients died and 7 in the out-

patient service. In 5 of the 7 the tampon was used. He thinks that the 2 deaths in hospital arose from intraperitoneal hemorrhage. In 1 not more than a pint and a half of blood was in the uterus and in the other, the patient was delivered by natural labor, dying after the third stage. In Tweedy's later work at the Rotunda, in three years he encountered 23 cases of accidental hemorrhage. Acting upon the knowledge that this complication often arises from toxemia complicating pregnancy, Cesarean section was performed when toxemia was producing the hemorrhage. Three of these operations were done successfully, and in all 3 there was blood in the abdominal cavity and in 1 the ovarian artery beneath the Fallopian tube was bleeding. Of the remaining 21 cases, 8 were treated by the tampon. There were no deaths from loss of blood, but 1 woman died from sepsis ten days after delivery. Taking both series of cases together, there were 72 in 18,000 deliveries with 2 deaths. In 30 the tampon was used. Before this method was adopted in the institution, in 3600 patients, there were 5 deaths. The writer is convinced that the use of the tampon is valuable because it impedes the circulation in the uterine vessels. It also causes the uterus to contract. The writer believes that the efficiency of the treatment depends on the way in which it is applied. The left hand should be passed into the vagina, with the palmar surface directed toward the hollow of the sacrum and the tips of the fingers lying behind the cervix. Small pieces of cotton wool, squeezed out of lysol solution, each the size of the thumb knuckle, are then taken and inserted by means of the right hand around the cervix. The fingers of the left hand are utilized to squeeze the pellets into a compact mass, forcing the spaces between them to permit the insertion of other pellets. This process is continued from above downward until the vulva is reached and no more cotton can be inserted. A T-bandage is then applied to keep the tampons in position and an abdominal binder is fastened tightly from above downward, and when it is removed, only so much blood will be found as escaped during the operation. Its application is not easy, nor without danger. If the first effort to stop bleeding in this way is not successful, the tampon must be removed entirely and the attempt repeated. Pain, distress and some shock follow its application and the mucous membrane of the vagina is wounded, rupture of the uterus may occur. The writer believes that in the vicinity of the internal os intraperitoneal hemorrhage is controlled by this method. A leak from an ovarian artery would not be prevented. The writer believes that hysterectomy is not indicated in accidental hemorrhage. He also states that the fact that the membranes have ruptured does not contraindicate the treatment.

In discussion, Shaw, of Manchester, had not used the method of packing because he believed that it predisposed to septic infection, and that, as applied by the general practitioner in private practice, it is not only dangerous but inefficient. His method consisted of rupturing the membranes, applying an abdominal binder tightly, and giving ergot or pituitrin. Williamson, at St. Bartholomew's Hospital, in 2600 patients had 98 cases of antepartum hemorrhage, with a mortality which varied in the different groups of cases. They were treated by various methods, and his experience had convinced him that tamponing the vagina is a valuable method in the treatment of antepartum hemorrhage and by

this bleeding in many cases can be arrested. He believes that cases of concealed hemorrhage caused by toxemia require Cesarean section, if uterine contractions are absent and the cervix is not dilated. In cases which are not toxemic, he would employ the tampon until dilatation developed, when he would practice bipolar version or introduce de Ribes' bag. He believes that the tampon acts by stimulating muscular contraction and he does not believe that it can check hemorrhage by pressing the uterine arteries.

In discussion, the majority of opinions seemed to be that midwives should not be shown how to apply a vaginal tampon; that if the method is taught to students, it should be taught as thoroughly as possible and that great stress should be laid upon the necessity for careful antisepsis.

GYNECOLOGY

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Fibroids of the Ovary.—Ovarian fibromata comprise approximately 2 per cent of all ovarian tumors and may occur from the time of puberty to an advanced age. The majority occur in single women about the time of menopause. The size and weight of these tumors vary extremely and the etiology has always been obscure. In reporting a case of this rare disease, CLARK and GABE (Am. Jour. Obst. and Gynec., 1921, i, 603) state that in the majority of the reported cases patients have complained of a swelling of the abdomen, pain of varying degree, often none at all, and not infrequently of feeling a hard mass through the abdominal walls. Other symptoms, such as frequency of urination, constipation, etc., are due to varying mechanical factors. Objectively, the tumor is usually palpated without difficulty. Its consistency, mobility and unilateral occurrence are significant. One feature, however, is of marked diagnostic importance when present, namely, ascites. The weight attached to this finding has been especially emphasized by English writers on the subject. It may be recalled that fibroma elsewhere, and especially in the uterus, is rarely associated with ascites. The presence of ascites with intra-abdominal carcinomatosis, located either primarily or secondarily in the ovary as a tumor mass, is common, but is associated with many other signs and symptoms not found in fibroma of the ovary. In other benign tumors of the ovary, ascites is usually lacking. It, therefore, seems of considerable diagnostic importance to find ascites together with a unilateral adnexal tumor in a case lacking signs of cachexia, great loss of weight, or symptoms

pointing to a focus of malignancy elsewhere in the body, as in the breast or stomach. In the absence of ascites, differential diagnosis from that of other adnexal tumors offers considerable difficulty. The tendency of ovarian fibromata to be unilateral, movable and hard, should be borne in mind. In the presence of ascites, where nephritis, cardiac decompensation, portal obstruction, abdominal carcinoma, tuberculous peritonitis, and the anemias can be ruled out, the occurrence of such findings should make one very suspicious of ovarian fibroma. The treatment, without exception is operation. The prognosis, as indicated from case reports, is excellent. The pathology of ovarian fibroma has been carefully studied by several investigators, showing that these tumors vary in size. Their consistency, likewise, is extremely variable, some, composed of a loosely woven network of connective tissue, being soft, while others require the use of a bone saw for their section. In a similar way, their shape, appearance on cross-section, color and general outline cover a wide range of possibilities. They show many forms of degeneration and it is on account of these as well as the possibility of a twisted pedicle, that their removal should be urged. The court of final judgment is the microscopic appearance of the tumor.

Treatment of Border-line Cancer of the Cervix.—In the opinion of WEISS (*Am. Jour. Obst. and Gynec.*, 1921, i, 661), cancer of the cervix is still to be classed as an operative condition when discovered early and the patient is a good risk. When a doubtful border-line condition is presented, treatment by radium is advisable and the question of subsequent operation should be determined by the reaction obtained; but if operation is contraindicated by age, general condition, heart, kidney or bloodvessel, radium alone should be used. A careful comparison between the cautery and radium type of treatment shows that both have advantages and disadvantages and that, in carefully selected border-line cases, far better results are obtained by a judicious combination of cautery amputation followed by moderate doses of radium. The author's results in a small series of border-line cases, while generally satisfactory, are far from conclusive. Similarly, the wide range of radium dosage in treating cervical cancer, varying from 1500 mg. hours in some clinics to 8000 mg. hours in others shows that no definite conclusions have been reached, and while favorable reports have been received from both extremes, the use of radium is still somewhat empirical. Definite conclusions can be drawn only after a definite tabulation of a long series of cases based on follow-up and end-results.

Clinical Experience with Corpus Luteum Extract.—The distressing symptoms of the menopause may be relieved quite frequently by the administration of corpus luteum extract, according to LEIGHTON (*Am. Jour. Obst. and Gynec.*, 1921, i, 613), since luteum extract supplies that element so necessary to the woman during her normal menstrual life. This therapy exerts its greatest benefit in the treatment of those women who have begun to exhibit the early manifestations of the climacteric. To avoid the unsatisfactory results which have been reported by some gynecologists, it is necessary that luteum extract be administered early and continuously once the diagnosis is made. Procrastination on the part of either the patient or the physician often means ill success, When menstrual irregularity makes itself known and the hot flushes.

mental confusion, tremor and hyperthyroideal symptoms are first evident, then is the proper time for ovarian organotherapy, not waiting until the height of the disorder has been reached or the woman has suffered for months or years with a "chronic" menopause. Early control is necessary and, once obtained, it is of easy maintainence. In over half of the 300 or more women to whom Leighton has given luteum extract, the indication for its use was solely the menopausal syndrome. Of this number there were not over a dozen who could not report exceptional benefit, even to absolute relief. To those women who during the menstrual life complain of so-called "sick headaches" of the frontal and temporal type, with nausea and vomiting, which occur with peculiar periodicity, at or about the time of menstruation, ovarian organotherapy offers much relief. In chlorosis, as an adjunct to hematinics, luteum is also indicated. The functional amenorrhea of women, in early adolescence or mid-menstrual life, responds in a miraculous manner. In the use of thyroid as a "reduction cure" the giving of luteum at the same time seems to obviate the occurrence of profuse sweating spells, muscular weakness, tachycardia, nausea and other vasomotor symptoms, occasionally following the ingestion of thyroid extract. Larger doses of thyroid are tolerated, if given in combination with luteum. While Leighton has not had 100 per cent of success, it has been his fortunate experience to observe a relief and cessation of many disorders, referable to deficient ovarian secretion, where proper diagnosis is followed by the continuous, thorough and regular use of luteum extract. It is important above all, that one should prescribe and the patient obtain a product from recent fresh material and care must be taken to see to it that the dispensing chemist has such on hand. The indiscriminate buying of luteum extract is one thing which Leighton is careful to prevent. A patient is directed to the shop where he knows fresh tablets are to be had. Each prescription calling for such, bears on the direction label, "These must be taken for ten or twelve weeks," and special emphasis is laid upon this point. He explains every time, at the commencement of treatment, that it is cumulative in action, that it is non-toxic, when fresh, and that one must be conscientious in its taking, as results are obtained slowly and relief is not immediate.

OPHTHALMOLOGY

UNDER THE CHARGE OF

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Treatment of Hysterical Amaurosis, Hemeralopia and Amblyopia by Suggestion and Hypnotism.—AUGSTEIN (*Ztschr. f. Augenheilk.*, 1920, xxiii, 47) calls the attention of ophthalmologists to the importance of

psychotherapy. In contrast to a preceding period, practitioners have laid too little stress, during the last ten years, upon the marked therapeutic effects of this method in the treatment of disease; indeed by many it has been regarded as unworthy of the scientific physician. The writer, based upon an extensive material, seeks to demonstrate the value of various psychotherapeutic methods; he has succeeded in curing by such methods hysterical hemeralopia and amblyopia. He cites a remarkable case of binocular amaurosis, the only symptom of hysteria demonstrable, which was cured by hypnotism after continuous blindness of twenty-one months. Such amaurosis is, in the author's opinion, solely the consequence of traumatism; the cause is to be sought in an injury of the highest centers of the cerebral cortex, determined in all probability by autosuggestion. The same influence also explains hysterical stasis of the pupil as well as the sluggish reaction sometimes observed in hysteria. Some trauma of material or psychic nature may well be regarded as the sole cause of hysteria, or as the determining factor where a predisposition to that neurosis exists. Every form of hysteria is a disturbance of normal brain function. As regards treatment, suggestion in connection with the faradic and galvanocurrent and injections of sodium chloride as a placebo, are as a rule, adequate for the cure of hysterical disturbances of the vision; the slight pain experienced from these agents plays a certain role in the cure; but in many cases hypnotism is indispensable; when properly conducted the application is never injurious.

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Strychnine in Ophthalmology.—LEOZ (*Arch. d. Oftal.*, 1921, i, 6) remarks that strychnine is a therapeutic agent which oculists sometimes employ, without much confidence, in desperate cases, but which, he thinks, can give good results if persevered in and in fairly large doses by injection. The medicament is evidently useless in complete optic atrophy and in peripheral paralyses of ocular nerves from compression or section; it is contraindicated in mydriasis dependent upon irritation or functional exaltation of the sympathetic. It finds its indication in pareses and paralyses of dyscrasic, toxic or infectious origin, in those dependent upon small nuclear hemorrhages and even in some cases of tabes; in non-paralytic latent strabismus, in muscular and accommodative asthenopia and especially in all such manifestations occasioned by general fatigue and exhaustion. Its value is undeniable in the so-called toxic amblyopias; it should likewise be employed in atrophic neuritis, retinitis and choroiditis, and in those grave cases in which nothing is to be hoped from any other treatment. To obtain definite results the initial dose should be 1 or 2 mg., to be increased to the point of tolerance and continued for some time, and repeated after intermission. By this method the author has been enabled to reach 76 mg. and even 82 mg. at a single dose. He begins with 1 or 2 mg., according to the patient's weight, for five days consecutively, then doubles the dose for five more; abstention for six days, followed by six injections of 3 mg., again followed by six days of withdrawal, when further injections of 4 mg. are given and so on up to 15 or 20 mg. The treatment is then to be suspended for two months and then resumed with larger doses to the point of tolerance. The symptoms of intolerance are well known: the most important are muscular jerking of the

extremities; a general sensorial excitability is frequently present; pruritus, tingling and great sensitiveness to sounds and jars. The writer has never met with any serious accidents.

Ocular Disturbances Consecutive to Inflammation of the Middle Ear. —GERDIL (*Paris Thèsis*, 1921) observes that ocular complications in the course of otitis media consist of paralysis of the abducens, encountered in 9 per cent of such cases, and papillary stasis with or without neuritis; the latter is of extremely frequent occurrence, being noted in 60 per cent of recorded observations. Paralysis of the sixth motor nerve is met with particularly in the course of the intracranial complications of otitis; it is due to quite diverse causes, such as circumscribed meningitis, cerebellar abscess, and thrombophlebitis; cases have, however, occurred in which the paralysis was not accompanied by intracranial complications; the pathogeny of such cases is very difficult of explanation; very probably the underlying condition is an affection directly involving the nerve. The alterations of the optic nerve in the course of otitis are of two forms: simple papillary stasis without immediate functional signs with ventricular hypertension alone; stasis with neuritis and rapid failure of vision when ventricular hypertension supervenes upon meningeal infection along the sheaths of the optic nerve. Systematic examination of the fundus, in the course of otitis media accompanied by symptoms of wider involvement, will reveal these alterations of the optic nerve. Treatment is based upon early diagnosis; good results may be obtained, particularly in papillary stasis. Lumbar puncture is of value in cases of slight hypertension, but it must be repeated several times. In cases of hypertension with papillary stasis recourse should be had to a decompressive craniotomy; to be of use, intervention should be practised before atrophy has had time to occur. In stasis with neuritis, vaccinotherapy is indicated, especially where the infectious organism has been isolated.

Amaurosis Provoked by Lightning.—Amaurosis from lightning is rare. An exhaustive study by VAN LINT, presented to the Belgian Society of Ophthalmology, November, 1909 embraced but 3 cases since 1843. DEPAS (*Clin. opht.*, 1921, xxv, 63) reports the following case: A young woman being in her kitchen during a violent thunderstorm, with the window open, experienced the impression that lightning was passing through the room, when she suddenly became blind; she collapsed without, however, losing consciousness, and was found in this condition shortly after. There were no appreciable lesions except two superficial red spots on the upper part of the breast and arm; they resembled urticaria, and disappeared in a short time. She was seen by the reporter two hours after the accident; there was such intense photophobia that examination was difficult. Blepharospasm was so severe as to be uninfluenced by cocain; ophthalmoscopic examination was impossible. The examiner could only discover slight hyperemia of the conjunctiva, and that the pupils, somewhat contracted, reacted normally. Vision was almost nil; there was a red cloud before the eyes, through which the test-card could be distinguished as an obscure whitish surface. Nevertheless the presence of the luminous reflex justified a favorable prognosis. Two days later there was not only no improvement but the sight was

even worse; pupillary reaction was still normal. An interesting fact to note is that during these two days very intense ocular and periorbital pain, with cephalalgia so severe as to prevent sleep, had appeared; three days later amelioration began; ophthalmoscopic examination failed to show the slightest trace of any lesion. From thence onward improvement was rapid, with perfect restoration of sight three weeks later, with normal fields. A first explanation of the loss of vision would ascribe the same to hysteria; but in view of our entire ignorance of the intimate mechanism of the act of vision it is possible that that mechanism may have been paralyzed for a period without alteration of the conductibility of the nervous fibers. Another conclusion from this case is that, independent of its visual powers, the retina also possesses sensation, otherwise it would be impossible to explain the intense pain provoked by light while vision was absent, and there was no external lesion capable of explaining the intense photophobia present. To this same sensory property may also be attributed the hyperesthesia to light which becomes a truly painful sensation in many persons exposed to intense light without the presence of any objective lesion.

Therapeutic Value of Injections of Milk in Diseases of the Eye.—CASSIMATIS (*La clin. ophthal.*, July, 1921, p. 378) gives his conclusions upon the value of this method of treatment based upon 604 injections in 134 patients, of whom, however, only 84 could be followed up regularly. The author's technic consisted in making the injections most usually deeply into the gluteal muscles, rarely into the subcutaneous tissue; he has never employed subconjunctival injections. The method is entirely harmless as regards both the eye and the general system. The treatment is para-specific, constituting a powerful therapeutic method as an adjuvant to appropriate local measures; the latter should be applied in every case. The injections should not be regarded as a panacea for all ocular affections; they are capable of real service as an adjuvant in all infections of the cornea and uveal tract, more especially in ulcer with hypopyon, rheumatic iritis and purulent conjunctivitis. They are also indicated in all operations in which postoperative infection is to be feared. They should be practised as early as possible, and in sufficiently large doses, although favorable effects upon the inflammatory process occur even in the later stages.

Atropin in Ophthalmology.—FRENKEL (*Arch. d. ophthal.*, July, 1921, p. 385) observes, from the fact of its great utility in ophthalmology, that there has been a tendency to overuse or abuse of this powerful drug; in fact, there has been a regular periodicity of protests which have been well summarized by Serie in his inaugural thesis. As an instance of the excessive use of atropin, the writer mentions all forms of keratitis, especially the superficial; this has been so distinctly recognized that certain writers have even recommended eserin in its place. He lays down as the principal indication for the use of atropin, iritis and associated conditions, such as cyclitis, iridocyclitis and interstitial keratitis, an affection so frequently complicated with cyclitis. Whether the iritis be primary or secondary, atropin is the remedy unless the inflammation depends upon some systemic condition which may also occasion hypertension; this is the case with certain forms of iritis in diabetes,

of iritis with a tendency to hemorrhage in ocular arteriosclerosis and also in certain cases of cyclitis occurring in the course of interstitial keratitis. Iridocyclitis from unrecognized intra-ocular foreign bodies (Morax) may also be accompanied by hypertension. Finally, atropin is also indicated in iritis complicating hypopyon and other exogenous infections. On the other hand the remedy is not indicated in nonsuppurative superficial keratitis, scrofulous, lymphatic, impetiginous forms of keratitis, pannus or herpetic keratitis not accompanied by iritis. In these affections it is not only useless but even injurious by increasing the photophobia. Eserin, or better still, pilocarpin, is preferable in these forms of superficial keratitis. Atropin appears also to be contraindicated in keratitis from vesicating gases or superficial burns without secondary infection, as also in electric keratitis. In bullous and filamentous keratitis, and in superficial erosions of the cornea, pilocarpin is superior to atropin. In episcleritis and scleritis the employment of atropin should depend upon the presence or absence of cyclitis or iridocyclitis as well as the state of the ocular tension. This is the guide also to its use in affections of the posterior segment such as non-neoplastic detachment of the retina. Although the treatment of strabismus by atropin has now fallen into disuse the method is of some value as an adjuvant to orthoptic treatment. True intolerance is due rather to improper indication or a septic condition of the solution used rather than to idiosyncrasy as invoked by the older writers. Among the succedanea of atropin, scopolamin is more toxic and should be used with discretion. The usual concentrated solution of atropin, 1:100 is too strong, even for exceptional cases; 1:200 is always sufficient if the proper treatment of the exciting disease (usually specific) is also given. Adrenalin adds to the efficiency of weaker solutions. As a résumé of the indications for atropin, Frenkel would subordinate them all to exact diagnosis of the ocular and systemic conditions and to the state of the intra-ocular tension.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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Studies on the Relation of Mineral Dusts to Tuberculosis: (1) The Relatively Early Lesions in Experimental Pneumokoniosis Produced by Granite Inhalation, and their Influence on Pulmonary Tuberculosis— GARDNER (*Am. Rev. Tuberc.*, 1920, iv, 734) exposed large numbers of guinea-pigs to granite dust over varying lengths of time by means of a special apparatus. The guinea-pigs were infected with a strain (R')

of tubercle bacilli, preceding, during and following the dust exposure by spraying with a de Vilbiss vaporizer. Control animals received either dust alone or tubercle bacilli alone. The lungs were prepared for microscopic examination after the methods of Miller, where intratracheal instillation of the fixative followed by removal *en masse* was employed. When only dust was given, small quantities of it could be found after three weeks' exposure, but it could not be recognized macroscopically until the seventh month. The dust was first encompassed in mononuclear intra-alveolar cells, the origin of which, the author believed, was reduced to a consideration of the local vascular endothelium, or the transitional cell of the blood-stream. In two months, the intra-alveolar dust cells mobilized, lying in the alveoli along the ductuli alveolares, and about the proximal sides of the alveoli adjacent to vessels and bronchioles. During a period of from three to seven months the process steadily increased, the invasion of lymphoid tissue becoming more extensive, and the larger nodules at the bifurcation of the bronchi becoming involved. If the dusting process were stopped, the lung rapidly attempted to remove the irritant, which was not found in mononuclear cells near enlarged lymph nodes, some, however, remaining within the aveoli along the ductuli alveolares. The first mobilization of the dust was within the air spaces, through which it was carried to the nearest lymphoid tissue, where it gained access to the lymphatic system and was removed from the lung. When inhalation of only tubercle bacilli was instituted by the twenty-nine-year-old strain (Ri), large, proliferative, subpleural tubercles with caseous centers appeared in three weeks. After two months these tubercles shrank and the midzonal tubercles increased in size. At six or seven months many of the lesions had practically disappeared, having healed with a morphological and functional restoration. In the coincident dust and infection experiments, the tubercles were more numerous, larger and had less tendency to a regular zonal arrangement. While the degree of caseation was not affected, an early and progressive fibrosis resulting from the stimulation of the dust not only distorted the tubercle, but retarded its healing. It would appear from these researches that both irritants—the dust and the bacilli—"enter and leave the lung by the same path." From his work to date, the author concluded that tubercles occur more frequently and tend to run a more prolonged course in the dusted than the undusted lung, and that the advent of the tuberculous process to the regional lymph nodes is not prevented.

Leukoplakia of the Pelvis of Kidney and Ureter.—RICHEY (*Jour. Lab. and Clin. Med.*, 1920, v, 635) reported a case of leukoplakia of the pelvis of right kidney and ureter from a man, aged forty-three years, who for twenty-two years had experienced periodic paroxysms of pain following an injury to the back. The kidney showed an advanced suppurative pyonephrosis, the leukoplakia, occurring as a white silvery, finely wrinkled membrane, looking not unlike the delicately corrugated skin of the scrotum of infants. Microscopically, the lining of the pelvis and ureter consisted of a thick layer of stratified squamous epithelium, presenting a large amount of keratinization of the free surface. No membrana propria could be demonstrated, the deepest layer of epithe-

lium resting directly upon a bed of granulation tissue. The culture of the urine yielded B. coli communior and B. acidi lactici. The author explains leukoplakia of the renal pelvis and ureter upon the theory of metaplasia "as a histogenic transformation induced by the alteration of environment, wrought by a long standing inflammatory process, with a resultant change in morphology of the cells from the normal transitional to stratified squamous epithelium even to the formation of a superficial layer of keratin."

The Sachs-Georgi Precipitation Test for Syphilis.—For several years investigators have attempted to find a test for syphilis less elaborate and complicated than the Wassermann test, and if possible, more delicate and specific. These endeavors have usually been directed along lines of precipitation tests. Some of them have been partly successful, but with the exception of the Lange colloidal-gold test on spinal fluid, none have been generally adopted. HULL and FAUGHT (*Jour. Immunol.*, 1920, v, 521) described a modification of the Sachs-Georgi test, using clear blood serum (0.3 cc) and an alcoholic extract of beef heart (1 cc), either cholesterinized or not. The entire volume of the test is 1.3 cc instead of 10.5 cc as advised in the original procedure. The authors emphasized the importance of vigorous shaking of the antigen when diluting it (1 to 5) with normal salt solution and of titrating the antigen to determine the optimum amount of precipitation. The prime requisite for the serum was its clearness, age and inactivation apparently making no difference. Centrifugalization enabled an immediate reading. As a rule, positive tests can be read when allowed to stand overnight. No change was noted after forty-eight hours. Optimum results were obtained with low temperatures for incubation, though no appreciable difference was noted in overnight incubation at room temperature and at ice-box temperature. Parallel precipitation and Wassermann tests were observed in 296 instances. Eighty-eight per cent of the samples agreed; in 7 per cent, the precipitation test showed a more delicate reaction, being positive where the Wassermann was negative; 2 per cent yielded a negative precipitation test with a definitely positive Wassermann, and in 3 per cent it was negative when the Wassermann was doubtful. Treatment of the patient apparently affected the results of the precipitation, causing it at times to become negative while the Wassermann was positive. Attempts to determine whether the precipitate formed in the Sachs-Georgi test was entirely responsible for the Wassermann reaction were unsuccessful. Similarly, TANIGUCHI (*British Jour. Exper. Path.*, 1921, ii, 41) compared the results between the Wassermann and Sachs-Georgi reactions on 296 cases. Ninety-one per cent gave the same result, while discrepancies were encountered in the remainder. The authors did not regard any of the discrepancies as serious, noting that the largest proportion occurred in cases which were suspicious to the Wassermann test but negative to the Sachs-Georgi reaction. When compared with the findings of other investigators, they felt that the discrepancies were, in all probability, not due to any essential difference in the nature of the two reactions and that, in general, the differences have been observed only in case of weak or doubtful reactions. The technic was essentially that as modified by Sachs-Georgi

and known as the "incubator method," where the readings were made after keeping the mixture for eighteen to twenty hours at 37° C. The alcoholic human heart extract, as used in the Wassermann reaction, was prepared by the double method. The human sera were inactivated by heating thirty minutes at 56° C. To each of two tubes containing 0.5 cc of emulsion a volume of 1 cc, consisting respectively of 0.1 and 0.05 cc serum diluted with saline, was added and mixed by slight shaking. From a practical standpoint, the authors believe that the Sachs-Georgi reaction suffers from the greater difficulty of distinguishing between negative and suspicious or weakly positive reactions. It was found that the precipitable substance in the Sachs-Georgi reaction consisted mainly of the lipoids contained in the emulsion. In a *resume* of the results of 1042 examinations, on serums and cerebrospinal fluids made with the Wassermann and Sachs-Georgi tests, LEVINSON and PETERSEN (*Arch. Dermat. and Syph.*, 1921, iii, 286) found a close parallelism of the two reactions (92 per cent). In 62 cases in which the Wassermann reaction was negative while the Sachs-Georgi reaction was positive or doubtful, the clinical history or examination revealed evidence of syphilis in 58 per cent. The authors employed a technic as modified by Mandelbaum, differing from the original in the use of smaller amounts of serum and antigen. Emphasis was placed on the preparation of a proper antigen and the careful reading of results. No superiority of ice-box over simple room temperature incubation was found. Because of its simplicity and the fact that it is frequently positive in syphilitic cases when the Wassermann test is negative, the authors are of the opinion the Sachs-Georgi reaction offers a valuable aid in the routine examination of syphilis when used in conjunction with the Wassermann reaction. KILDUFFE (*Arch. Dermat. and Syph.*, 1921, iii, 416) reported the results of parallel Wassermann and Sachs-Georgi tests on 296 human sera. The technic for the latter test corresponded to that described by Galli-Valerio. Twenty-three per cent gave positive Wassermann reactions while in the Sachs-Georgi tests the total number of positive reactions was 14 per cent, some of which were in Wassermann negative sera. By the Wassermann, 70 per cent were negative while by the Sachs-Georgi, 60 per cent were negative, some of these occurring in Wassermann positive sera. Of 16 anticomplementary serums, 2 gave a weakly positive Sachs-Georgi reaction. Twenty-three sera reacted only with the cholesterinized heart extract and the acetone insoluble lipoid extract, the syphilitic liver extract being negative; of these 6 gave positive Sachs-Georgi reactions. The worker concluded that a diagnosis of syphilis or a conclusion as to treatment cannot be based on the results of a Sachs-Georgi test with safety.

Tuberculosis in Guinea-pigs with Experimentally Produced Endothelial Leukocytosis.—McJunkin (*Jour. Med. Research*, 1921, xlii, 2–201) studied the effect on tuberculous guinea-pigs of producing in them an endothelial leukocytosis by the intraperitoneal injection of cultures of B. phlei, B. smegmatis, and non-virulent tubercle bacilli. The type of leukocyte increased was the large mononuclear of transitional leukocyte which was differentiated by the benzidine polychrome stain. It was found that those tuberculous animals in which the leu-

kocytosis had been induced usually lived a few days longer than the control untreated tuberculous guinea-pigs. The chief difference in pathological features at autopsy was that the spleen of the treated animals was quite small, bound down by adhesions, and was free from definite tubercles, while in the untreated tuberculous animals the spleen was enlarged and showed necrotic areas.

HYGIENE AND PUBLIC HEALTH

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Experiments on Alastrim.—LEAKE and FORCE (*Public Health Rep.*, 1921, xxxvi, 1437), working with material in the shape of crusts and vesicle contents from cases of alastrim, a mild form of smallpox or a smallpox-like disease, found that the virus immunized monkeys against vaccine virus. Rabbits gave similar results, while rabbits previously inoculated with vaccine virus showed cutaneous sensitization to small-pox, alastrim and vaccine virus, but were negative to chickenpox. The authors hold that this work indicates the identity of alastrim and smallpox.

A Guide to the Proper Rat-proofing of Buildings.—HAUER (*Public Health Reports*, 1921, xxxvi, 930) points out that trapping and poisoning result in only temporary reduction of the number of rodents in a community, though these measures are valuable in a plague emergency. On the other hand, rat-proofing gives lasting results, though the warning is given that we cannot expect to make any community rodent-free. The classification of buildings according to rat hazard and subclassification with reference to construction and uses are given, as are the measures applicable to each group. Details of the proper use of concrete and of other important features of rat-proofing are given.

Industrial Dermatosis Among Printers.—McCONNELL (*Public Health Reports*, 1921, xxxvi, 979) investigated an eruptive condition known as "ink poisoning" among printers. The condition was found only among those who have "dry" skins and was not accompanied by any constitutional symptoms. The lesions varied from erythema to ulcers and were confined to the regions exposed to the ink. A calamine gelatine paint was found to remedy the dermatitis promptly. As a prophylactic it is recommended that lanolin or a mixture of lanolin and olive oil be rubbed into the hands and forearms.

Anopheles and Sea-water.—GRIFFITS (*Public Health Reports*, 1921, xxxvi, 990) reviews earlier observations on the subject and records his own experiences. The latter lead to the following conclusions: (1) *A. crucians* was found to propagate in sea-water diluted to a maximum salinity of 10,088, or slightly more than 50 per cent average sea-water. The transfer to sea-water of *A. crucians* larvæ which had started their development in brackish water did not unfavorably affect their subsequent development. (2) *A. quadrimaculatus* was not found to breed in numbers sufficient to be of sanitary importance in a higher salinity than 10,003, or 1.5 per cent sea-water. In one case two larvæ found in water with a salinity of 10.048 developed into *A. quadrimaculatus* imagoes; but this observation requires confirmation as to whether this species may complete its entire water cycle in so high a percentage of sea-water. The question is raised as to whether *A. quadrimaculatus* larvæ may not withstand a much higher salinity intermittently than continuously. Specimens of *A. quadrimaculatus* transferred from fresh pond-water to sea-water, salinity 10,160, were all killed within twelve hours. (3) *A. punctipennis* was not found developing in salt or brackish waters. This species breeds under a wider range of conditions than either *A. quadrimaculatus* or *A. crucians*, but apparently does not survive in salt or brackish waters. Larvæ of *A. punctipennis* all died within seven hours when put into sea-water.

Typhoid Fever in Cleveland, Ohio, for the Years 1918, 1919 and 1920.—PERKINS (*Public Health Reports*, 1921, xxxvi, 1095) gives a detailed discussion of recent experiences in Cleveland with typhoid fever, considering especially the possible sources of infections. The evidence excludes flies and milk as sources of any appreciable amount of infection; food, contact, and infection acquired by bathing in contaminated water are allocated a fairly definitely though relatively small number of cases. The city water supply, though part is filtered and all is chlorinated, is regarded as the chief source of infection. The author does not regard the chlorination as adequate to make the water supply safe, a point on which the water department of the city disagrees. A plea is made for the providing of a supply which shall at all times conform to Federal requirements from a bacteriological point of view, *i. e.*, not to exceed one colon bacillus in 50 cc. It is noted that whenever an improvement has been made in Cleveland's water supply a drop in typhoid incidence has followed.

Recovery from Rabies, with Reports of Cases of Treatment Paralysis and of Recovery of Animals Apparently Rabid.—PHILLIPS, BERRY and SNOCK (*Jour. Infect. Dis.*, 1921, xxix, 97) state that spontaneous recovery from rabies naturally acquired, while rare, does occur. The saliva of an animal which recovers from rabies may have been extremely virulent during the course of the disease. As early as thirty-eight days after recovery from street rabies in a dog, the infectivity of the brain may disappear and Negri bodies be absent. And that therapeutic measures to control the symptoms in developed rabies in man should not be so heroic as to themselves endanger the life of the patient, for there is a possibility of recovery.

Fake Arsphenamine.—(*Public Health Reports*, 1921, xxxvi, 1510). The Public Health Service issues a warning in regard to spurious arsphenamine, quoted from the weekly Bulletin of the Health Department of the City of New York: "The Department of Health having made an investigation relative to the sale, in the city, of arsphenamine of supposedly German origin, by seamen and other unscrupulous venders, submitted several samples purchased to its chemical laboratory for analysis. The chemist's report shows the samples to be a fraudulent substitution, being a combination of sodium chloride and a yellow dye. Physicians and druggists are accordingly warned against purchasing such products from unknown persons."

Observations on the Spread and Persistence of the Hemolytic Streptococci Peculiar to Scarlet Fever. The Streptococci Isolated from Attendants and Surroundings of Scarlet Fever Patients.—TUNNICLIFF, (*Jour. Infect. Dis.*, 1921, xxix, 91) states that hemolytic streptococci may be isolated from the floor and walls of rooms occupied by patients with scarlet fever and diphtheria, and from the fingernails, face masks and shoes of the attending nurses and from the eating utensils used by patients harboring hemolytic streptococci. Only 5 of 20 strains thus isolated were opsonified and agglutinated by the serum of a sheep immunized with a hemolytic streptococcus from scarlet fever and hence to be considered as specific for scarlet fever. Four of these strains were isolated from the eating utensils of scarlet fever patients and one from the face mask of the nurse in attendance. These results indicate the value of face masks and the necessity of disinfection of eating utensils used by patients with infectious diseases. It would appear also that persons associated with scarlet fever patients may develop tonsillitis without an exanthem and harbor hemolytic streptococci which belong to the same biologic group as those isolated from typical cases of scarlet fever. Agglutination of hemolytic streptococci from suspected cases of scarlet fever, by immune sheep serum specific for streptococci from scarlet fever, has proved helpful in diagnosis. These results suggest, further, that while patients with scarlet fever generally rid themselves of hemolytic streptococci specific for scarlet fever in from three to four weeks, patients with discharges may retain them much longer, and that the streptococcus specific for scarlet fever disappears at the time when the patient becomes non-infectious, according to clinical experience.

ORIGINAL ARTICLES.

ACUTE CEREBELLAR ENCEPHALITIS (ACUTE CEREBELLAR ATAXIA).*

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The great interest which has been awakened in the subject of acute non-suppurative encephalitis, owing to the prevalence of an epidemic of the disorder, leads me to a further elaboration of an earlier study of this form of inflammation of the brain, particularly as it affects the cerebellum and as it is manifested in children. It has been my fortune to encounter four isolated cases in which the symptoms indicated that the cerebellum suffered very decidedly from the attack, if, indeed, it did not bear the brunt of it. These have been reported in two earlier publications,[1] together with the abstracts of all the cases I had discovered recorded in journal literature up to 1915, making twenty-one in all. In all of these the attack was acute and the affection occurred in early life.

It will not be necessary to repeat here the abstracts of the cases which I have already collected. They were of reports by Shepherd,[2] Schepers,[3] Feith,[4] Bastian,[5] Lenhartz,[6] Hammarberg,[7] Lüthje,[8]

Frederick Taylor,[9] Voelcker,[10] Guthrie,[11] Batten,[12] Nonne[13] and the four seen by myself, making a total of twenty-one cases in all. The following are abstracts of cases which have appeared in medical journal literature since the time mentioned, now about six years ago, or of the cases which were inadvertently omitted from my paper, those being selected which seem with good reason to belong to this category:

Clapton.[14] Female. Well until four years, when, after measles, was unable to walk or talk for six months. Then up to fifteen years walked unsteadily. Could not use her hands with certainty or ease and was dull mentally. Must have then gradually improved, and when married at thirty-two years could take long walks, although she had to walk slowly. With pregnancy gait became more unsteady and she was dull of comprehension, but could still attend to domestic duties. Died shortly after confinement. Autopsy showed decided atrophy of cerebellum.

NOTE. This case is very much like the one reported by Hammarberg. The onset was distinctly acute and the condition must have been an encephalitis; but many data are lacking. Recovery, although partial, had yet been very decided.

Fairbanks.[15] Child, sex not given, aged five years. Had a severe attack of measles when four and a half years old—about six months before seen—followed in two weeks by prolonged screaming, unsteady gait, staggering, ataxia of right hand. Mind clear; speech unaffected. Examination showed Romberg's symptom; staggering gait; no nystagmus; normal speech; ataxia of the right hand; right knee-jerk slightly greater than left; plantar reflex normal; Babinski reflex present. Under observation about one month (?), during which time there was decided improvement.

NOTE. The connection with measles and the acute condition seem to be undoubted, and the degree of improvement renders ultimate recovery to be hoped for.

E. S. Taylor.[16] Case 1, girl, aged ten years. Measles nine weeks before admission, followed in a week by headache. When taken from bed a week later had a nodding movement of the head backward and in four days was unable to stand and had pain in the left chest. Examination showed movements of the head when the child was in a sitting position; speech slow and hesitating; knee-jerks present; pupils normal; no nystagmus; extreme ataxia when placed on feet and apparently vertigo. Improvement remarkably rapid

[9] Lancet, 1904, **2**, 1416.   [10] Brain, 1905, **28**, 360.   [11] Ibid., 363.
[12] Brain, 1905, **28**, 489, 490; Clin. Soc. Tr., 1907, **11**, 276, 277.
[13] Neurolog. Centralbl., 1909, **28**, 885.
[14] Tr. Pathol. Soc. of London, 1871, **22**, 20.
[15] Arch. Pediat., 1907, **24**, 770.   [16] Guy's Hospital Rep., 1913, **67**, 98.

and seemingly complete in about twelve weeks from the onset of the measles.

E. S. Taylor. Case 2, girl, aged seven years. While in apparently perfect health fell suddenly and could not stand. Headache the next morning. Examination two days later showed speech monotonous and abrupt; child apathetic; knee-jerks present; no nystagmus; irregular movements of the head; could not sit without assistance; completely ataxic when standing and support was necessary; no vertigo; an intention-tremor of both arms; spinal fluid normal; slight fever; well-marked asynergia and adiadokokinesia. In less than three weeks no signs of cerebellar disease remained.

Note. Taylor emphasized the occurrence in both cases of sudden onset, extreme ataxia without loss of power and a characteristic slow, jerking speech.

Strümpell.[17] Boy, aged four and a half years. One day, about four weeks after the beginning of a moderate whooping-cough, complained that eyes did not feel so well. Better the next morning, but on the day following was taken suddenly with inability to stand and could scarcely see. This attack was not immediately preceded by any severe paroxysm. Examination four days later showed normal intelligence; dilatation of pupils; apparently a diminution of power of movement of the eyes; complete bilateral amaurosis; typical bilateral optic neuritis; no ataxia of arms; knee-jerks not obtained; well-developed ataxia of the trunk; sways greatly when placed on his feet and could not stand alone. Lumbar puncture was negative. Improvement was very rapid and complete in about six weeks.

Note. Strümpell describes this case as an undoubted one of ataxia of the cerebellar form, but is uncertain whether the lesion was in the cerebellum or in the corpora quadrigemina.

A. Gordon.[18] Child, aged seven and a half years, sex not stated. At five years had a very severe diphtheria followed by ataxic gait and station; increased knee-jerks; ataxia of the upper extremities; nystagmus; the child appeared dull and to understand with difficulty. Under observation for a year without improvement.

Note. This would appear to have been an acute encephalitis of the cerebellar type after diphtheria. Basing the opinion upon the histories of certain other cases it is possible that improvement or even recovery might yet take place.

Seham.[19] Boy, aged ten years. Condition commenced acutely with a drunken gait. During two months this grew worse; there

[17] Deutsch. Ztschr. f. Nervenheilk., 1914–15, **53**, 321.
[18] Jour. Nerv. and Ment. Dis., 1918, **47**, 370.
[19] Arch. Pediat., 1919, **36**, 531.

was trouble with writing; diplopia; slow, uncertain and scanning speech; static ataxia and support needed; nystagmus; strabismus; incoördination of hands; sensation normal; patellar reflexes increased; intelligence normal. Improvement went on slowly. In four months he could stand without difficulty, although the gait was reeling. Three and a half years later a letter states that the boy goes to school, walks alone sometimes for miles and speech is much better.

NOTE. The sudden onset points distinctly to an acute lesion, such as an encephalitis, and the existence of this condition is borne out by the almost complete recovery at the last note.

Mills and Wilson.[20] Girl, aged three years. Shortly after an attack supposed to be influenza she grew gradually more unsteady on her feet, and three months later a severe attack of indigestion and vomiting was followed by great difficulty in standing and walking and then by inability to sit upright. Examination showed cerebellar gait and station; some marked cerebellar asynergy in the upper extremities, with inability to control the motion of the hands; alternating strabismus and nystagmus. No note made of condition of speech or of psychic symptoms. Improvement steady during two weeks of observation.

NOTE. This case apparently dates from the attack of influenza, with a recurrence of the intracranial disturbance at the time of the severe attack of indigestion.

Skoog.[21] Girl, aged four years. Measles followed on the twelfth day by unsteadiness of hands and interference with walking. In a short time she could hardly get about. Examination on the third day after the onset showed the patient a little sulky or obstinate, but otherwise cerebration good; coarse tremor of tongue; slight nystagmus; no paralysis; sensation normal; deep reflexes slightly increased; all movements of extremities moderately ataxic; standing and walking difficult; all incoördination typically cerebellar in type; cerebellar asynergia evident. Improvement rapid and in seven weeks after onset of the nervous symptoms was complete.

Reh.[22] Girl, aged seven and a half years. Grippe developing on the fourth day into delirium, yet no unconsciousness, and the child could hear and obey orders given. There was very marked static ataxia, with difficulty in keeping from falling when on her feet. Apparently no other disturbance of motility; sensibility unimpaired; knee-jerks exaggerated; slight rigidity of the neck. Spinal fluid showed no noteworthy alteration. By the seventh day the delirium was replaced by moderate temporary somnolence

[20] Arch. Neurol. and Psych., 1919, **1**, 567.
[21] Jour. Am. Med. Assn., 1920, **74**, 1697.
[22] Arch. d. méd. des enf., 1920, **23**, 362.

and the fever had ceased, By the ninth day the ataxia had disappeared. By the thirteenth day there was some sciatic pain. The patient was out of bed, apparently well, in a month.

It has not been possible to make a search for cases clearly belonging to the present epidemic of encephalitis and which have been reported and are to be classified as perhaps constituting a cerebellar form of this disease. A number of such have been described in adults, as, for instance, by Redlich,[23] and seen in soldiers in whom ataxia of a cerebellar type was present; but I have not read of any in children, although in the vast literature of the present epidemic there are doubtless such on record. There have repeatedly been described during the epidemic instances of a myoclonic form of encephalitis which to a slight degree suggests the tremor seen in some of the reported instances of cerebellar ataxia, but without exhibiting any true ataxia or other symptoms which would form this complex. I have myself seen at least three instances of this condition in children. As already indicated a number of cases have also been described of a choreiform or choreo-ataxic or choreo-athetotic encephalitis, in some of which the movements appear to hold a mid-situation between those of chorea and ataxia. Such cases in children have been reported, for instance, by Roge,[24] Stertz,[25] Zimitz,[26] Massary,[27] R. C. Hamill[28] and others, and one or two have come under my own observation; and Economo[29] in discussing such cases expressed the view that the lesions are especially in the tissues leading from the cerebellum to the thalamus. Cases of this sort, although approaching in symptoms those described in this communication, exhibit other features distinguishing them. All go to support the accepted view that the lesions of encephalitis, epidemic or otherwise, are by no means confined to any one region and that borderline cases must of necessity occur.

It is difficult to give any synoptical account of the onset and course of the disease, since these vary so greatly. The description of an imaginary typical case would read somewhat as follows: The onset is acute, with unconsciousness and absence of speech, these possibly being preceded by initial vomiting or convulsions. The unconsciousness disappears in a few days, yet with this occurrence it is noted that the mentality is not quite normal; that the returning speech is affected in various ways, suggesting difficulty in enunciation rather than in thought; that there is a very decided degree of ataxia of the limbs, and often of the head and trunk; and that the patient cannot walk at all or only with a staggering gait.

[23] Ztschr. f. d. ges. Neurol. u. Psychiat., 1917, **37**, 1.
[24] Bull. et mém. de la Soc. méd. des hôp., 1920, **36**, 246.
[25] München. med. Wchnschr., 1920, **67**, 225.
[26] Wien. med. Wchnschr., 1920, **70**, 474.   [27] Ibid., 542.
[28] Arch. Neurol. and Psych., 1920, **4**, 44.
[29] Wien. med. Wchnschr., 1920, **70**, 475.

Convalescence progresses more or less slowly; less often rapidly, the mentality usually soon becoming normal, the ataxia and disturbance of speech disappearing more gradually, and the case recovering in many instances with little if any trace of the disorder remaining; often, however, with evidences of permanent damage, especially of a psychic nature.

The great variation in symptoms spoken of makes it necessary to review some of them more in detail: Some disturbance of the sensorium has been observed in the majority of the cases. This is often transitory, sometimes long continued, and is of a varied nature. Unconsciousness is comparatively common. It was stated to have been present in 12 of the 31 cases. It is usually of brief duration, but sometimes prolonged, in one instance lasting as long as seven weeks (case of Lüthje). Although it was seen in only the fourth of my personal cases, in this it lasted, with entire immobility, four or five days, and after that a soporose state continued for a decidedly longer time, the condition very strongly suggesting the four instances of epidemic stupor reported by Batten and Still.[30] Convulsions have been reported in but three or possibly four cases. In my fourth case frequently repeated convulsions continued during the first sixty hours.

Vomiting is not common. It was observed in 8 cases, but was only occasional and insignificant. Pain of any sort, oftenest in the head, is distinctly uncommon. It was recorded in only 6 of the 31 cases. Among disturbances of mentality observed other than unconsciousness may be mentioned a lethargic or dazed condition; apathy; delirium; violent and prolonged screaming; a state of fear; a maniacal state; and a diminution of intelligence. Some such affection of mentality was present in 19 of the 31 cases. This has been of variable duration. One of the shortest, in those in which the psyche was affected at all, was in the first patient under my own care, in whom attacks of screaming and a dazed or dull condition of the intellect lasted for more than a week. In some of the cases the continuance has been several months and in not a few others it was still present after several years in the form of mental backwardness and gave promise of being permanent.

Speech was reported affected in 22 of the 31 instances, and I refer only to the condition after any unconsciousness which might have been present had disappeared. In many instances there was for a time entire inability to speak. Later, after the power of speech began to return, utterance remained still far from normal, being described as drawling, or slow, or jerking, or irregular in some way, according to the case. In at least 9 cases speech was entirely absent for a time; and although the continuance of this state was usually brief, sometimes it was decidedly prolonged. Periods of

[30] Lancet, 1918, 1, 636.

one and a half, three, five and six months are on record. One of my own cases did not speak at all for five months. So great a duration of absolute absence of speech is unusual; but, on the other hand, the recovery of perfect speech is generally distinctly delayed. In one of my cases speech had become entirely distinct within seventeen days from the onset while in one of the collected cases it was still abnormal a year after the attack. Other cases give likewise a duration very variable in time. Even as much as three and a half years after the attack the speech was still affected in one case, that of Frederick Taylor, which finally recovered entirely. The slowness with which all speech-defect disappears is shown by the fact that in only 10 of the 22 cases who had disturbance of speech is it indicated that the recovery of it was complete. In the remainder the patients passed from observation with the defect still present to some extent, although in many of these there was nothing but a slight hesitation or slowness remaining. There seems no doubt that in some of the more persistent instances of delay in recovery the trouble was to be assigned, at least in part, to the continuance of a disturbed mental state, and this statement perhaps applies as well to the early entire disappearance of the power of speech; but in the greater number of cases the defects of utterance were of a nature clearly dependent upon incoördination.

A very prominent symptom was ataxia, present in all the cases. It was sometimes slight, and then of later appearance and entirely of less importance than were the cerebral symptoms. In nearly all, however, it has been a very early and prominent manifestation. It affected most frequently the legs, interfering with standing or producing a drunken cerebellar gait. Nearly always the arms were involved as well, and sometimes the head and the trunk. A rhythmic nodding of the head, which might be classed as a manifestation of static ataxia, is recorded in six instances. The degree of ataxia was variable. In some cases it entirely interfered for a considerable time with standing or walking, even as long as twenty-two months in one instance (Frederick Taylor). Generally in the course of a few weeks the power to walk was regained, although with a gait which was decidedly incoördinate. The duration and course of the ataxia progressed to a large degree *pari passu* with the disturbance of speech. In the mildest cases all evidence of it had disappeared within three weeks.

Other symptoms which have been described are less constantly present. In some of the cases in which tremor is mentioned it is doubtful whether this may not have been a manifestation in reality of ataxia. Whatever its indication it has not been seen frequently— in only 6 of the 31 cases in all. Nystagmus was peculiarly marked in 2 of my own cases and absent in 2. Taking all the 31 reported cases as a group, nystagmus was observed in 10 instances. Strabismus was seen in 5 or possibly 6 instances. Optic neuritis was found

in but 2 cases. Loss of sphincter control was observed in 3. "Loss of power" or "paresis" has been reported in a number of instances. It was not present in the sense of paralysis in 3 of my 4 cases, and in the remaining 1 was no more than hypotonia lasting during the comatose phase of the attack. It is extremely likely that in nearly all instances which have been observed it is in reality a loss of control, not of power. The reflexes as represented by the knee-jerks are active or normal so far as any reports have been made on the subject by the writers. This was the condition mentioned in 17 instances. Ankle-clonus has occasionally been found—4 cases in all. Vertigo or dizziness has, as a rule, not been reported. It was complained of slightly in 2 of my own cases, but there has been mention of its presence in but 1 other. Still, with the presence of ataxia in every case and with the youth of the patient precluding any very accurate description by him, it is difficult to determine just what influence vertigo may have had in the production of the staggering gait. It is reasonable to conclude that, apart from the ataxia, vertigo may have shared in the action in some instances. Disturbance of sensibility has been rarely reported, anesthesia being mentioned only once.

The age of the 31 patients ranged from three to twelve years, 18 of them being six or more years old. The immediate causes of the disease without reference here to the actual nature of the affection itself have been varied. The occurrence of some infectious disorder appeared to have been the precursor in 24 of the 31 cases, measles immediately preceding in 8, influenza in 5 and typhoid fever in 4. It is interesting to note that 3 of the typhoid fever cases occurred in children of one family (Lüthje). In all of the 24 cases the encephalitis immediately followed upon or developed during the infectious disease. In 1 case dysentery was the precursor, and this might perhaps with reason be included among the cases of infection. In another case the attack was preceded by trauma of the head, but just what the etiological relationship may have been is uncertain. In 4 instances there had been no previous illness observed. As to the sex, 17 of the patients were females and 12 males and in 2 no statement is made.

The nature of the affection is naturally of the greatest interest. There appears to be no question that it is an encephalitis, and also that it is a process not limited to any one portion of the brain. Symptoms other than those supposedly cerebellar have been seen in practically every case referred to in this report. Fever, unconsciousness, delirium, convulsions and the like, which may occur, certainly cannot be called cerebellar symptoms, nor can the various later alterations of the mentality. After the unconsciousness passes away the presence of the cerebellar symptoms becomes manifest. The absence of speech, at first probably cerebral, is replaced later by various affections of utterance, which indicate in most instances,

as I have said, rather a lack of control, although mental defect may have had some influence in others.

The possible relationship of the disease to the epidemic encephalitis which is now so prominently before our attention is of great interest. With an increasing knowledge of the numerous types of this latter disorder it would appear very probable, as I have already stated, that in many instances of this cerebellar symptoms are naturally to be expected. As a matter of fact we do know that the lesions of lethargic encephalitis, which affect predominatingly the gray matter at the base of the cerebrum, may involve also the cerebellum or other regions. So far as the cases now under consideration are concerned it must be said that they have occurred for the most part independently of any epidemic, in connection with various other possible causes, and cannot be attributed to an encephalitis of any specific microbic nature.

We know little regarding the actual lesions which were present in any of the 31 cases, for the reason that only 2 of them came to autopsy, and that this was years later, death being preceded by symptoms of mental failure. The prognosis, therefore, as to survival is good, but that of complete recovery is far more uncertain. In my first case recovery was complete in one month, while in one of the cases observed by E. S. Taylor the child was well in three weeks. Complete recovery in less than six months was reported in 8 instances and nearly complete recovery in less than one year in 3. The case reported by Frederick Taylor still showed symptoms three and a half years after the onset, but none when an examination was made twenty years after the attack. It is evident, therefore, that we must be guarded before making a decision that progress toward recovery has fully ceased. A total duration of three or four months might perhaps be assumed as an average for the more acute symptoms, but this is only an approximation. In about one-third recovery was absolutely complete when the patient was last seen, while in some others it was almost entirely so when the last note was made, and in still others we may fairly assume that complete recovery soon took place. In quite a number of instances, however, we are in doubt as to the final disappearance of symptoms, and in certain of these the symptoms might be expected to persist for certainly a long time, and perhaps even permanently. The disquieting element is that in about one-quarter of the cases there was at the last observation some evidence of mental defect.

CLINICAL STUDIES IN FUNCTIONAL DISTURBANCES.

STUDY I.   FUNCTIONAL THYROID TESTS AS AN AID TO DIFFERENTIAL DIAGNOSIS.[*]

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Introduction.   During the past few years a great deal of interest has been centered upon the use of various functional tests as aids to the clinician in the diagnosis of suspected thyroid disease and as a measure of the degree of thyroid activity where a functional disturbance of this gland has been recognized to exist. The tests of thyroid function which have found widest application are the estimations of the basal metabolic rate, the glucose tolerance and the adrenalin sensitivity.

Our purpose in offering the ensuing study was to correlate these three tests in disturbances of the thyroid and to note the results of their use in other endocrinopathies and various conditions of chronic disease. Heretofore no study based on the joint application of all these tests has been made, although there have been many published in which one or two have been used.

While it is not the purpose of this paper to present a complete bibliography, it is not perhaps amiss to recall some of the more important contributions to this subject.

Bibliography.   BASAL METABOLISM.   It has become a generally accepted teaching, as a result of the extended researches of numerous competent workers, that the basal metabolic rate is a reliable index of the degree of thyroid activity. Thus, Means[1] states in a recent publication: "So characteristic of thyroid disease are changes in the basal metabolism that, personally, I believe that in the metabolism level we have a functional test of that gland, increase meaning hyperthyroidism and decrease meaning hypothyroidism, provided, of course, that other diseases that alter basal metabolism are excluded." The above sentence summarizes well the feeling of numerous others who have made use of this test. DuBois,[2] Boothby,[3] McCaskey[4] and Sandiford[5] have all subscribed to the same view. Peabody, Wearn and Tompkins[6] are of the opinion that a normal metabolic rate is sufficient evidence in itself to eliminate a previous diagnosis of hyperthyroidism.

[*] Read before the American Climatological and Clinical Association, June, 1920.

GLUCOSE TOLERANCE. A vast amount of work has been carried out in recent years on the utilization of glucose in various conditions, and it is the opinion of most workers that alimentary hyperglycemia occurs in almost every case of hyperthyroidism. Hamman and Hirschman,[7] Denis and Aub,[8] Janney,[9] McCaskey[10] and Lueders[11] are among those who have contributed toward forming this conclusion.

ADRENALIN SENSITIVITY. Numerous observations, alike of clinicians and physiologists, lend support to the view that the active principle of the thyroid sensitizes the sympathetic nerve-endings to the action of adrenalin. Foremost among the American workers in this field are Goetsch,[12] Barker and Sladen,[13] Cannon and Cattell[14] and Levy.[15][16] A good working bibliography and a brief theoretical discussion are presented in Goetsch's paper. Since the appearance of his work the adrenalin sensitivity test has been widely used in this country, though the conclusions reached as to its diagnostic significance have not always agreed with those of Goetsch himself. In this country Peabody and his associates showed that 60 per cent of cases of "irritable heart" in soldiers reacted positively to adrenalin.[17] They confirmed Goetsch's statement that normal subjects are not sensitive to the dosage employed (0.5 c.c. of 0.001 solution of adrenalin chloride or its equivalent in the solid form). The normals studied by Peabody and his associates were soldiers in training. O'Hare[18] showed that cases of hypertension exhibit a definite hypersensitiveness to adrenalin, although the type of response is not identical with that obtained by Goetsch and others in cases of hyperthyroidism. Boothby and Sandiford[19] find that there is no relationship between the character of the adrenalin reaction and the degree of thyroid activity. Woodbury[20] alone thinks that there are certain cases of thyrotoxicosis, dependent upon toxic adenomata, which, while showing hypersensitiveness to adrenalin, may present no increase in the basal metabolic rate. His ideas are identical with those of Goetsch,[21] though the latter did not make any estimations of the basal metabolism in the cases which he reported. A few foreign writers have made contributions to the subject, notably Ramon Turro,[22] Bernard[23] and Troell,[24] whose ideas are strikingly similar to those of Goetsch and Woodbury.

Methods. In order to secure a clinical impression independent of the results of the functional tests a complete history was taken of every case and a careful physical examination recorded. In all cases the blood-urea nitrogen was determined, and in most cases blood counts, urinalyses and Wassermann tests on the blood serum were carried out.

BASAL METABOLISM. The portable respiration apparatus devised by Benedict[25][26] was used in making all the determinations recorded in this paper. The calculation of the basal metabolic rate was based entirely on the oxygen consumption. The standard method of

determining surface area was employed as outlined by DuBois,[27] while the standards of sex and age were taken from *Clinical Calorimeter*, Study XXX.[28] We had the opportunity of controlling this method with others in two instances in which the variation proved to be less than 5 per cent, a fact which makes us feel that this method in our hands was sufficiently accurate for clinical purposes. Furthermore, the results obtained conformed very well to the clinical impression of the cases and were borne out by their subsequent progress. The operation of the apparatus, while not tedious or complicated, offers a few technical difficulties which must be constantly borne in mind in order to secure accurate and uniform results.

GLUCOSE TOLERANCE. A slight modification of the technic employed by Janney was used for the determination of the glucose tolerance. Samples of blood and urine were taken on a fasting stomach. The patient was then given an amount of glucose corresponding to 1.75 grams per kilo of body weight. This was administered orally in a 40 per cent aqueous solution flavored with the juice of a lemon, which was prepared the night before and kept in the ice-box. The blood sugar was determined on the fasting specimen and again two hours after the administration, and the urine tested for sugar hourly over a period of four hours. The blood sugar was determined by Myers's[29] modification of the Lewis and Benedict method. For the purpose of describing in a roughly quantitative fashion the degree of intolerance exhibited to glucose we have made use of the following arbitrary scale:

Plus minus (±), a reaction of doubtful significance.

1. Two-hour blood sugar more than 150 mgm. and less than 200 per 100 c.c. of blood—no glycosuria.

2. Two-hour blood sugar less than 150 mgm. with glycosuria (trace) in one specimen.

One plus (+), a slightly positive reaction.

1. Two-hour blood sugar less than 150 mgm. with definite glycosuria in more than one specimen (traces, not complete reduction).

2. Two-hour blood sugar more than 200 mgm. without glycosuria.

Two plus (++), a moderately positive reaction. Two-hour blood sugar less than 200 mgm. with glycosuria (complete reduction) in more than one specimen.

Three plus (+++), a strongly positive reaction. Two-hour blood sugar more than 200 mgm., with complete reduction in more than one specimen.

ADRENALIN SENSITIVITY. The sensitivity of all patients to adrenalin was determined by the subcutaneous injection of 0.5 c.c. of a 1:1000 solution of adrenalin chloride (Parke, Davis & Co.), the effect on pulse and blood-pressure being noted, and observations taken on the subjective and objective response in accordance with the technic recommended by Goetsch.[12] While no physiological tests were made to assay the strength of the solutions used, the frequency of positive responses was considered sufficient proof of

their activity. During the later tests a rest period of at least one-half hour was employed, in order to bring the pulse and blood-pressure to a steady base line and to observe the effect of a subcutaneous injection of 0.5 c.c. sterile water. All the tests in this series except

TABLE I.—Hyperthyroid cases

Key to column headings on tables: Basal metabolism test:
Weight: Figures given represent net weight in kilograms.
Calories: Figures given represent calories per square meter per hour.
Metabolism: Figures given represent percentage variation from normal for an individual of same age and sex.

The column headings under the glucose tolerance test represent time intervals following administration of glucose.

Figures under columns entitled pulse, blood-pressure (systolic and diastolic), and respiration represent values obtained before injection of adrenalin (figure to left of oblique line) and the maximum rise or fall following the injection (figure to right of line). By this graphic method the maximum rise of pulse, systolic blood-pressure and respiratory rate can be readily noted in each individual case as well as the maximum drop in diastolic pressure.

The degree of subjective and objective change following the adrenalin injection is noted by the number of plus signs in the columns entitled subjective and objective respectively, the scale running as follows: Plus-minus, doubtful; one plus—slightly noticeable; two plus—definite; three plus—marked.

N. D. = Not done.

V. = Vascular type of response; described elsewhere by O'Hare.

twelve were carried out by the same observer in order to eliminate as far as possible differences in interpretation. As was done in the case of the glucose tolerance test, an arbitrary scale was established in order to quantitate approximately the degree of response as follows:

Plus minus ($\pm$), cases showing a degree of response probably within the limits of normal:

1. Rise of pulse or blood-pressure, or both, of more than ten points, without evidence of much subjective or objective disturbance.

INITIALS	SERIES NUMBER	LAB. NUMBER	AGE	SEX	BASAL METABOLIC RATE				GLUCOSE TOLERANCE TEST							ADRENALIN SENSITIVITY TEST							REMARKS
					BUCCAL TEMPERATURE	WEIGHT	CALORIES	METABOLISM	BLOOD		URINE					BLOOD PRESSURE		PULSE	RESPIRATION	OBJECTIVE	SUBJECTIVE	INTERPRE-TATION	II HYPOTHYROID CASES
									FASTING	2 HOURS	FASTING	1 HOUR	2 HOURS	3 HOURS	4 HOURS	INTERPRE-TATION	SYSTOLIC	DIASTOLIC						
S G	1	135	36	♀	97.0	164.0	27.9	−20	90	200	O	O	O	O	O	O					−	−	N.D.	Myxœdema
L C	2	179	46	♀		130	27.3	−24	90	80	O	O	O	O	O	O					−	−	N.D.	Migraine Menopause
E M	3	146	44	♀	98.0	59.0	25.2	−35.7	−	−	−	−	−	−	−	N.D.					O	O	O	Myxœdema
M T	4	174	30	♀	97.3	59.5	30.7	−19	110	160	O	−	CR	Tr	O	++					++	++	++	Migraine
T C	5	179	19	♂	97.0	437	34.5	−35	90	80	O	O	O	O	O	O					++	++	+++	Thyroid Adenomata Puberty
R S	6	85	45	♀	98.1	173	34.7	−36	90	90	O	O	O	O	O	O					±	±	±	Migraine Menopause
E A	7	123	48	♀	97.0	61	29.7	−33	100	100	O	O	O	O	O	O					++	++	++	Menopause
B M	8	221	11	♂	99.0	320	30.0	−25	100	60	O	O	O	O	O	O					−	−	N.D.	Cretinism
R W	9	227	74	♀	98.0	130	31.0	−43	100	110	O	Tr	Tr	O	O	+					+	+	+V	Hypothyroidism Arterio-sclerosis
H	10	234	29	♀	99.0	190	29.0	−20	110	110	O	O	O	O	O	O					++	++	++	Migraine
S A	11	246	42	♀	98.0	160	27.6	−23	100	190	O	O	O	O	O	O					−	−	N.D.	Manorrhagia
M C	12	186	43	♀	97.0		26.2	−28.5	90	110	O	O	O	O	O	O					++	+	++	Post-infectious Fatigue
H K	13	192	48	♀	98.0		24.8	−39	140	250	O	CR	CR	CR	O	+++					±	O	O	Migraine Menopause

TABLE II.—Hypothyroid Cases

2. Slight subjective and objective disturbance without perceptible rise of pulse and blood-pressure.

One plus ($+$), slightly positive response. Rise in pulse and blood-pressure of over ten points, with slight but definite subjective and objective disturbance.

INITIALS	SERIES NUMBER	LAB. NUMBER	AGE	SEX	BASAL METABOLIC RATE				GLUCOSE TOLERANCE TEST							ADRENALIN SENSITIVITY TEST							REMARKS
					BUCCAL TEMPERATURE	WEIGHT	CALORIES	METABOLISM	BLOOD		URINE					BLOOD PRESSURE		PULSE	RESPIRATION	OBJECTIVE	SUBJECTIVE	INTERPRE-TATION	III FATIGUE CASES
									FASTING	2 HOURS	FASTING	1 HOUR	2 HOURS	3 HOURS	4 HOURS	INTERPRE-TATION	SYSTOLIC	DIASTOLIC						
L R	1	169	39	♀	98.0	54.2	39.5	+7	120	190	O	O	O	O	O	±					+	+	+	Thyroid Adenomata Thyroidectomy
M H	2	177	27	♀	97.4	410	38.5	+4	100	−	O	Tr	Tr	Tr	O	±					±	+	±	Thyroid Hyperplasia Visceroptosis
R R	3	133	36	♀	98.0	54.5	37.2	O	130	110	O	Tr	Tr	O	O	+					++	++	++	Slight Thyroid Hyperplasia
M D	4	168	23	♀	98.8	52.8	31.3	−16	90	180	O	O	Tr	O	O	+					++	+	++	Thyroid Hyperplasia
C T	5	169	26	♂	97.0	67.0	42.8	+9	100	100	O	O	Tr	O	O	±					++	++	+++	Thyroid Hyperplasia
R D	6	189	30	♀	97.0	64.5	37.7	+3	100	100	O	O	O	O	O	O					++	++	+++	Thyroid Slightly Enlarged Visceroptosis Post-influenza
A M	7	190	25	♀	98.6	44.7	26.4	−26	100	160	O	Tr	CR	O	O	+++					++	++	+++	Gastric Ulcer Thyroid not enlarged
H J	8	195	30	♀	99.0	57.0	32.1	−13	80	70	O	O	O	O	O	O					+++	++	+++	Thyroid Hyperplasia Menorrhagia
L C	9	214	34	♀	97.4	61.0	33.5	−13	−	−	−	−	−	−	−	N.D.					+	+	+	Thyroid Adenomata
B M	10	225	35	♀	99.0	50.0	34.0	O	100	100	O	O	O	O	O	O					+	++	+++	Post-influenzal Convalescence
P D	11	196	30	♂	97.8	64.9	37.4	−9	110	90	O	O	O	O	O	O					++	++	++	Post-influenzal Convalescence Neplasia
P K	12	197	21	♂	98.4	54.3	35.5	−10	100	90	O	O	O	O	O	O					+	+	++	Effort Syndrome
P R	13	204	34	♂	99.4	73.7	40.7	+36	120	100	O	Tr	CR	Tr	O	+++					+	+	+	Anginal Attacks
M R	14	247	34	♀	95.8	55.0	28.6	−21	100	90	O	O	O	O	O	O					++	++	++	Tachycardia
E V	15	188	34	♀	99.2	47.2	33.5	−4	90	260	O	O	CR	Tr	O	+++					++	++	++	Thyroid Hyperplasia

TABLE III.—Fatigue Cases.

Two plus ($++$), definitely positive response. Rise in pulse and blood-pressure of over twenty points, with increased degree of sub-

jective and objective disturbance to the point of considerable discomfort for the patient.

Three plus (+++), strongly positive response. Rise in pulse and blood-pressure of over thirty-five points with an alarming degree of subjective and objective disturbance.

INITIALS	SERIES NUMBER	LAB. NUMBER	AGE	SEX	BUCCAL TEMPERATURE	WEIGHT	CALORIES	METABOLISM	BLOOD FASTING	BLOOD 2 HOURS	URINE FASTING	URINE 1 HOUR	URINE 2 HOURS	URINE 3 HOURS	URINE 4 HOURS	INTERPRETATION	SYSTOLIC	DIASTOLIC	PULSE	RESPIRATION	OBJECTIVE	SUBJECTIVE	INTERPRETATION	REMARKS
IM	1	39	27	♀	98.0	69.8	36.5	-1	130	180	0	Tr	Tr	0	0	+	153/123	80	76	-/-	++	++	+++	Hypertension
HP	2	81	41	♀	98.0	87.9	35.5	+1	100	180	0	0	CR	CR	Tr	++	153/139	66	112	24	++	++	++	Hyperthyroidism Improved
IO	3	124	34	♀	97.0	47.0	42.0	+14	130	150	0	0	0	0	0	O	122/134	72	104/124	22/22	+	0	±	Vertigo No Organic Disease
AG	4	131	42	♀	98.2	37.3	35.5	-2	100	110	0	0	0	0	0	O	94/152	69/58	53/106	21	++	+	++	Hyperthyroidism cured Gastric Ulcer
ND	5	134	40	♀	97.6	60.5	35.7	-1	90	100	0	0	0	0	0	O	96/173	66/82	144/112	33/36	++	++	++	Arterio-sclerosis Anginoid Attacks
SB	6	140	45	♀	99.4	46.9	41.2	+12	90	120	0	CR	Tr	0	0	+	153/173	86/82	76/132	18/22	±	0	±	Pulmonary Tb Hypertension
EJ	7	153	43	♀	98.4	72.0	31.4	-19.3	-	-	-	-	-	-	-	ND	192/191	80/70	76/10	-/-	+	+	+	St Hypertension Thyroid Adenomata
ES	8	156	34	♀	99.6	48.0	40.9	+12	90	110	0	0	0	0	0	O	112/136	72/70	90/76	20/28	++	+	+	Raynaud's Disease
WV	9	160	36	♂	98.0	79.5	40.2	+2	110	100	0	0	0	0	0	O	110/104	72/70	78/70	20/20	0	0	0	Bronchial Asthma
HH	10	163	32	♀	98.0	63.0	35.0	-4	90	100	0	Tr	Tr	0	+	134/140	70/70	44/104	20/16	++	++	++	Chr Appendicitis
AM	11	167	49	♀	98.4	70.0	36.5	+1	110	130	0	0	0	0	0	O	130/153	78/84	76/96	22/26	±	±	±	Menopause
ME	12	175	51	♀	98.6	55.8	39.3	+11	100	150	0	0	0	0	0	O	-/-	-/-	99/-	20/-	0	0	0	Sinusitis
EW	13	177	51	♂	98.0	68.2	38.4	+1	90	90	0	0	0	0	0	O	-/-	-/-	60/-	20/-	-	-	ND	Chr Alcoholism
MS	14	178	22	♀	91.8	86.8	28.3	-24	100	140	0	0	0	0	0	O	96/104	73/76	72/108	24/23	++	++	++	Gastric Neurosis
CK	15	180	28	♀	99.0	39.5	41.5	+13	100	160	0	Tr	CR	Tr	0	++	112/123	64/53	80/91	13/20	+	±	±	Raynaud's Dis
AD	16	182	52	♀	97.0	46.4	32.8	-6	100	125	0	0	0	0	0	O	100/160	64/62	68/104	21/16	+	±	V	Pulmonary Tb Arterio-sclerosis
FH	17	183	23	♀	99.0	66.5	38.4	+4	90	115	0	0	0	0	0	O	118/126	64/58	80/120	21/26	++	+	+	Gastric Neurosis
OD	18	199	28	♀	98.4	77.0	36.0	-2.7	125	125	0	0	0	0	0	O	96/121	56/49	72/96	22/30	++	++	++	Chr Anaemia Cholelithiasis Amenorrhoea
BA	19	201	30	♀	97.0	65.6	31.0	-16.3	100	160	0	0	0	0	0	±	119/123	79/75	76/92	22/22	++	++	+	Periodical Amenorrhoea
AV	20	202	29	♀	98.0	45.7	37.3	+1	110	110	0	CR	0	0	0	+	104/126	65/52	72/92	18/22	++	++	++	Dysmenorrhoea with Associated Tetany
VE	21	205	33	♀	98.6	49.4	31.3	-14	90	250	0	CR	CR	CR	0	+++	102/139	58/50	104/146	14/16	++	++	+++	Mucous Colitis
LH	22	207	32	♂	98.2	52.6	39.4	0	90	220	0	CR	CR	CR	0	+++	119/133	70/66	64/109	16/30	+	+++	+++	Paroxysmal Tachycardia
BR	23	208	27	♀	98.6	62.0	39.7	-5	110	110	0	CR	-	-	Tr	++	174/164	64/46	64/100	21/26	++	+	++	Exoph. Goitre After Thyroidectomy
AS	24	210	19	♀	98.2	59.8	33.2	-13	110	90	0	0	0	0	0	O	110/138	80/36	80/112	14/20	+	+	+	Adolescent Goitre Eczema Hay Fever
RV	25	214	35	♀	99.0	61.0	36.2	-1	130	125	0	0	0	0	0	O	126/158	88/54	84/96	14/16	+	±	+	Charcot's Bile Abscess Pre Pancreatic & Prostatic
NN	26	219	49	♀	97.8	35.0	39.0	+10	100	90	0	0	0	0	0	O	140/166	80/72	76/100	10/14	0	0	V	Arterio sclerosis
MV	27	230	31	♀	98.2	57.0	36.7	0	110	80	0	0	0	0	0	O	110/116	66/74	74/109	14/34	++	++	++	Pulmonary Tb
PZ	28	236	30	♀	98.9	80.0	31.5	-14.4	150	130	0	Tr	0	0	0	±	111/134	72/70	76/104	16/14	+	+	+	Obesity
MC	29	237	22	♀	98.6	42.0	37.6	+2	110	110	0	0	0	0	0	O	92/103	60/72	72/114	13/14	±	+	+	Duodenal Stenosis
HB	30	238	49	♀	97.8	58.0	30.5	-14	100	80	0	0	0	0	0	O	90/110	50/60	60/70	18/20	++	++	++	Thyroid Adenomata Menopause
EB	31	242	26	♂	97.4	70.5	35.7	-14.7	110	80	0	0	0	0	0	O	104/150	66/46	64/90	18/14	++	++	++	Idiopathic Epilepsy
DB	32	240	21	♀	98.4	76.3	29.5	-20	110	140	0	0	0	0	0	O	90/116	58/46	76/96	16/14	+	+	+	Amenorrhoea Chronic Hyperthrosis
FB	33	253	23	♀	98.0	45.0	31.6	+6	100	140	0	0	0	0	0	O	100/146	63/58	80/104	13/16	++	++	++	Visceroptosis
CC	34	236	30	♀	98.0	70.5	30.0	-20	110	110	0	0	0	0	0	O	100/116	72/58	90/104	16/16	+	+	+	Migraine
LH	35	145	30	♀	97.0	43.6	33.6	-9	120	110	0	Tr	0	0	0	±	132/196	70/70	84/84	22/22	±	±	±	Syphilis of C.N.S.

TABLE IV.—Miscellaneous cases.

Clinical Groupings. HYPERTHYROIDISM. All cases in this group may be classified under two headings: (*a*) True exophthalmic goiter and (*b*) toxic adenomata without exophthalmos. They all without exception presented a majority of the signs and symptoms ordinarily considered cardinal in the diagnosis of thyrotoxicosis (exophthalmos, restlessness, tachycardia, tremor, loss of weight and hyperhidrosis).

HYPOTHYROIDISM. Among the cases listed as hypothyroidism are included three in which an unqualified diagnosis of myxedema could be made clinically. The remainder, while presenting certain

findings suggestive of thyroid insufficiency, were not diagnosed until functional tests were carried out and the administration of thyroid extract had effected a disappearance or amelioration of the predominating symptoms.

FATIGUE CASES.   We have considered it excusable to describe certain cases under this heading because of the predominance of subjective and objective fatigue in the clinical picture, and in spite of the fact that they cannot be classified among the recognized clinical entities.   In this conception we do not claim priority, as Rogers[30] has already recognized the syndrome.   We believe that most of these cases are identical with those described by Goetsch as cases of latent hyperthyroidism of a type hitherto unrecognized. They usually present in addition to subjective and objective fatigue, perceptible thyroid enlargement, labile pulse and vague symptoms ordinarily described as neurasthenia.   Two of the cases showed palpable nodules in the thyroid while in three no enlargement could be demonstrated.   One classical case of effort syndrome is included in this series.

MISCELLANEOUS.   In this large and motley group we have placed cases which were studied with a view to the elimination of possible disturbance in the endocrine system.   In some of them the existence of thyroid disturbance had been established at some previous period; in others clinical evidences of pluriglandular disturbance were present, though the variations in clinical findings preclude the possibility of placing them in definite categories; in a few all evidence of endocrine disease was found lacking and the presence of organic disease established, while another small group may be classed as essentially normal.

Discussion.   In looking over the records of the cases here presented it appears quite evident that ordinary careful clinical methods are entirely satisfactory from a diagnostic standpoint in all cases of frank hyperthyroidism.   However, in four of these cases (171, 215, 232 and 235) functional tests proved of distinct value in confirming a strong clinical impression of mild thyrotoxicosis.   In the general run of cases these tests showed their greatest value in allowing a quantitative estimate of the degree of intoxication and in forming a basis for studying the effect of treatment.

A glance at Table I should convince any impartial critic that the only functional test showing an invariably positive response in cases of hyperthyroidism is the basal metabolism.   However, it is evident that any subject of thyrotoxicosis must pass through an incipient stage in which functional tests might be expected to yield negative results.   Our attention was directed to this possibility by the behavior of one case in particular (215) whose basal metabolic rate was plus 6 per cent at a time when several clinicians were convinced that her symptoms were due to hyperthyroidism.   One month later subjective and objective signs had increased and her basal metabolic rate was found to have risen to plus 17 per cent.

Alimentary hyperglycemia and glycosuria have been found to be consistently present in hyperthyroidism, but inasmuch as these are also found to occur in other conditions, where their presence is sometimes difficult to explain, their value as specific tests of thyroid function is correspondingly diminished.   Several workers have called attention to a characteristic blood-sugar curve occurring in hyperthyroidism, i. e., a rapid rise in the blood sugar to a moderately high level followed by a rapid fall to the fasting level, as contrasted with the slow rise and fall which is common to diabetes.   It has been suggested that this type of reaction is due to a rapid mobilization of sugar and that it is another manifestation of accelerated metabolism.   Although we have not considered it necessary to make hourly blood-sugar determinations, we have noticed the tendency for glycosuria to occur usually within the two hours following the administration of glucose and for many cases to have a normal or nearly normal blood sugar at the end of two hours.   The cases which showed this reaction most strikingly did not necessarily show an excessively heightened metabolism.   In fact, there was no close agreement between the basal metabolic rate and the degree of intolerance to glucose.   Thus, whereas five cases showed negative sugar reactions and a maximum basal metabolic rate of plus 36 per cent, six other cases whose metabolism was less than plus 36 per cent showed positive sugar reactions.   In one case (255) the response was very marked, although the basal metabolism was only plus 15 per cent.   It is to be noted, however, that this curve was similar to that described in potential diabetes, although no other evidence of the condition was found in this case.

In the adrenalin sensitivity test there was no direct relationship established between the intensity of the reaction and the basal metabolic rate.   In fact, some of the strongest adrenalin reactions were observed in which the metabolism was less than plus 25 per cent, and *vice versa*.   Two cases having a basal metabolic increase of over 50 per cent showed a reaction to adrenalin which, according to the standards proposed by Goetsch, would be construed as negative.

As far as a comparison can be drawn between the glucose tolerance test and the adrenalin sensitivity, it may be said that in looking over the hyperthyroid series some degree of similarity may be traced in the results observed.   This correspondence, however, is not constant and is not sufficiently marked to allow an accurate forecast of the result of one of those tests in a given individual on the basis of the response observed to the other.

It will be noticed that several of the positive adrenalin reactions are designated as vascular in type.   By this is meant that the rise observed in pulse and blood-pressure was not as sustained as in the cases showing the type of response alleged to be typical of hyperthyroidism.   In the hyperthyroid group three of the four showing

a vascular response had no hypertension, although showing evidence of bloodvessel disease, whereas three cases of hypertension showed the typical sustained rise of pulse and blood-pressure, this rise being equally high with that noted in the vascular type (rise in the systolic pressure of at least fifty points).

One noteworthy observation that is suggested by a study of the records in the hypothyroid group is that the glucose tolerance test was found to be distinctly positive in only two cases, both of which showed severe headache of the migraine type as the only symptom. In one of these the evidence was very suggestive of associated pituitary disease. On the other hand, of those which were subjected to the adrenalin test, 55 per cent showed a definitely positive response. These cases were all distinctly improved by the administration of thyroid extract. We regard this fact as the strongest clinical evidence hitherto adduced that the adrenalin test in itself affords no criterion of the presence or absence of thyrotoxicosis. No correspondence could be established between the basal metabolic rate in these cases and the response to glucose and adrenalin.

Among the fatigue cases it will be noted that in 40 per cent the basal metabolic rate was minus 10 per cent or less while in the remainder it fell within normal limits. In no case was an increased metabolism demonstrated. We feel that at the present time it is impossible to say whether or not these cases which show a lowered metabolism are definitely hypothyroid, as we have not had the opportunity to carry the therapeutic test to a satisfactory conclusion. In one case (190) in which the basal metabolic rate was minus 26 per cent and the response to adrenalin distinctly positive, thyroid extract was tolerated well and was administered long enough to bring the metabolism to normal—a change which was unaccompanied by improvement in her clinical condition. Goetsch[21] and Woodbury[20] have recently advanced the view that cases of this type show clinical improvement following thyroidectomy, and state that the excised glands show a picture of diffuse adenomatosis with an increase in the mitochondrial content of the cells and other signs of increased functional activity. We are therefore watching our cases with eagerness for the development of clinical evidences of hyperthyroidism—the more so because with one exception all of them responded positively to adrenalin.

In view of the magnificent quantitative work of Kendall[31] and Plummer,[32] which has shown the definite relationship between thyroxin and the basal metabolic rate, it does not seem rational to make a diagnosis of hyperthyroidism, in the absence of the classical symptoms and signs of this condition, when the basal metabolism is within normal limits. The possibility of the existence of a second active principle in the thyroid gland, independent of thyroxin and with a different physiological action, has been suggested. Up to

the present time there is not sufficient clinical or physiological evidence to afford this theory much support. Although both Goetsch and Woodbury claim clinical improvement in almost all their cases following thyroidectomy, in no instance had their patients been followed over a period exceeding nine months. Furthermore, we do not feel that the degree of subjective improvement reported is sufficiently striking, in the absence of careful control by direct personal observation and the repeated use of functional tests, to justify any dogmatic statement on this most important point. Particularly is this true since the psychological effect of operation and the recognized value of a subsequent rest period might together be sufficient to produce a definite, if temporary, amelioration of symptoms. We must not be unmindful of the danger of hypothyroidism developing in these cases as a result of thyroidectomy. As far as we know no report has yet been published of basal metabolic estimations following these operations.

In regard to the glucose tolerance test 20 per cent of the fatigue cases showed a moderately and another 20 per cent a slightly diminished tolerance, while the rest showed doubtful or negative reactions. No relationship could be demonstrated between this response and the basal metabolism or adrenalin sensitivity tests.

In the large and varied miscellaneous group a few points of interest are to be noted: One case only (173) showed a decided increase of the basal metabolic rate. This patient had a definite pan-sinusitis and showed no clinical evidences of hyperthyroidism or of disease of any other endocrine organ. Five cases showed increases of from 10 to 13 per cent; 2 of these were cases of Raynaud's disease, 1 of active pulmonary tuberculosis, 1 of vertigo of vestibular origin and 1 of arteriosclerosis with menopause. Three of these were individuals of unusually short stature, while with one exception they all showed an exceptionally poor state of nutrition. These facts may in part account for an apparent slight increase in their basal metabolic rate. On the other hand 11 cases showed a decrease in the metabolic rate of from 12 to 24 per cent. Of these 8 were considered to be possible hypothyroid cases and were given thyroid gland. They were left, however, in the miscellaneous group because the period of observation was not considered long enough to warrant a final diagnosis of hypothyroidism. Of this small group of 11 cases showing decreased metabolism 4 were distinctly sensitive to adrenalin and 5 slightly so, the remaining 2 giving a questionable response.

Five cases in the whole miscellaneous group showed distinct intolerance to glucose, 2 of which were clinically well following definite hyperthyroidism. One case had Raynaud's disease, 1 paroxysmal tachycardia and 1 mucous colitis.

In regard to the adrenalin sensitivity test, excluding those cases showing a decreased metabolism, 40 per cent showed a dis-

tinctly positive response and 20 per cent a mild one. Thus on cal-
culating the number of definitely positive responses to adrenalin
in the whole series of 85 cases we find that there were 40, (47 per
cent). Of these 10 were seen in the hyperthyroid group (45 per
cent), 5 in the hypothyroid group (38 per cent), 10 in the fatigue
group (66 per cent) and 15 in the miscellaneous group (45 per cent).
On the basis of these figures we consider that the phenomenon of
hypersensitivity to adrenalin may occur in a variety of disease
conditions which have not as yet been exhaustively studied from
this angle.

Summary and Conclusions. A clinical and functional study is
presented of 85 cases showing symptoms either definitely attrib-
utable to disturbance of the endocrine glands, particularly the
thyroid, or not readily explainable on any other basis.

The functional tests employed were the basal metabolism, glucose
tolerance and adrenalin sensitivity tests.

The cases studied were divided into four groups: hyperthyroid,
hypothyroid, fatigue and a large miscellaneous group.

Clinical methods were found satisfactory in the diagnosis of frank
hyperthyroidism, myxedema and to a lesser extent in the third and
fourth groups. In apparent hypothyroidism—not myxedematous
in type, however—the ordinary clinical methods usually failed to
suggest the probable diagnosis. In such cases the diagnosis was
made entirely on the basis of a decreased basal metabolic rate,
together with definite improvement after the administration of
thyroid extract.

Of the functional tests used the basal metabolism was the only
one to yield uniform results, which could be reasonably interpreted
in association with the clinical findings and subsequent progress of
the cases studied. As a result of this study it is our firm conviction
that an apparatus for the determination of the basal metabolic
rate is indispensable in a diagnostic clinic. We share the belief of
other workers that this test affords the best index of the degree of
thyroid activity.

Both of the other tests yielded positive results in almost all cases
of hyperthyroidism, but the frequency of similar responses in a
variety of other conditions, in some of which the diagnosis of hyper-
thyroidism was not even a remote possibility, necessarily detracts
from their value as specific tests of thyroid function.

Special emphasis is laid on three points brought out by the data
here presented. These are: (1) That there are some cases showing
definite hypersensitiveness to adrenalin and intolerance to glucose
who tolerate thyroid extract well and improve under its administra-
tion; (2) that it is dangerous to attribute much importance to a
positive adrenalin response in the diagnosis of suspected hyper-
thyroidism; and (3) a corollary of the point just mentioned that
an occasional case of classical exophthalmic goiter showing marked

increase of the basal metabolic rate may exhibit no hypersensitiveness to adrenalin.

We wish to take this opportunity of expressing our appreciation to the physicians and surgeons of the Buffalo General Hospital for the privilege of studying their cases, their interest in the work and for many valuable suggestions, as well as to the hospital administration, through whose good will it was possible to use the personnel and equipment of the routine laboratory, although no special financial provision had been made.

We also wish to thank Miss Helen Markey and Miss Mary B. Watters, laboratory assistants, for their tireless energy in making the many chemical determinations, and Miss Blythe Gager, for assistance in the performance of the adrenalin sensitivity tests.

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A CLINICAL CLASSIFICATION ON ASTHMA BASED UPON A REVIEW OF SIX HUNDRED AND FORTY-EIGHT CASES.[1]

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It is clearly recognized today that asthma is always a symptom and never a disease as such. The diagnosis is usually made by the patient. The term "asthma" is here used to include all those cases in which a type of dyspnea characterized by difficult inspiration or expiration, or both; "wheezy" breathing is the predominant symptom. Such breathing occurs in a variety of conditions. The patient with a typical barrel chest full of squeaks and musical rales over which the breath sounds are prolonged usually has asthma, but his diagnosis should be pulmonary emphysema. Bronchial asthma is a loose term which is ordinarily applied to those patients with asthma in whom the physical examination between the attacks is essentially normal. As to the mechanism by which this peculiar type of dyspnea is produced we know little, although the theory of bronchial spasm with edema of the mucous membrane seems adequate.

In the study of each case of asthma at least two factors in its cause are important. There is for each case of asthma an underlying basis the nature of which is quite unknown, except that it tends to be inherited, especially in those cases in which the asthma is due to foreign proteins. This basis may be referred to as the "asthmatic state" which underlies not only the various forms of asthma but such other conditions as hay fever, food and drug idiosyncrasies and certain cases of urticaria, angioneurotic edema, eczema, etc. On top of this basis recent investigation has identified a variety of types of asthma which it is the purpose of the present paper to review, with particular reference to their relations one with another.

The simplest and most obvious classification already discussed, especially by Walker and by myself, divides asthmatics into two main groups: First, those sensitive to foreign proteins in which the cause is outside of the body (extrinsic), and second those not sensitive where the cause is inside of the body (intrinsic).

During the past three years patients with asthma have been studied in the clinic for anaphylaxis at the Massachusetts General Hospital and in private practice. The accompanying chart shows an arrangement of these cases and is an attempt to demonstrate the clinical relation in the various groups. In the management and treatment of cases this chart has been found to be of great practical value.

Foreign proteins may enter and act upon the body in several ways, particularly through the respiratory tract, as in Groups A and B of the chart and through the gastro-intestinal tract, as in Group C.

Group A. Pollen Hay Fever and Asthma. Group A represents cases which were sensitive to the plant pollens. There were 71 cases of early hay fever (sensitive to the graminaceæ, timothy, red top and June grass), 227 cases of late hay fever (sensitive to the compositæ ragweed) and 49 cases of double hay fever—a total of 347 cases of hay fever. (These cases of simple hay fever are not included among the 648 cases of asthma.) Pollen asthma describes the asthma which occurs as an aggravation of hay fever. Pollen asthma must, in its pure form, be limited in its dates of onset and subsidence to the true hay fever season. Pollen asthma occurred in only 9 cases of early hay fever (12.6 per cent), in 81 cases of late hay fever (35.7 per cent) and in 9 cases of double hay fever (18.3 per cent), "and in a total of 99 cases (28.5 per cent) of all types of hay fever." This is the most typical form of asthma known: the easiest to diagnose and the simplest to treat. Desensitization with pollen extract relieves this asthma even better than it relieves hay fever.

A CLINICAL CLASSIFICATION OF 648 CASES OF ASTHMA.
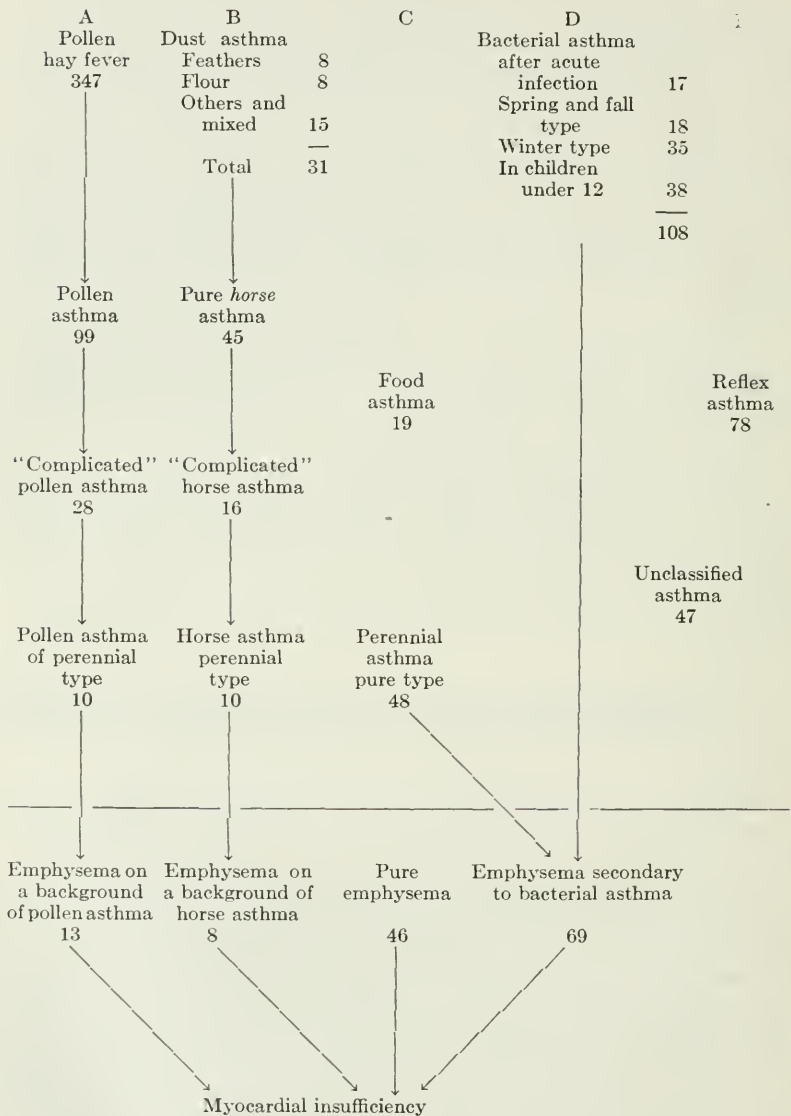
In certain cases this pollen asthma once started does not end abruptly with the end of the hay fever season but continues on into the fall or winter. Such cases, 28 in number and nearly 28 per cent of the 99 cases of pollen asthma, are here called cases of complicated pollen asthma. This term is, however, applicable only to those cases in which asthma continues in one single attack, which lasts not more than a few weeks beyond the true hay fever season.

Some cases which give a history compatible in the early stages with a pollen asthma—and later with a complicated pollen asthma—will say that still later, after the apparent end of their usual fall attack, they will have other attacks during the winter and spring. It is obvious that these other attacks of asthma can have no relation to any pollens and must therefore be due to bacterial action or in certain cases to some reflex action. It might be presumed that other foreign proteins in dust or food might perhaps be responsible for the later attacks in such patients, and, indeed, 7 patients reacted positively to one or other cereal proteins and 1 of them to eggs as well. However, in the 7 cases the removal of the corresponding food had no effect on the asthma.

The diagnosis of pollen asthma can be made in most cases by a careful history and without skin tests. Occasionally a case of supposed pollen asthma was found that failed to react to pollens. Study, however, revealed the fact that such patients had no eye or nose symptoms preceding their asthma, which of course emphasizes the importance of care in history-taking.

Up to this point the physical examination of these patients between their attacks of asthma is always normal. As the asthma progresses, as the attacks become longer and the intervals shorter, evidence of a secondary pulmonary emphysema develops. This will be discussed at greater length later. Suffice it to say that of the 99 cases of pure pollen asthma, 23 cases went on to develop perennial asthma, and 13 of these had emphysema. Two cases which had late hay fever and also had a perennial asthma had never been worse during the fall, so that in them a diagnosis of pollen asthma was not made.

Group B. DUST ASTHMA. Group B is a group closely related to Group A, and includes 76 cases of individuals sensitive to foreign proteins other than the pollens, but is confined to those cases in which the contact is by way of the respiratory tract, and in which the exposure is to proteins in dust. Here are 45 cases of horse asthma, 9 of which were sensitive to the pollens as well and one of which reacted to egg-white. In addition there are 8 cases of asthma due to feathers, 8 cases of asthma in bakers and housewives due to wheat flour dust, 1 case due to cats and 1 to dogs, 1 to coffee, and 11 cases of asthma due to some unknown dust, only 6 of which had positive tests, and these tests were incompatible with the history. In this last group of 11 cases this diagnosis was made because of the peculiar circumstances: a theater, a musty house or a farm which invariably precipitated the attack. It is felt that more comprehensive tests might have revealed the offending protein, for as long as the patient avoided the particular circumstances there was no asthma. Walker, quoting Goodale, has lately defined such cases as reflex in nature (through the olfactory nerves).

The 8 cases of asthma from wheat flour dust are of great interest. They were all in bakers. In spite of the fact that they gave satisfactory tests to the wheat proteins they had no symptoms at all referable to eating white bread. Symptoms developed only during or shortly after exposure to wheat flour in the form of dust. In other words, symptoms were caused only by contact through the respiratory tract. Treatment, however, included the withdrawal of cereals in the diet, as a cumulative action is a distinct possibility. Cases of susceptibility to other dusts, such as orris-root powder, rice powder, rabbit, guinea-pig and miscellaneous hair, perhaps leather dust and a variety of others, should be mentioned for the sake of completeness, although in the present study no such case was identified. In an analysis of 198 cases of vasomotor rhinitis susceptibility to orris-root powder was found in 13 (6 per cent), but none of the patients had asthma.

As in the case of pollen asthma, so horse or dust asthma may readily be complicated by bacterial infections to a greater or less extent, and these complications may ultimately produce emphysema. In this Group B, 16 cases in the total of 76 were so complicated and 10 went on to develop perennial asthma, and 8 of them emphysema as well.

Group C. Food Idiosyncrasy. Group C represents those individuals who are obviously poisoned by certain definite foods or food combinations. This poisoning manifests itself by asthma, by urticaria, by angioneurotic edema or occasionally by violent gastro-intestinal upsets or by eczema.

In 19 cases, or only 3 per cent of the 648 cases of asthma, proteins in food were considered to be the cause, not only because each patient gave a well-marked test to the protein in question, but also because the patient's symptoms were definitely relieved when the particular food was eliminated.

These 19 cases were sensitive in 10 cases to egg, in 4 to wheat, in 2 to meat and in 1 each to nuts, fish and milk; 4 cases were sensitive each to a number of different foods, the most frequent combination being to eggs and wheat. Eleven of these 19 cases were in children. It so happened that no case of food asthma in this series was found which had a complicating bacterial asthma.

Thirty-five cases of urticaria and 6 cases of angioneurotic edema have been tested[2] but no case of either urticaria or angioneurotic edema was found to have asthma.

Twenty-nine cases of eczema were tested and 5 of these also had asthma which seemed to come and go with the eczema. Four of these 5 cases had positive tests each to one or more food proteins.

Group D. Bacterial Asthma. Group D represents perhaps the most common group, which can be subdivided as follows:

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[2] For results see paper on Skin Tests with Foreign Proteins, which will appear in an early issue of this Journal.

1. Where asthma dates from a definite acute respiratory infection, 17 cases (13 adults and 4 children).

2. Eighteen cases in which there is each year a rather sharp and severe but relatively short attack of asthma occurring with the first cold spell of autumn and often recurring with the violent changes in temperature in March. Seven of these 18 cases were in male adults over thirty-five years old.

3. Thirty-five cases of "winter" asthma where the symptoms are closely associated with the cold weather of New England; are persistent and present practically constantly until the spring. Any fresh cold makes them markedly worse. All of these cases were in adults. Their separate classification is perhaps artificial, since many cases closely resemble the cases of perennial asthma to be discussed later. The group should be recognized, however, because a change to a warmer climate is an efficient and valuable treatment.

4. Bacterial asthmas in children, 38 cases, which come on most often after a cold and last for variable periods—the important point being that between the attacks these children are quite well. In case they are not quite normal between the attacks and still retain a certain amount of wheezing and dyspnea on exertion, it is usually found that they have mild emphysema, large peribronchial lymph nodes or some other organic cause for the symptoms. In each of these subgroups the tests are ordinarily negative, but 7 children have been added in spite of a positive test, since nothing in their story seemed to agree with the test.

Group E. Reflex Asthma. While it is usually accepted that in many cases asthma depends upon the action of foreign proteins, yet in other cases the relation of proteins to the etiology is much less clear. In many of these latter some organic condition outside of the respiratory tract can be discovered and can be assumed to be indirectly responsible for the asthma, although the precise mechanism of its effect is usually unknown.

In the present study 78 cases are placed under the heading of reflex asthma. In 16 of these cases, mostly in children, bad nutrition was considered to be the cause rather than the result of the asthma, largely because treatment directed toward the regulation and enlargement of the diet, but without attention to specific foods, caused a great relief of the asthma. In at least 4 cases the asthma was associated with and presumably due to a faulty posture with ptosis. In 4 cases with disturbances of the gastro-intestinal tract, asthma was associated with constipation, the relief of which relieved the asthma. In 9 cases with diseased tonsils, 1 with lung abscess, 4 with bad teeth, and 11 with chronic pulmonary tuberculosis the absorption of toxic material is easy to understand, as at least a contributory cause to poor general condition and asthma. In 8 cases various pelvic disturbances were associated with the asthma, including the menopause and pregnancy, and in 2 cases asthma was invariably associated with the catamenia.

Referring to the definition of the term asthma as given in the first paragraph of this paper, it is of interest to note that recently a patient was referred to the writer for asthma in whom a tumor, probably luetic in nature but of sufficient size to obstruct the breathing, was found in the bronchial mucous membrane.

In the group of reflex asthma also are placed 13 cases of nervous asthma in which excitement or association with some disagreeable undertaking (return to college, beginning summer work, preparations for a journey) was the exciting cause of asthma in these patients with a general nervous instability; and finally, in 5 cases asthma seemed to follow a long period of stress and strain. Several of these latter cases have been undoubted results of the war, and a prolonged period of rest and relaxation, without other treatment, has caused a great improvement.

One case of this type is that of a widow who, left entirely alone, broke down under the strain of settling her husband's estate, sending the children to school and trying to do all the housework when her servants abandoned her. With a complete rest and change of environment the asthma largely disappeared.

Perennial Asthma. It is obvious that as asthma progresses the attacks become more frequent and of greater duration, but as a diagnosis of emphysema cannot be made in these cases, this way-station in the chart is justified. It would only be confusing to attempt to trace here the origin of the many cases of perennial asthma; but for the treatment of each case, this origin must be traced, if good results are to be obtained.

In addition to 23 cases in Group A and 10 cases in Group B who have reached this stage of perennial asthma there is a group of 48 cases who state in their history that their asthma has from its start been chronic with comparatively short intervals between attacks. Most, if not all, of these cases are of bacterial origin—their skin tests are all negative. Their separate classification is artificial and perhaps unnecessary.

Emphysema. On the chart a horizontal line is drawn between perennial asthma and emphysema. This line represents the onset of a demonstrable organic change in the patient which will remain constantly present even though the patient is sure that he "is entirely well."

Such patients have dyspnea on exertion which is usually associated with wheezing. If they are examined at any time, even between their attacks of asthma, they will show a more or less barrel-shaped chest with rounded shoulders. The breath sounds are most often diminished in intensity and high pitched in quality. Musical, whistling or squeaky rales are almost always present or can be brought out if the patient coughs a few times. In well-marked cases the pulse is often of poor quality; there is usually some cyanosis depending on the amount of associated bronchitis; the pulmonic

second sound is accentuated, due to the increased intrapulmonary pressure, while the heart seems on percussion to be small, due to the overlying lung. Such patients suffer from a markedly increased dead space in their air passages and from a markedly diminished vital capacity due to the large amount of retained air which they cannot expel.

Such patients are prone to develop chronic infections of the bronchi which are very resistant to treatment, in that these infections aggravate the emphysema just as the emphysema aggravates them, so that a vicious cycle is promptly established.

Emphysema may be acute compensatory following a severe attack of asthma. It may be idiopathic—that is, may be itself the primary condition arising in an unknown manner and not following an attack of asthma, and finally it may obviously be a late secondary result of chronic asthma.

In this series a total of 136 cases are diagnosed emphysema. Thirteen have already been included under pollen asthma, 8 under dust asthma and 4 under reflex asthma. Of the other 111 cases 14 gave a positive skin test to one or more foreign proteins, ragweed pollen, horse-hair extract and the wheat proteins being the most common. These cases have not been included in other groups because there was no history of hay fever or horse asthma which might have justified the test-finding. Twenty-one of these 111 cases were acute and of less than two years' duration. Twenty-five cases followed a history of chronic asthma and were of over twenty years' duration.

That prolonged emphysema with its associated chronic bronchitis may lead to myocardial insufficiency and arteriosclerosis seems undoubted whether the cause depends upon the burden to the circulation added by the almost constant effort to breathe or whether the cause is referable to the absorption of toxic material from the bronchi. It is, however, difficult to tell in just how many cases the myocardium is damaged, so that no figures can be given here.

In the foregoing, 648 cases of asthma have been discussed and classified. In addition to the above, 47 cases, or nearly 7 per cent of the whole, remain to date unclassified, most of whom have not been seen since their first visit.

Treatment. Treatment depends, obviously, on the type of asthma from which the patient suffers. Treatment by removal of foreign proteins or by attempts to desensitize the patient to them is sufficient in certain cases. On the other hand the treatment of perennial asthma, for example, will never be satisfactory until the etiology of each case is worked out. In the cases classified below, the "line of organic change," no treatment will be entirely satisfactory, although much can be done for the patient's comfort. In the cases above the line everything possible should be done to prevent the progress of the disease downward, and the hope of success is not unreasonable.

The chief function of such a classification of asthmatics, as is described above is, of course, to aid in the treatment of these patients. As is seen, most of the cases of asthma have neither a basis of definite foreign proteid susceptibility nor have they any abnormality which might justify a diagnosis of "reflex asthma," so that most of the cases come under the heading of "bacterial asthma" or, at all events, are complicated by bacterial infection. The subdivisions of this great group of bacterial asthmatics as given here are made on an empirical basis, usually not founded on any definite scientific basis but simply depend upon clinical observations and characteristics. In practice, however, these subdivisions have been found to be of some importance in treatment.

Vaccines have come to play an even more important role in the treatment of asthma, although their value from the strictly scientific viewpoint is as yet unknown. If it is assumed that the attacks of asthma depend upon a low-grade focus of bacterial action, say in the bronchial tubes, and if the use of vaccines is found to relieve these symptoms, it may be assumed that this relief depends upon the irradication, permanent or temporary, of this focus, and this irradication in turn is probably caused by the production of an active immunity. The possibility that the patient may be sensitized to bacteria and that the results of vaccine treatment are good because of a production of desensitization is another theory. There is little or no scientific basis available to date to help us choose between these two theories. The second theory has been advanced largely because of the desire to correlate all these cases with the simpler and more obvious cases of pollen and other foreign proteid sensitiveness. At all events it should be borne in mind that vaccines produce their greatest effect, at least in other conditions than asthma, by producing an active immunity, and therefore it may be assumed that vaccines will work best in those cases of asthma whose attacks are isolated by fairly definite intervals of more or less complete freedom from symptoms.

Another point about vaccines: in a previous paper the writer attempted to show that vaccines do good in asthma only in case a local reaction is produced at the site of inoculation. This finding has been many times confirmed and in many cases has furnished a method by which the proper vaccine for treatment has been selected. This method consists roughly in making separate vaccines from each of the various organisms isolated from the patient's sputum and then giving small doses of each vaccine subcutaneously. In twenty-four hours the local reactions from one or two of these vaccines may be fairly definite (heat, redness and tenderness), while there will be no reaction from the other strains used. If this is found to be the case, treatment with the organisms producing the reaction will usually give satisfactory results, whereas if the other non-reacting organisms are used in vaccines the further doses can be tremen-

dously increased without producing either local reaction, aggravation or improvement of the symptoms.

The object of this paper will have been attained if it has emphasized that not only are there many forms of asthma, but also by proper classification and by proper selection of the form of treatment a great deal can be done for these unfortunate sufferers.

Conclusions. 1. A chart showing the interrelation of various groups of asthmatics is presented in the hope that it will prove of service in the classification of these patients.

2. The importance of a careful study of the patient, and especially of his history, is emphasized.

3. The importance of a proper classification and of a knowledge of the origin of asthma in any given case as a precursor to the successful treatment of that case is demonstrated.

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OBSERVATIONS ON THE TREATMENT OF AURICULAR FIBRILLATION BY QUINIDIN SULPHATE.*

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QUINIDIN, one of the cinchona alkaloids, was isolated as a pure base by Van Heijningen in 1848. It is chemically isomeric with quinin and has somewhat similar physiologic properties. Occasionally it has been used in therapeutics as a substitute for quinin, particularly in the treatment of malaria.

Quinin was recommended as a remedy in heart disease seventy years ago by Beletti.[1] Such distinguished authorities as Huchard and Lancereaux considered it of value in cardiac palpitation, tachycardia and vascular erethism. According to Wenckebach, quinin was often used by the older clinicians in combination with digitalis. Nevertheless, its use in cardiac therapy was practically abandoned until Wenckebach,[2] by accident, discovered its effect in restoring normal rhythm in a case of auricular fibrillation. He then tried it a number of times, but was successful in restoring the normal rhythm in but one additional case.

Wenckebach's observations stimulated a number of studies of the effect of quinin on abnormal rhythms. It has been definitely established that quinin exerts an inhibitory effect against auricular fibrillation, but the percentage of cases in which the normal rhythm can be restored is so low that the use of the drug in clinical medicine for this purpose is scarcely warranted. Frey[3] studied the effects of the three other well-known cinchona alkaloids, namely, cinchonin, cinchonidin and quinidin. The first two he found to be of no particular value in interrupting fibrillation, but quinidin yielded striking results in auricular fibrillation and flutter. Of the first 22 cases treated, 11 regained the normal type of rhythm.

Comparatively little experimental work in respect of the effect of quinidin on the heart has thus far been reported, so that the information on this point is somewhat fragmentary. Santesson,[4] in 1893, studied its effects along with those of quinin, cinchonin and cinchonidin on the frog's heart. He concluded that its toxicity is about one-half that of quinin, as it required nearly double the con-

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[1] Quoted from Pezzi and Le Clerc: La Médecin, March, 1921, p. 443.
[2] Die unregelmässige Herztätigkeit und ihre klinische Bedeutung, Leipzig and Berlin, 1914.
[3] Berl. klin Wchnschr., 1918, **55**, 417 and 450.
[4] Arch. f. exp. Path. u. Pharm., 1893, **32**, 321.

centration to bring about complete cardiac arrest. Both cause reduction of pulse volume and frequency, but while quinin tends to influence volume more than frequency, quinidin exerts comparatively more effect on frequency. Occasionally quinidin brought about actual increase in pulse volume. All the cinchona alkaloids studied were believed to be cardiac depressants and to exert their effects by acting as heart-muscle poisons. It was noted that quinin and cinchonidin were able to abolish irregularities in cardiac rhythm produced in the preparation of the hearts for the experimental procedures.

Hofmann[5] found in dog and cat hearts perfused with quinidin that the most conspicuous effect was on contractility; this effect was not due to the influence of cardiac rate, as the changes in rate were small. He believed it to be a direct effect of the poison on the cardiac muscle. Excitability was also greatly diminished, so that the threshold of stimulation necessary to produce extrasystoles or fibrillation of the auricle rose. Finally, it became impossible to bring about fibrillation.

Boden and Neukirch[6] by perfusion experiments on isolated rabbit and fetal human hearts found a marked depression of stimulus production which was manifested by bradycardia and slowing of artificially produced tachycardia. They like Hofmann found that a heart perfused with sufficient concentration of quinidin could not be made to fibrillate, or if fibrillation were already present it was abolished by the drug. Quinidin also caused a decrease in the strength of contraction of the auricles and ventricles. The coronary arteries were found to be widened by perfusion with quinidin. Hedbom[7] had previously found that quinin caused increased blood-flow through the heart, but at the same time decrease in strength of contractions.

Schott[8] made electrocardiographic studies of the effect of large doses of quinidin in guinea-pigs. He found progressive decrease of auricular rate, shallower and broader P-waves, marked alterations in the ventricular complex and increase in the conduction time going on to a high-grade incomplete heart-block with as many as five auricular contractions to one ventricular. Ordinarily complete dissociation would have developed instead of such a high-grade incomplete block, but Schott explains the failure of the ventricle to develop an independent rhythm on the ground that stimulus production was depressed in the lower levels of the heart as well as the higher by quinidin. But it would appear from electrocardiograms published by Boden and Neukirch[9] that the auriculoventricular node, at any rate, is able to assert itself as pacemaker for the

5 Ztschr. f. Biol., 1920, **71**, 71.
6 Deutsch. Arch. f. klin. Med., 1921, **136**, 181.
7 Skand. Arch. f. Physiol., 1899, **9**, 1.
8 Deutsch. Arch. f. klin. Med., 1920, **134**, 208.
9 Loc. cit.

ventricles under the influence of quinidin. In some tracings there was no evidence of the spread of an excitation wave through the auricles. There were marked changes in the form of the ventricular complexes.

In studying the effects of quinidin on normal persons in therapeutic doses, Frey[10] was unable to discover any depression of cardiac contractility, but he as well as Hecht and Matko[11] found a flattening of the T-waves in electrocardiograms. Boden and Neukirch[12] found no electrocardiographic changes when the drug was given to normal persons. It is possible that the diversity of findings may be due to differences in administration of the drug. The details of the experiments are not given by the writers. Boden and Neukirch found no changes in urine output nor cardiac rate in normals unless the drug was given intravenously, when there was a slight increase of rate for a short time.

Weichman[13] studied the urinary excretion of quinidin. He found that excretion began quickly and was greatest during the first twenty-four hours. Smaller amounts were excreted during the next two days. With increase of urine output the excretion of quinidin was also increased. It was not affected by the administration of digitalis but apparently was increased by muscular activity of the patient. Fractionation of doses also favored rapidity of excretion. Quinidin sulphate was excreted more rapidly than quinidin, probably on account of the fact that the sulphate is more soluble and more easily absorbed than the pure alkaloid.

Boden and Neukirch[14] treated 12 cases of sinus tachycardia by oral or intravenous administration without result. They believed that a favorable effect was obtained in extrasystoles, but, as they point out, extrasystolic arrhythmia is so changeable that it is difficult to judge the results of treatment. In 6 cases of paroxysmal auriculoventricular and ventricular tachycardia the attacks were terminated in 4 and the rate decreased in 2 by intravenous injection.

It is in auricular fibrillation and flutter that the effects of the drug have been most striking. In 147 cases collected from various European sources, 4 reported by Levy[15] in this country and 12 from our clinic, 163 in all, the normal rhythm was restored in 83, a percentage of 51.5. Frey,[16] who has had the largest experience, has reported and analyzed his results in 50 cases. Of the 50 cases a normal rhythm was restored in 21, fibrillation was converted to flutter in 6 and 23 remained uninfluenced. Neither the age of the patient nor the type of cardiac disease, including the presence or absence of valve lesions, seemed to influence the results. On the

[10] Deutsch. Arch. f. klin. Med., 1921, **136**, 70.
[11] Quoted from Frey: Deutsch. Arch. f. klin. Med., 1921, **136**, 70.
[12] Loc. cit.   [13] Inaugural Dissertation, Kiel, 1918.
[14] Loc. cit.   [15] Jour. Am. Med. Assn., 1921, **76**, 1289.
[16] Loc. cit.

other hand, patients with decompensation did not react nearly so well as those whose function was less impaired. The duration of fibrillation was also found to be of importance. Those who had fibrillated only a short time reacted well, only 8 out of 24 remaining uninfluenced as compared with 13 out of 19 among those who were known to have had fibrillation for over a year. Fibrillation in thyroid disease was also found to be refractory to quinidin.

The duration of normal rhythm following its restoration by quinidin for the most part has been merely temporary. Many patients have reverted to fibrillation after a few days or weeks, although 1 patient of Boden and Neukirch's[17] at the time their paper was written had retained a normal rhythm for nine months. In Frey's[18] experience two-thirds of the patients retained a normal rhythm for at least a month. He believes that the more or less continuous administration of small amounts of quinidin tend to prevent, in a measure, the recurrence of fibrillation.

The reports on the effects of quinidin on subjective symptoms and cardiac decompensation have been somewhat conflicting. Frey has stated that the drug exerts no favorable influence on passive congestion or diuresis, in spite of the fact that the rhythm may return to normal and the patients feel better. Von Bergmann,[19] on the other hand, considered the drug life-saving in a patient with severe decompensation who was not benefited by digitalis. Under quinidin the rhythm was restored to normal and the severe decompensation and passive congestion disappeared. Leschke and Ohm[20] report that not only does quinidin bring about a restoration of the normal rhythm but improvement in the mechanical power of the heart. They give the details of one case in which passive congestion improved and exhibit venous pulse curves which they regard as evidencing cardiac improvement.

Electrocardiographic studies during the course of treatment have shown graphically the profound effect of the drug in flutter and fibrillation. Even in the cases in which fibrillation was not abolished the oscillations due to the spread of the excitation wave in the auricle tended to become less rapid and larger. In a number of cases it was observed that fibrillation was converted first either to pure flutter or to what appeared to be a transition stage between fibrillation and flutter, and then to normal rhythm. Frey noted that the T-wave might become less high, the P-waves altered in shape and conduction time increased over the normal, following the restoration of sinus rhythm. Boden and Neukirch noted prolongation of the $P–R$ interval in 2 cases. On the other hand, von Bergmann found no alterations in conduction nor in the T-waves. A number of observers have commented on the fact that auricular extrasystoles are often found shortly after the restoration

[17] Loc. cit.
[19] München. med. Wchnschr., 1919, **66**, 705.
[18] Loc. cit.
[20] Ibid., 1921, **68**, 65.

of sinus rhythm. Von Bergmann believes that further treatment with quinidin tends to abolish them.

In a number of cases there have been untoward results. Benjamin and von Kapf[21] report two deaths that were due apparently to quinidin. One patient was decompensated with a pulse-rate of 80 to 100. Under quinidin therapy the pulse rose rapidly to 160 and the patient died of cardiac failure. In the second case, a few hours after the restoration of normal rhythm, there was sudden cardiac arrest followed about ten minutes later by respiratory failure and death. The dosage given was small. In a third case there was a lung infarct after the restoration of normal rhythm. This the authors regard as due to the improved circulation whipping a thrombus from the heart to the pulmonary artery. The patient recovered. Frey states that in some cases he saw alarming symptoms which he regarded as due to hypersusceptibility to quinidin. Such symptoms as nausea, vomiting, epigastric discomfort and pain, dizziness, fainting and even temporary arrest of respiration have been reported. Frequently the ventricular rate has increased in an alarming manner, especially in auricular flutter, where slowing of the auricular rate in some unexplained way seemed to bring about a degree of "unblocking." The explanation of this phenomenon is at present obscure, especially in view of the fact that there is evidence to indicate that quinidin depresses auriculoventricular conduction.

Report of Cases. CASE I.—J. G., white, male, aged fifty-five years. Diagnosis: Chronic myocardial disease; auricular fibrillation; cardiac decompensation; arteriosclerosis. Symptoms referable to the heart for three years, worse recently. Dyspnea, weakness, precordial pain, palpitation, swollen legs. History of excessive alcoholism. Examination showed wide aortic arch, large heart with transverse measurement of 16 cm., auricular fibrillation with ventricular rate about 90. Systolic murmur at the apex. Free fluid in the abdomen.

He received digitalis for about ten days, with moderate improvement, and was then given quinidin sulphate, 0.2 gram b. d., for one day followed by 0.4 gram t. i. d., the dose being gradually increased to 0.8 gram five times a day over a period of ten days. At this time he complained of stuffiness of the ears and slight deafness, so the drug was discontinued. The normal rhythm was not restored, nor was there any apparent effect on the cardiac rate. The patient thought he felt a little better while taking quinidin, but there was no significant change noted in his condition.

CASE II.—H. S., white, male, aged thirty years. Diagnosis: Multiple serositis, with abdominal, pleural and pericardial effusions;

[21] Deutsch. med. Wchnschr., 1921, **42**, 10.

chronic myocardial disease; auricular fibrillation. Well until five years ago, when he had attacks of dyspnea, dizziness and unconsciousness. One year ago had abdominal swelling and edema of the legs. Three months ago the abdomen was tapped and 7000 cc fluid removed. On admission there was a large area of precordial dulness and pericardial friction sounds. Total arrhythmia with ventricular rate of 75. Signs of a great deal of fluid in the abdomen and also fluid in the right chest. Teleroentgenogram showed a very large heart shadow and evidences of pericardial fluid.

After seventeen days' treatment with moderate-sized doses of digitalis the cardiac rhythm became regular and for several days there was sinus rhythm with P-wave in the electrocardiogram and a well-defined wave in the jugular tracing. Fibrillation was then reëstablished. About a week later quinidin sulphate was given, first two small preliminary doses then 0.4 gram t. i. d. for four days and 0.6 gram for two days. At this point in the treatment the patient left the hospital. The fibrillation was unaffected, no change was observed in his general condition and no disagreeable symptoms were noted as a result of the quinidin.
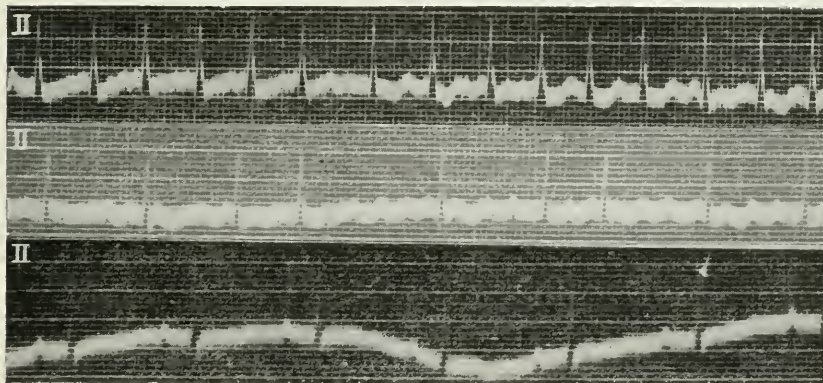
Fig. 1 (Case 3).—Top tracing made July 20, 1921. Auricular fibrillation with a ventricular rate of approximately 155. Second tracing made July 26 after 10.2 grams quinidin sulphate had been taken. Fibrillation still present but ventricular rate 92 and oscillations of auricular origin coarser and less rapid. Third tracing made July 27. Sinus rhythm. Had taken 12 grams quinidin sulphate in seven days. $P-R$ interval 0.22 second. All three tracings are Lead II.

CASE III.—B. T., white, female, aged forty-five years. Diagnosis: Mitral stenosis; auricular fibrillation; moderate cardiac decompensation. First seen in the Outpatient Department February 9, 1921, when the cardiac rhythm was normal. On May 25 she was found to have auricular fibrillation. Had had symptoms referable to the heart for four years, which were much worse recently. Palpitation, precordial pain, dyspnea and hemoptysis. No history of rheumatic fever but has had syphilis. Heart markedly enlarged,

with a transverse measurement of 18 cm.   Clear-cut signs of mitral stenosis.   Auricular fibrillation with a ventricular rate of 100.

She was given two preliminary small doses of quinidin sulphate, followed by 0.4 gram t. i. d. for one day, when her rhythm became normal.   After a few days she was discharged but was readmitted six weeks later with a history that she had felt well for two weeks after leaving the hospital, but since then had been worse than before.   Again there was fibrillation, this time with a ventricular rate of about 130.   Received quinidin sulphate, 0.4 gram t. i. d. for five days and 0.6 gram t. i. d. for three days, when the normal rhythm was again restored.   During the first four days of quinidin therapy the rate became more rapid and was counted as high as 155. It then fell to below 100 and the auricular oscillations in the electro-cardiogram became larger, more nearly uniform and regular and less rapid, somewhat resembling flutter.   After the restoration of sinus rhythm she was given quinidin sulphate, 0.2 gram b. d., and began to improve rapidly.   Five weeks later the rhythm was still normal and she felt well.   Two weeks after this she was seen again—was feeling worse and was again fibrillating.   No disagreeable effects were noted from quinidin.
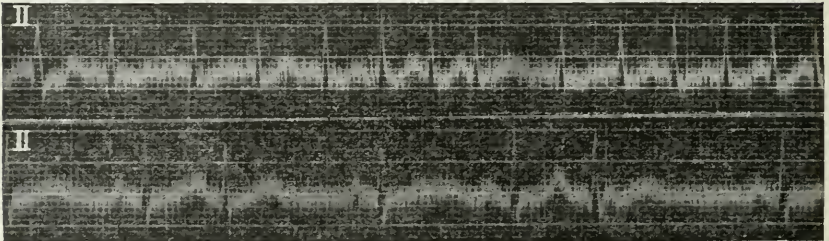
Fig. 2 (Case 4).—Upper tracing made July 5, 1921. Auricular fibrillation, ventricular rate about 150, constantly varying form of ventricular complexes. Lower tracing made July 6 after having received 1.6 grams quinidin sulphate. Normal type of rhythm. *P–R* interval 0.20 second. Both tracings are Lead II.

Case IV.—E. W., white, female, aged fifty-eight years.   Diagnosis: Adenoma of the thyroid; syphilis; chronic myocardial disease; auricular fibrillation.   Has had swelling of the neck for seven years.   Moderately nervous.   No exophthalmos.   Heart enlarged; transverse measurement, 16 cm.   No evidence of valvular disease.   Ventricular action rapid and irregular; a few rales at the bases of the lungs; liver enlarged; moderate edema of the legs. Basal metabolism, 37.7 per cent above the normal.   Electrocardiogram showed auricular fibrillation, with a ventricular rate around 150.

Received preliminary doses of quinidin sulphate, 0.2 gram b. d. followed by 0.4 gram t. i. d. for one day.   The next morning the rhythm was normal and the rate 84.   She was then given 0.2 gram

b. d. for three weeks, the rhythm remaining normal while the cardiac function improved remarkably. Her son reported a month later that her improvement had continued. No disagreeable effects were noted as due to the quinidin.
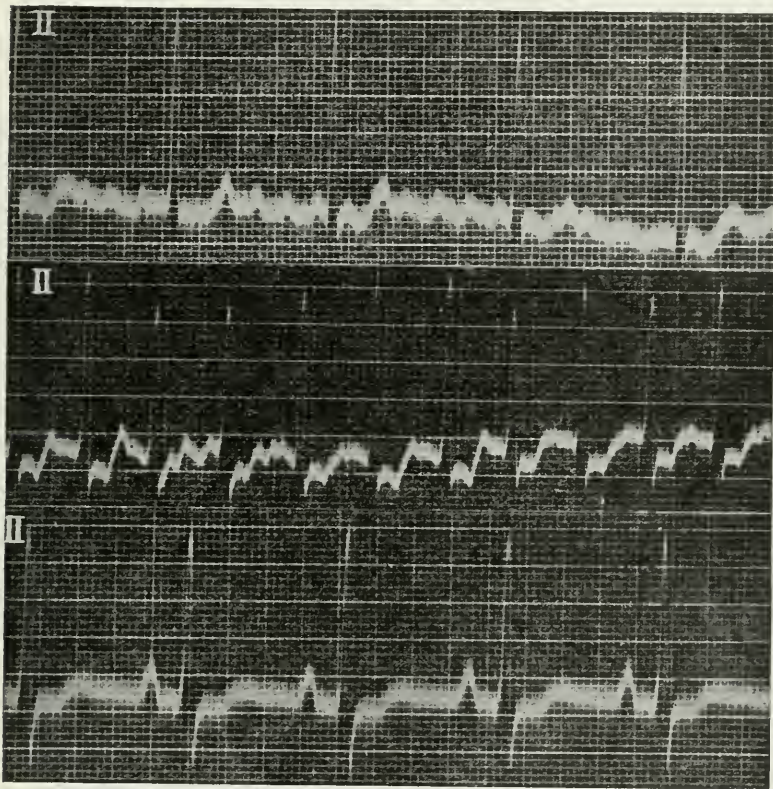
Fig. 3 (Case 5).—Top tracing made June 27, 1921, after 6.2 grams quinidin sulphate had been taken in five days. Fibrillation still present with ventricular rate averaging 65. Second tracing made June 29 after 9.8 grams quinidin. Ventricular rate 155 and nearly regular. Probably impure flutter. Third tracing made July 1 after 13.8 grams quinidin. Sinus rhythm restored with rate of 71. *P–R* interval 0.21 second. All tracings are Lead II.

CASE V.—C. N., white, female, aged twenty years. Diagnosis: Mitral stenosis and regurgitation; auricular fibrillation. Under observation constantly since 1919 and has had auricular fibrillation continuously for over two years. The heart is very large and the signs of mitral disease clear-cut. Two attacks of rheumatic fever. Does well on digitalis but quickly becomes severely decompensated if she neglects treatment. Was fairly well-compensated when she was sent to the hospital for quinidin.

Received quinidin sulphate: First day 0.2 gram b. d., then 0.4 gram t. i. d., the dose being gradually increased to 0.6 gram q. i. d.

over a period of eight days, when her rhythm became normal. After six days' treatment the ventricular rate jumped to 155, but she felt no worse at this time. After the restoration of normal rhythm she received 0.2 gram b. d. and was sent home. At this time she said she had less palpitation than usual, but otherwise felt no better. When she reported two weeks later she was again fibrillating. No disagreeable subjective symptoms were noted as due to quinidin.
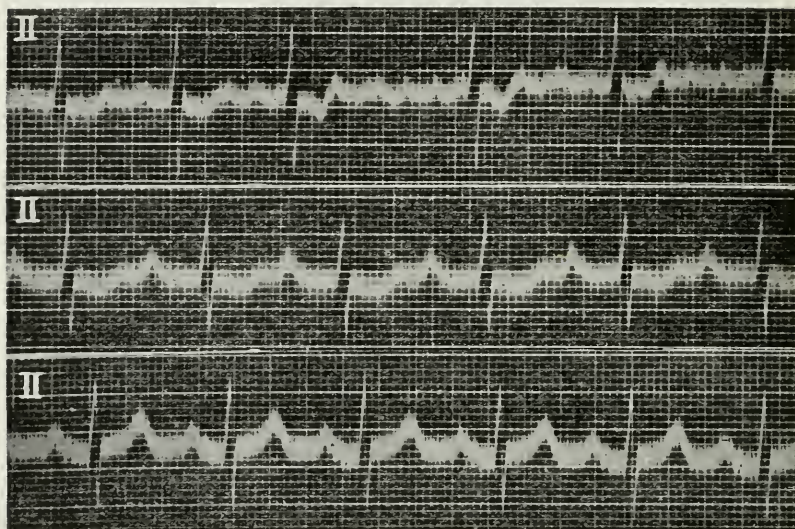
Fig. 4 (Case 6).—Top tracing made July 8, 1921. Auricular fibrillation. Had taken no drugs for several weeks. Second tracing made July 11 after 2.8 grams quinidin sulphate. Sinus rhythm. *P–R* interval 0.3 to 0.32 second. Third tracing made September 7. Had been receiving 0.4 gram quinidin daily. *P–R* time 0.23 second. Marked increase in height of *T*-wave. All tracings are Lead II.

CASE VI.—B. K., white, male, aged fifty years. Diagnosis: Aortic regurgitation and auricular fibrillation. Well until six months ago, when he began to suffer from digestive symptoms. Slight cardiac palpitation and marked dyspnea on exertion. Unable to do much work. Heart only moderately enlarged. Auricular fibrillation of the slow type.

Treated with digitalis for about a month without improvement. Was given quinidin sulphate 0.2 gram b. d. for one day followed by 0.4 gram t. i. d. for two days, when the rhythm became normal. Continued to take 0.2 gram b. d. There has been no recurrence of fibrillation in over two months. Has steadily improved; has no symptoms except on exertion and is able to work all day as a clothes-presser and tailor. During the first week of quinidin therapy even small doses caused epigastric distress, but later the drug was well tolerated.

CASE VII.—L. C., white, male, aged forty-seven years. Diagnosis: Hyperthyroidism, chronic myocardial disease and auricular fibrillation. Had been under observation for about one year on account of hyperthyroidism and cardiac condition, which was considered secondary to the thyroid disease. Treated by roentgen ray, with marked clinical improvement and fall in the metabolic rate. Had received digitalis therapy a number of times without much effect on his cardiac condition.
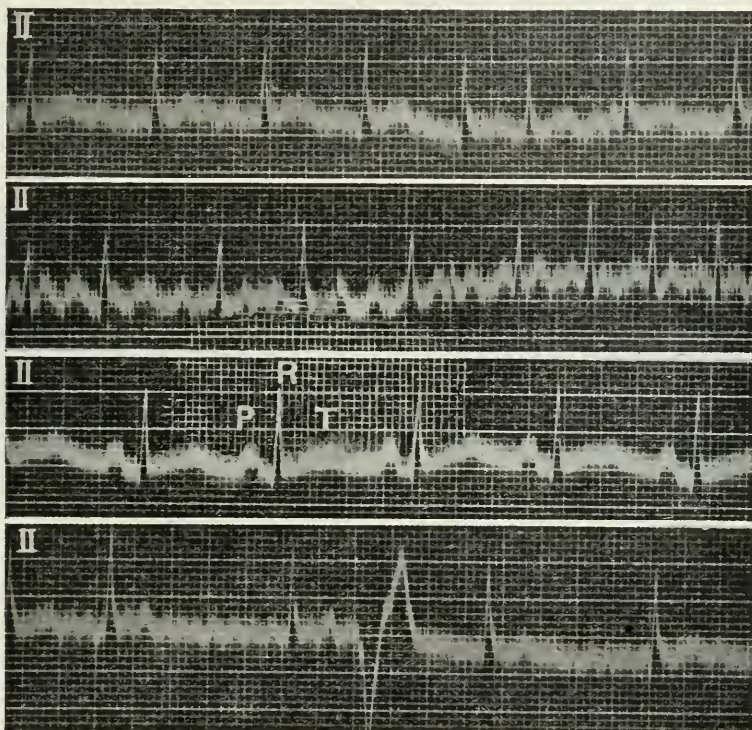
FIG. 5 (Case 7).—Top tracing made June 20, 1921. Auricular fibrillation, ventricular rate 110. Second tracing made June 22 after 2 grams quinidin sulphate. Auricular oscillations larger and less rapid. Third tracing made June 27 after 13.6 grams quinidin sulphate. Sinus rhythm, P–R interval 0.18 second. Fourth tracing made July 7. Auricular fibrillation. All tracings are Lead II.

He was given quinidin sulphate, 0.2 gram b. d. for one day, 0.4 gram t. i. d. for two days and 0.6 gram t. i. d. for six days, when the rhythm became normal. He was then discharged and ordered 0.2 gram b. d., which he did not take. When he reported the next week he was fibrillating again.

Two days before the restoration of normal rhythm the ventricular rate became quite rapid and the electrocardiographic auricular

oscillations larger, slower and almost uniform, approaching the type of tracing found in flutter. No disagreeable symptoms were noted from taking quinidin.

CASE VIII.—E. P., white, female, aged forty-two years. Diagnosis: Chronic myocardial disease, auricular fibrillation and cardiac decompensation. Shortness of breath and cardiac palpitation for several months; worse recently. Heart greatly enlarged; auricular fibrillation with ventricular rate of 160.

Received quinidin sulphate 0.2 gram b. d. for one day and 0.4 gram t. i. d. for one day, when the rhythm became normal and the rate dropped from 160 to 70. Continued to take 0.2 gram b. d. Discharged eight days later with normal rhythm. Readmitted after five weeks with fibrillation again. She had felt better for several weeks after leaving, but recently was worse again. Given
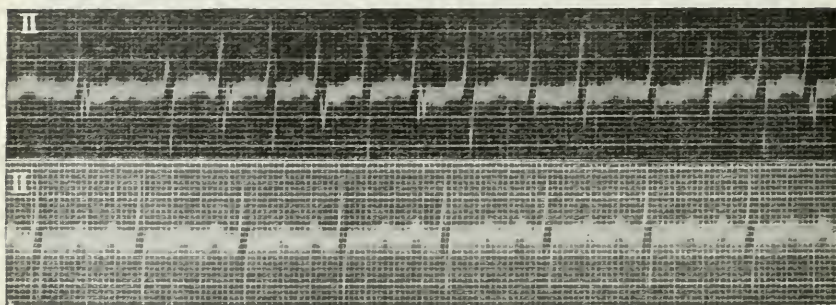
Fig. 6 (Case 8).—Upper tracing made July 2, 1921. Auricular fibrillation, ventricular rate 155. Lower tracing made July 5, 1921. Had received 2.8 grams quinidin sulphate. Sinus rhythm with auricular extrasystoles. Rate of dominant rhythm 68. Both tracings are Lead II.

0.4 gram quinidin sulphate t. i. d. and the dose gradually increased to 0.6 gram q. i. d. over a period of twelve days without interrupting the fibrillation. After three days without quinidin it was again given in dosage of 1 gram t. i. d. and the normal rhythm was restored in one day. During the entire period she received also 1 cc tincture of digitalis t. i. d. The rhythm remained normal for about a week and then reverted to fibrillation again in spite of the fact that she was taking 0.2 gram quinidin sulphate b. d. During the time the largest doses of quinidin were given she complained of feeling weak and dizzy.

CASE IX.—J. C., white, male, aged fifty-three years. Diagnosis: Chronic myocardial disease and auricular fibrillation. Well until six months ago, when he began to have digestive disturbances. His physician diagnosed heart disease. Came to the cardiac clinic with severe decompensation and auricular fibrillation with very rapid

ventricular rate, and was immediately referred to the ward. He improved markedly on rest and digitalis therapy and the evidences of passive congestion disappeared. Was then given quinidin sulphate, 0.2 gram b. d. for one day, 0.4 gram for five days and 0.6 gram for one day, when his rhythm became normal. Then received 0.3 gram for five days, when fibrillation recurred, but was restored to normal again by 0.6 gram t. i. d. for two days. The dosage was then tapered down to 0.2 gram b. d. and digitan 0.03 gram t. i. d. was also given. Ten weeks after discharge the rhythm was still normal; he had regained a considerable degree of compensation and was able to walk long distances and climb stairs without distress. He felt better immediately after the interruption of fibrillation both times. The most striking thing to him was the disappearance of palpitation. No disagreeable effects were noted from the quinidin.

CASE X.—R. R., white, female, aged twenty-five years. Diagnosis: Mitral stenosis, auricular fibrillation. Had been under observation for about two years in the Pennsylvania Hospital Medical Dispensary. The fibrillation had been present all that time. Responded well to digitalis. Became pregnant and shortly before term was sent to the University Hospital Maternity for delivery. She was kept well digitalized and Caesarean section was performed without any cardiac embarrassment. One week later quinidin sulphate was begun, 0.2 gram b. d. followed by 0.4 gram t. i. d. for eight days, without any noticeable effect on the fibrillation. There were no disagreeable effects ascribable to quinidin.

CASE XI.—M. M., white, female, aged fifty-one years. Diagnosis: Chronic myocardial disease and auricular fibrillation. Cardiac symptoms for twenty months. On admission she was severely decompensated with edema of the back and legs, congested pulmonary bases, enlarged liver and ascites. Heart markedly enlarged with transverse measurement of 17 cm. Loud systolic murmur at the apex. Auricular fibrillation with very rapid ventricular rate.

There was a slight improvement after ten days' rest in bed and digitalis therapy. She then received quinidin sulphate 0.2 gram b. d. the first day, 0.4 gram t. i. d. for six days and q. i. d. for five days. At the same time 3 cc digalen was given daily by hypodermic. The fibrillation was not interrupted. After three days' intermission she was given 1 gram quinidin sulphate t. i. d. for three days, again without interrupting the fibrillation. No disagreeable effects were noted from the quinidin.

CASE XII.—G. H., white, male, aged twenty-four years. Diagnosis: Aortic and mitral regurgitation; auricular fibrillation; moderate cardiac decompensation. Said to have had valvular heart disease since the age of eight, when he had diphtheria. At

fifteen had some shortness of breath. About three months ago it was noticed that he had "extra beats" of his heart. Up to then he had done heavy work but since has grown rapidly worse. Heart greatly enlarged; clear-cut signs of mitral and aortic regurgitation; auricular fibrillation with ventricular rate of about 150. Moderate orthopnea; no passive congestion.
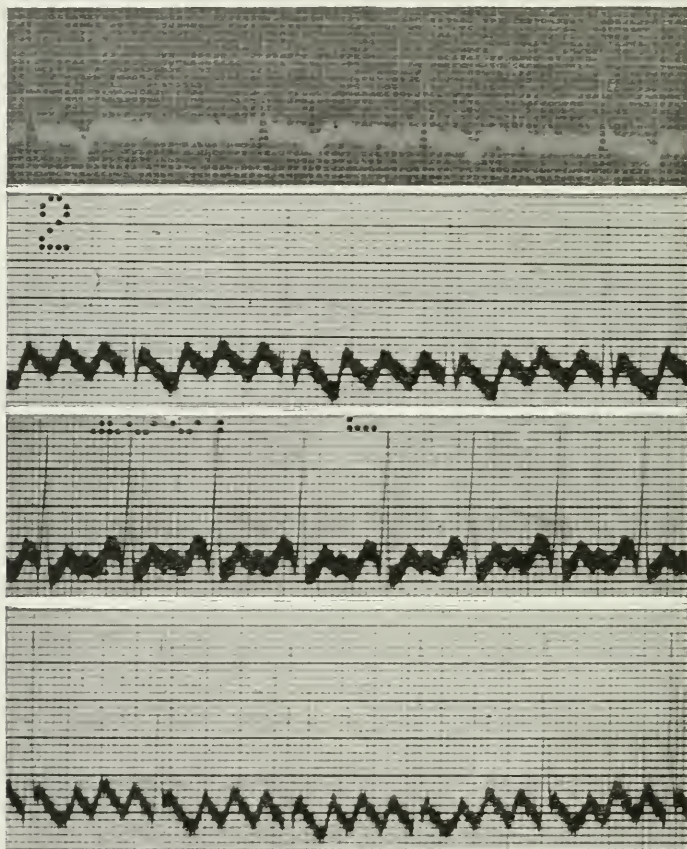
Fig. 7 (Case 12).—Top tracing made September 30, 1921. Auricular fibrillation with slow ventricular rate. Second tracing made October 3 after 2.4 grams quinidin sulphate had been taken. Auricular flutter four to one block, auricular rate, 271. Third tracing made October 6 after 6 grams quinidin sulphate. Auricular flutter two to one block, auricular rate 245. Fourth tracing made October 13, 1921, after withdrawal of quinidin for five days and substitution of digitalis. Auricular flutter four to one block, auricular rate, 316. All tracings are Lead II.

He received quinidin sulphate—the first day 0.2 gram b. d. and then 0.4 gram t. i. d.—which was increased to 0.8 gram t. i. d. in five days, when it was stopped because of ringing in the ears. The ventricular rate had dropped to around 95 and the patient stated

that he felt much better.   Five days later quinidin was again given, 0.4 gram t. i. d.   On the third morning of this treatment a regular four to one flutter developed.   After the dosage was increased to 0.6 gram t. i. d. the auricular rate became slower, but on account of the development of a two to one block the ventricular rate was much more rapid.   With the rapid ventricular rate dyspnea quickly ensued and the treatment had to be discontinued.   Ten days later fibrillation was reëstablished.

Discussion.   Of the 12 cases of auricular fibrillation treated with quinidin the normal rhythm was restored in 7, the fibrillation converted to flutter in 1, while in 4 the treatment failed to abolish the fibrillation.   In the last group the dosage was probably inadequate in 2 cases (Cases II and X), but in the other 2 it was increased to the point where symptoms due to the drug appeared.   It is of some interest that in 1 of the cases in which quinidin was not successful (Case II) there had been a period of normal rhythm a short time previously during the administration of digitalis.

In 2 cases (Cases V and VII) there was no clinical benefit from the restoration of normal rhythm, as the fibrillation was reëstablished within two weeks.   In two others (Case III and VIII) the results might be regarded as moderately successful.   Fibrillation was abolished for periods of several weeks and the patients stated that they felt better during that time.   But in both fibrillation returned and was much more refractory to a second course of treatment, although it was again possible to restore sinus rhythm temporarily.

In 3 cases (Cases IV, VI and IX) the results of quinidin therapy were excellent.   Case VI had been thoroughly treated by digitalis through at least two prolonged courses of treatment without much benefit.   His fibrillation was easily abolished by quinidin and his rhythm has remained normal for a period of more than two months. There has been striking clinical improvement.   Case XI had been severely decompensated but had improved somewhat under digitalis. There was a further very distinct improvement after the restoration of normal rhythm by quinidin.   His normal rhythm has now remained for nearly three months, during which time there has been a steady improvement in cardiac strength.   Case IV showed the most striking effect of all.   From one day's treatment the heart action changed from fibrillation, with a ventricular rate of 150, to normal rhythm, with a rate of 88.   It is noteworthy that her cardiac condition had probably been due to hyperthyroidism, a type that Frey found especially refractory to treatment.

During the periods that attempts were being made to abolish fibrillation the subjective effects were various.   Four patients, including 2 in whom the treatment was unsuccessful, said they felt better, but in the remainder there was no improvement.   One complained of weakness and dizziness, 1 of epigastric distress,

1 of a sensation of stuffiness in his ears and slight deafness and 1 of ringing in his ears. No visual disturbances were complained of. In no case did alarming symptoms develop. Several patients who were annoyed by perception of their heart action were either entirely relieved of this symptom or much benefited during the time the rhythm was normal.

There was no significant effect noted on urinary excretion either in the direction of increasing or diminishing the output. Even after the return of normal rhythm there was no particular change, although it should be said that none of the patients had much edema at the time quinidin was being given.

In 3 patients there was rather sudden marked increase in ventricular rate, which was considered an effect of quinidin. In 1 of the 3 symptoms of cardiac embarrassment quickly began to develop and the drug was discontinued, but in the other 2 the rapid rate was well tolerated and in both normal rhythm was soon established.

In Figs. 1, 3 and 5 are seen effects of quinidin on the auricular waves of the electrocardiogram during fibrillation. The oscillations tend to become larger, less rapid, more nearly uniform, somewhat approaching in form the curves of flutter. In only one case was pure flutter observed (Fig. 7). From such evidence it would seem that quinidin must exert a profound effect on the transmission of the excitation wave through its abnormal path in non-specialized auricular muscle. It seems not unlikely that such an effect of the drug may play an important part in the abolition of fibrillation and flutter.

After the restoration of normal rhythm in our cases the auriculoventricular conduction time appeared to be increased above the average. In only 2 was the $P-R$ time as short as 0.18 second, In 2 others it was about 0.2 second while in 3 it was 0.21 second or more. One patient (Case VI) received only a small amount of quinidin but the $P-R$ interval was 0.3 to 0.32 second shortly after the restoration of normal rhythm, while another (Case IX) took large amounts of quinidin without increasing the $P-R$ interval above the normal limit. It is therefore scarcely justifiable to assume that the alterations in conduction from the normal that were observed are necessarily due to quinidin.

The presence or absence of valvular disease, so far as can be judged from this small series, did not appear to affect the efficacy of the treatment. Of the 5 cases with valvular disease 3 had the normal rhythm restored as compared with 4 successful cases out of 7 without valvular disease. Likewise the age of the patient did not seem to make any particular difference. The normal rhythm apparently is not more nor less difficult to restore in the elderly than in the young.

Treatment. The use of quinidin in the treatment of auricular flutter and fibrillation is, to a certain extent, in an experimental

stage, but certain points in respect of the types of cases in which the drug may be employed and details of treatment have been established.

The most favorable cases for treatment are those with (1) relatively good heart muscle and at least fair compensation, and (2) flutter or fibrillation that has been present only a short time.

In cases with good heart muscle the restoration of sinus rhythm with the abolition of the mechanical disadvantage to the heart of such profound disturbances of its mechanism, as fibrillation or flutter may be expected to yield good results. But the use of the drug in patients with weak heart muscle is not so likely to be beneficial. Not only is it dangerous to use so depressant a drug as quinidin in such cases, but the chance of restoring the normal rhythm is much less. It is doubtful whether the advantages that may be gained by the restoration of normal rhythm in a comparatively low percentage of cases in this group counterbalances the disadvantage of still further disturbing the compensation in some cases and the possibility of meeting disaster.

The importance of the duration of flutter or fibrillation has been mentioned. It is agreed by most observers that if the abnormal rhythm is of recent origin it is much more easily removed. Not only may a small amount of quinidin be sufficient to restore the normal rhythm, but apparently the recurrence of fibrillation is more easily prevented in these cases.

In the management of patients under quinidin therapy a close observation should be maintained. The possibility of the rapid development of alarming symptoms makes it necessary that immediate attention be available. Consequently the patient would better be in a hospital or under the care of a well-trained nurse. On account of the abrupt changes in the cardiac mechanism it is a decided advantage to make frequent electrocardiographic examinations.

The sulphate of quinidin has been found preferable to the pure alkaloid in treatment on account of the insolubility of the latter. Thus far the drug has usually been given by mouth. Because of the possibility of hypersusceptibility of the patient one or two small preliminary doses, such as 0.2 gram, should be given. If any symptoms develop from such small amounts the treatment should not be undertaken. If there is no hypersusceptibility, larger doses may be given, beginning with approximately 0.4 gram t. i. d. and gradually increasing to 1 gram t. i. d. in a person of average size. It is probably not worth while to continue a course of treatment more than ten days. After a rest period a second course may be instituted if the first is unsuccessful.

As soon as normal rhythm is discovered the large doses of quinidin should be discontinued. The problem then changes to one of maintaining the normal rhythm. Thus far the results have not

been brilliant, but this may be due in part to lack of knowledge of the proper amount of quinidin the patient should take. It has been customary not to give more than 0.2 gram b. d. A great deal of work remains to be done in this field. It would appear reasonable to avoid any strain on the heart for a long time after the restoration of normal rhythm, since a strain might be expected to help convert the mechanism back to fibrillation.

The types of disagreeable effects that may occur during quinidin administration have already been stated. In the present state of our knowledge extreme caution should be observed in giving the drug if any of them develop. Such symptoms as increasing weakness, dyspnea, dizziness or precordial distress or manifestations of cinchonism, such as ringing in the ears, deafness or stuffiness in the head, should call for withdrawal of treatment. The development of a rapid ventricular rate presents a problem. If the fibrillation has been converted to flutter or a transition stage between fibrillation and flutter it is desirable to continue the treatment if possible in spite of tachycardia, since the prospect of the return of normal rhythm is good. But if symptoms of cardiac embarrassment supervene the treatment should be discontinued. Likewise should tachycardia develop before the course of the excitation wave in the auricle has been much altered the treatment would better be stopped.

Summary. 1. Studies of the physiologic action of quinidin have shown that it is a cardiac depressant influencing chiefly the functions of contractility, excitability and conductivity.

2. Quinidin has been found effectual in restoring the normal rhythm in auricular fibrillation and flutter in slightly over one-half the cases thus far reported.

3. Observations on 12 cases of auricular fibrillation treated with quinidin are reported and the effects of treatment discussed.

4. Quinidin therapy is still in the experimental stage. If it is used there must be careful selection of cases and constant observation during the course of treatment.

NON-SPECIFIC WASSERMANN REACTIONS IN DIABETES MELLITUS.

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In a series of 168 cases of diabetes mellitus treated in this clinic during the last four years, 2 cases have been observed which gave strongly positive Wassermann reactions upon their blood, there

being no history or other signs or symptoms of a specific infection. Both cases were treated for their supposed syphilitic infection over a short period of time, with marked and rapid decline of their carbo-hydrate tolerance. This effect upon their carbohydrate tolerance was so striking that it seemed to justify a report.

SERIAL CASE I.—Case No. 27672. Male, aged five years. Weight, 15 kilos. First admission April 11, 1918. First symptom of poly-uria about February 1, 1918. Glucose was first found in the urine March 15, 1918. There was no loss of weight; no history of head injury; and the heredity was negative. There had been no previous treatment. Physical examination was negative. Treatment was instituted and the patient was discharged on June 21, 1918, with an intake of protein, 60 grams; fat, 70 grams; carbohydrate, 70 grams; giving 4 grams of protein with 73 calories per kilo body weight. Weight on discharge was 14.8 kilos. There was no acidosis and the fasting blood sugar ranged from 0.07 to 0.08 per cent.

Subsequent to discharge the patient remained almost continually free from glycosuria until September, 1919. During this time his intake was protein, 60 grams; fat, 69 grams; carbohydrate, 70 grams; and his weight had increased to 19.9 kilos.

Due to the breaking of his diet he was readmitted on October 1, 1919, with marked acidosis and a greatly lowered carbohydrate tolerance. A Wassermann upon his blood was positive ($+ + + +$) on November 1 and 11, 1919. These were both fasting bloods; there was no lipemia and the reactions were performed with both human and guinea-pig complement-fixation taking place both at 37° C. and at 5° C. The family history was negative. Blood Was-sermanns upon both parents were negative. The patient was given intravenously 0.15 gram and 0.4 gram of neophenarsenyl (manu-factured by Phenarsenyl Company, Montreal, Canada) on November 18, 1919, and November 25, 1919, respectively, without reactions. Blood Wassermann upon November 29, 1919, was negative. A further injection of 0.45 gram of neophenarsenyl was given on December 3, 1919.

Table I shows the course of this patient's treatment while in the hospital, with the effect of the specific treatment upon the carbo-hydrate tolerance:

Subsequently at home during the first week after discharge he had glycosuria on an intake of protein, 15 grams; fat, 10 grams; carbohydrate, 10 grams. By January 27, 1920, his tolerance had increased to protein, 30 grams; fat, 18 grams; carbohydrate, 15 grams without glycosuria. Subsequently glycosuria appeared at more frequent intervals, with a marked decrease in the carbohydrate tolerance, death following on March 23, 1920. There was no ter-minal coma.

TABLE I.—ALL BLOOD SUGARS WERE DONE BY THE LEWIS-BENEDICT TECHNIC.

Date, 1919.	Intake.			Glycosuria, grams.	Blood.		Weight, kilos.	Neophen-arsenyl, grams.
	Protein, grams.	Fat, grams.	CHO, grams.		Sugar, per cent.	CO_2 vols., per cent.		
Oct. 2	7.5	1.3	60.0	54.0	0.402	36.1	19.18	
8	6.0	1.0	24.0	14.4	. . . . .	. . . .	19.09	
9	Fast	day	. . . .	0.0	0.360	50.0	19.54	
12	5.4	1.0	15.0	0.0	. . . . .	. . . .	20.90	
24	20.0	1.0	15.0	0.0	0.194	. . . .	17.72	
Nov. 3	30.0	20.9	25.0	0.0	0.174	. . . .	16.25	
14	40.0	20.5	30.0	0.0	0.197	. . . .	16.37	
18	40.0	25.1	30.0	0.0	0.190	. . . .	17.37	0.15
24	40.0	30.7	40.0	0.0	0.211	. . . .	17.37	
25	40.0	30.7	40.0	3.69	. . . . .	. . . .	17.37	0.40
26	40.0	30.7	40.0	9.01	. . . . .	. . . .	17.37	
Dec. 1	40.0	30.0	35.0	3.36	. . . . .	. . . .	16.92	
2	40.0	30.0	35.0	8.00	. . . . .	. . . .	16.81	
3	40.0	30.0	35.0	7.42	0.272	. . . .	16.81	0.45
5	40.0	30.0	35.0	8.12	. . . . .	. . . .	16.59	
6	Fast	day	. . . .	0.0	. . . . .	. . . .	16.59	
7	Discharged							

A summary of the more important fasting blood sugars showing the increasing hyperglycemia after the neophenarsenyl follows:

TABLE II.

Date, 1919.	Blood sugar, per cent.	Remarks.
Oct. 2	0.402	With glycosuria.
9	0.306	First day free from glycosuria.
16	0.288	No glycosuria.
Nov. 10	0.163	No glycosuria.
18	. . . . .	Neophenarsenyl, 0.15 gram.
20	0.192	No glycosuria.
24	0.211	No glycosuria.
25	. . . . .	Neophenarsenyl, 0.40 gram.
27	0.277	No glycosuria.
Dec. 3	. . . . .	Neophenarsenyl, 0.45 gram.
4	0.272	Slight glycosuria.

Nitrogen studies show an inability on the part of the patient to maintain a nitrogen equilibrium both before the neophenarsenyl with an intake of 22.8 calories per kilo and after its injection when receiving 32 calories per kilo. During both of these periods the grams of protein per kilo body weight were practically the same. With the latter period there was almost the same loss of nitrogen per day, 1.48 grams as against 1.14 grams for the former period. This shows that the nitrogen metabolism was greatly stimulated subsequently to the neophenarsenyl administration, the patient needing an increased supply of calories.

SERIAL CASE II.—Case No. 31112. Female, aged nineteen years. Admitted October 2, 1919, complaining of weakness. Was quite well until February, 1919, when she noticed increased thirst. Glucose was first found in the urine in April, 1919. Since May, 1919, she had lived upon a restricted carbohydrate diet. No history of head injury. One aunt on her mother's side died of diabetes at the age of thirteen years. Physical examination was negative except for a pruritus vulvæ.

Upon admission the first twenty-four-hour glycosuria was 52 grams upon an intake of protein, 82 grams; fat, 80 grams; carbohydrate, 128 grams. There was a slight acidosis. No blood sugar was done until October 6, the first day free from glycosuria, when it was 0.228 per cent. Under treatment the glycosuria rapidly disappeared, the acidosis cleared up and the fasting blood sugar fell to 0.094 per cent. By November 18, 1919, her tolerance had been built up to protein, 75 grams; fat, 80 grams; carbohydrate, 110 grams, without glycosuria and with a fasting blood sugar of 0.17 per cent.

On November 1, 1919, a blood Wassermann was four plus $(++++)$. Repeated on November 11, 1919, it was the same with both human and guinea-pig complement-fixation taking place both at 37° C. and at 5° C. Both of these bloods were fasting specimens and there was no lipemia. The personal and family histories were negative. On November 18, 1919, she was given 0.15 gram of neophenarsenyl intravenously. A second injection of 0.55 gram was given on November 25, 1919. On November 27, 1919, the blood Wassermann was negative. No further treatment was given.

In Table III is tabulated the reaction of the specific treatment upon the carbohydrate tolerance:

TABLE III.

Date. 1919.	Intake.			Glycosuria, grams.	Blood sugar, per cent.	Weight, kilos.	Neophenarsenyl. grams.
	Protein. grams.	Fat, grams.	CHO, grams.				
Nov. 10	75	70	90	0	0.130	44.31	
13	75	70	100	0	0.170	44.09	
17	75	80	100	0	0.180	44.09	
18	75	80	110	0	.....	44.09	0.15
19	75	90	110	0	.....	44.09	
20	75	90	110	0	0.166	44.09	
21	85	90	110	7.13	.....	44.09	
22	85	90	110	9.45			
23	43	45	55	0			
24	75	90	110	0	0.210−		
25	75	90	110	4.67	.....	.....	0.55
26	75	90	110−	8.74	.....	44.54	
27	Discharged		...	....	0.208		

Subsequent to discharge the patient's tolerance dropped off very rapidly, as shown in Table IV.

TABLE IV.

Date. 1919.	Intake.			Glycosuria.
	Protein, grams.	Fat, grams.	CHO, grams.	
December 1920.	80	90	70	+ +
January	75	80	80	+
February	70	80	70	+
March	30	40	50	+

On March 17, 1920, she was readmitted to the ward with a tolerance as shown in Table V.   Her blood Wassermann on March 23 was negative.

TABLE V.

Date. 1920.	Intake.			Glycosuria. grams.	Blood sugar, per cent.	Weight. kilos.
	Protein, grams.	Fat, grams.	CHO, grams.			
March 18	52	49.0	50.0	54.7	0.308	45.90
19	52	49.0	50.0	54.2	..	45.67
20	52	49.0	50.0	43.7	..	45.75
21	25	25.0	25.0	22.3	..	45.75
22	Fast day		....	4.9	0.258	45.22
23	20	....	....	0	..	45.76
24	20	....	....	0	..	45.00
25	25	....	....	0	0.170	45.00
26	40	0.5	10.0	0	..	44.54
27	50	0.8	15.0	0	..	44.22
28	60	0.7	20.0	0	..	44.76
29	60	10.9	20.0	3.36	0.200	44.76
30	20 (Breakfast only)	3.5	8.9	0		

Since her second discharge from the hospital, on March 31, 1920, her tolerance has still remained very low.   Most of the time she has continued to have glycosuria and the diet has not been so strictly controlled as before.

Discussion.   The occurrence of these strongly positive Wassermann reactions in cases of diabetes mellitus where there is no history or evidence of a past infection must be considered conservatively. Why they should have become negative so promptly with only slight treatment is difficult to explain, as it would appear that the reactions

were due to some disturbed physico-chemical relationship, which two injections of neophenarsenyl one would not expect to influence.

Working with the sera from known cases of diabetes mellitus, Van Saun[1] came to the conclusion that "with carefully controlled tests non-specific fixations can always be checked." Likewise Williams[2] is willing to state there is no danger of obtaining non-specific reactions.

The reported facts would indicate that material damage was done to the patients by the arsenic treatment. Probably the arsenic acted as a toxic agent upon the weakened pancreatic cells, altering the quantity or nature of their internal secretion. That it acted generally upon the glucose burning cells of the body is difficult to believe, as it apparently has no effect upon the carbohydrate tolerance when administered to syphilitic patients.

LEAD POISONING, WITH SPECIAL REFERENCE TO POISONING FROM LEAD COSMETICS.

REPORT OF FOUR FATAL CASES OF ENCEPHALOPATHIA SATURNINA OCCURRING IN ONE FAMILY.

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Introduction.—The importance of lead and its compounds in producing disease is known to very few—doctors as well as laymen—in spite of the fact that, from the standpoint of industrial poisons alone, it is the most subtle and most productive of ill-health. "If a pound of lead drops on a workman's head the catastrophe is more obvious than if minute quantities of lead are taken into the system day by day, but the poisoning may be as fatal as the accident."[1] Its foremost rank among the etiologies of the occupational diseases is to be explained by the fact that it is more or less essential in about 150 industries.[2] But great as may be the extent of its use in the industries, there is another purpose for which it is perhaps even more extensively used, that of cosmetics. Its ravages in this form,

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[1] Jour. Med. Research, 1917, xxxvii, 205.
[2] Jour. Am. Med. Assn., 1918, lxx, 365.

though by far less intensive, are very probably more widespread, and in the sum total cause greater unhappiness, discomfort and illness because of the fact that owing to its insidious and intangible poisonous action on the human body it remains unsuspected and unrecognized.

The fact that cases of poisoning due to lead-containing cosmetics usually remain undiagnosed, may perhaps explain why there is so little to be found in the literature relative to this type of poisoning. Oppenheim[3] makes the statement that the use of cosmetics containing lead (rouge) sometimes produces poisoning. Similarly, Rosenau[1] states that lead poisoning may be caused by the absorption through the skin from cosmetics containing lead. Lewandowsky,[4] Osler and McCrae[5] and Sollmann[6] mention the occurrence of poisoning from lead-containing cosmetics (paint, rouge, hair-dyes) as not uncommon. Cooley,[7] in 1866, stated that the daily use of oil or pomatum containing a few grains of lead carbonate or lead plaster are unsafe for long-continued use. "Atrophy of the scalp, baldness and even local paralysis have sometimes though rarely been caused by them." But none of these authors gives any details beyond these meager statements. Out of hundreds of references in the literature dealing with lead poisoning in its various phases only one was found to bear directly upon poisoning from lead-containing cosmetics, and by a remarkable coincidence the cases and conclusions bear a very close resemblance to those which form the basis of the present study.

This article, published forty years ago by J. W. Holland,[8] warns against the dangers lurking in cosmetics which are not guaranteed to be free from lead and its compounds. In the two cases cited by him, curiously enough, the cosmetic involved is identical with that which was found to be the etiological factor in the poisoning which forms the subject of this paper.

His first case is that of a seamstress, aged twenty-eight years, who presented a blue line on the gums, double wrist-drop, pale and sallow complexion and yellowish, discolored eyes. She asserted that to her knowledge she had not been exposed to lead in any form. However, a very evident application of powder on her face led to the disclosure of the fact that for two years she had made unstinted use of a fine white powder sold by druggists under the name of "Flake White." During this period she had repeatedly suffered from constipation and colic which were attributed to indigestion. She also had had spasmodic attacks of vertigo and headache. After she had used the powder for about a year she was treated by her doctor for melancholic mania. During the second year she developed weakness, tremors of the hands, and became depressed in spirits and irritable. Her doctors had been unable to diagnose her case and it was only when she had developed double wrist-drop that she consulted Holland, who made the correct diagnosis.

On her second visit she was accompanied by her younger sister, who had stopped working because of failing health and loss of power in her right hand. She had lost in weight and suffered from attacks of rheumatism in the shoulders and the right elbow. Twice her doctors had treated her for supposedly epileptic convulsions. She also admitted having used the same cosmetic during the previous two years.

Holland very aptly points out how insidious and undetected are the effects of lead cosmetics when the melancholic delirium and epileptiform convulsions were not recognized as part of the syndrome of lead encephalopathy, when lead arthralgia was treated for rheumatism, and when lead colic and constipation were regarded as merely phases of a weak digestion.

Before proceeding with the discussion of the major cases in this study it is interesting to note that among 20,000 admissions to the University Hospital, Minneapolis, there were 7 cases admitted which were diagnosed at the hospital as chronic lead poisoning. Of these 6 were men and 1 a woman. Of the 6 cases 2 were painters who had been sent to the hospital with the diagnosis of chronic lead poisoning. These had the classical signs of constipation, severe headaches, colicky pains in the region of the umbilicus and the lead lines on the gums. A third was a paint filler who was sent in with a diagnosis of diabetes mellitus and probable stone in the left kidney. A fourth was a painter sent in as a case of neuritis. A fifth, occupation not mentioned, was sent in with the diagnosis of duodenal ulcer or gallbladder disease. He presented characteristic symptoms and findings of lead poisoning, including basophilic granulations of the red cells. The sixth case, occupation not given, was sent in with the diagnosis of gastric ulcer, carcinoma or gastritis. This case also gave the symptoms and findings of lead poisoning. He had been in one of the large hospitals of the city six months previously, suffering from the same complaints that he had on entering the University Hospital—colic, vomiting, weakness, loss in weight and anemia—but the correct diagnosis had not been arrived at. Of these 6 cases only 2 had been correctly diagnosed by the physicians who referred them. Of the remaining 4 cases 2 presented symptoms and findings sufficient for a proper diagnosis. The other 2 cases were men employed in occupations which should have strongly hinted at the probable etiology of the symptoms, and yet so unknown and unsuspected are cases of lead poisoning that they went unrecognized even when the occupation alone should have been sufficiently suggestive.

REPORT OF CASES.

CASE I.—The seventh case, G. D., Hospital No. 9618, that of a woman, is almost a duplicate of the first case cited by Holland.[8] The patient, also a seamstress and of the same age, twenty-eight

years, was admitted on the service of Drs. Rowntree and Richards
on September 21, 1916, complaining of pain in the epigastrium,
insomnia, nervousness and pain in the arms. Her doctor sent her
in with the diagnosis of an indeterminate pelvic condition. She
stated that she had had attacks of severe cramp-like pains in the
epigastrium, accompanied by nausea and vomiting, for about ten
years. These attacks would last about two weeks and recurred two
or three times a year. Nothing seemed to relieve the pain.

During the three months previous to her admission the symptoms
of weakness, nervousness, dyspnea, loss of weight, constipation,
abdominal cramps and vomiting became so severe that she had to
quit her work. She also developed pains in her arms. She stated
that she had had two operations: one for appendicitis, seven years
ago, and the other a laparotomy five years ago. She did not know
the character of the second operation.

Examination at the hospital showed a marked emaciation, her
weight having dropped from her normal weight of 98 pounds to
the present weight of 72 pounds. There were coarse tremors of the
fingers, hands and arms. There was atrophy of the interossei
muscles of both hands. A bilateral wrist-drop of mild degree
developed in the hospital. There was gingivitis, dental caries and
a grayish-blue line on the gums. The patient was restless and
complained of severe headaches. The anemia was marked. Exami-
nation of the blood showed 45 per cent. hemoglobin, 3,600,000
erythrocytes, 9100 leukocytes and a moderate degree of basophilic
granulation. The urine showed a trace of albumin and a few
hyaline casts. The phenolsulphonephthalein test was normal. The
anamnesis and the clinical and laboratory findings of the case sug-
gested the diagnosis of lead poisoning very strongly. In carefully
questioning the patient as to any possible source of exposure to lead
the information was elicited that she had used "Flake White" face
powder very freely for over fourteen years. As early as three years
previously her dentists had remarked about a blue line on her gums.

This case shows that not only had the condition remained unrec-
ognized for at least three years after unmistakable evidence of lead
poisoning had developed, but that the symptoms at times had
probably simulated surgical conditions and that the two previous
operations very likely resulted from an improper diagnosis of the
case. Mention of uncalled-for surgical intervention in cases of
lead poisoning is not infrequent in the literature.

The most flagrant examples of the dangers lurking in lead-con-
taining cosmetics and the facility with which proper diagnoses
are overlooked will be found in the following four fatal cases of
encephalopathia saturnina occurring in one family.

CASE II.—On August 30, 1920, a girl, L. F., aged sixteen years,
Hospital No. 19,723, was brought to the University Hospital in an

ambulance in a stuporous, semiconscious condition. She was entered on the service of Drs. S. Marx White and R. I. Rizer, to whom we wish to express our gratitude for the opportunity of studying and reporting this case. The following history was obtained from the father of the girl:

The patient has always been strong and healthy. She has had the usual diseases of childhood: whooping-cough, diphtheria and measles. At the age of eight years she had acute nephritis. She had bronchitis and pneumonia twice before she was four years old, but without complications. She has had several mild attacks of sore-throat. Otherwise her past history has been entirely negative. Her present illness began about July 12, 1920, with an attack of sore-throat and severe headache, which lasted only for a day but left the patient in a very weak and easily fatigued condition. This weakness continued during the next two weeks. On August 1, 1920, she was suddenly seized with severe colicky cramps in the abdomen, which caused her to double up, vomit and cry out with pain. The attack lasted only for a few minutes and then passed away, but during the following week she experienced five similar attacks. The next week she was able to be up and around, but she complained of extreme nervousness and of pain in the legs and feet. She was taken to a hospital in a nearby town where she remained for a week, with no improvement. No diagnosis was made of her condition. She was then removed to a hospital in another town, where she remained for about a week. While in this hospital she sank into a stupor and became irrational and semiconscious, talking incoherently. The pain in the abdomen, arms and legs became very severe. She developed an obstinate constipation. There were twitchings of the muscles about the face and arms. She had several convulsions and became incontinent of her urine and feces. Her skin began showing an increasingly marked pallor. The physician who sent her to the University Hospital stated on her application that the diagnosis of this case had not been determined and that during the past year the patient's mother, sister and aunt had died under similar circumstances.

Physical examination on admission showed a fairly well-developed but poorly nourished young female with a mask-like expression of the face, lying quietly in bed in a stuporous and semiconscious condition. She was in no apparent pain or discomfort. Occasionally she would open her mouth as if she wanted to speak. She would respond sluggishly to commands, such as to protrude her tongue. The eyes were partially closed and showed no paralysis, ptosis or strabismus. Nystagmus could not be elicited. The left pupil was slightly larger than the right and somewhat irregular. Both reacted sluggishly to light. The lips were dry, cracked and encrusted. There was a very offensive odor to the breath. The tongue showed a coarse tremor. The gums appeared in good condi-

tion and showed nothing abnormal. There was a marked rigidity and stiffness of the neck. Attempted movements of the head seemed to cause pain. The heart and lung findings were negative. The abdomen was somewhat rigid and tender to deep palpation. It was otherwise negative. The extremities showed slightly hyperactive reflexes of the knees, ankles, biceps and triceps. There was no ankle-clonus, Babinski or Oppenheim present. Kernig's sign was positive. The blood-pressure was 118/75 mm. of mercury. A tentative diagnosis of tuberculous meningitis or lethargic encephalitis was made on admission.

Examination of the eye-grounds showed no choked disk, and because of the evidences of meningeal irritation a spinal puncture was performed. About 10 c.c. of clear limpid fluid were withdrawn. It escaped under slightly increased pressure. Examination of the fluid showed a cell count of 6 c c per millimeter. Nonne colloidal gold and Wassermann tests were negative. Examination of the urine showed a trace of albumin and an occasional granular and hyalin cast and a small number of leukocytes. Examination of the blood showed hemoglobin 45 per cent., erythrocytes 2,500,000, leukocytes 18,600. The differential count showed 88 per cent. polymorphonuclears, 7.5 per cent. lymphocytes, 0.5 per cent. eosinophiles and 4 per cent. basophiles. Several myelocytes were seen. There was a moderate anisocytosis and slight poikilocytosis. There was an occasional normoblast present, a moderate polychromatophilia and a very marked basophilic granulation of the erythrocytes. The basophilic granulation was the most striking finding obtained in the entire examination of the patient, both physical and laboratory. It was the more striking because it was so unsuspected. This finding at once suggested lead poisoning as a strong possibility in this case, but we were completely puzzled as to the source of exposure. We approached the father for further history. We inquired about the water supply and plumbing at their home. He said that they lived on a farm where they had an iron pump which had been there for many years, and that to his knowledge there were no lead pipes in the system. To all questions relative to the possibility of exposure to lead he was able to give no definite clue.

He volunteered, however, the suggestive information that this mysterious disease had peculiarly afflicted only the female members of his family, himself and ten-year-old son alone having been exempted.

CASE III.—Concerning the histories and findings of the other members of the family, we were informed by the father and the doctors then in charge that L. P. F., an aunt of the patient, took sick about September 4, 1919, complaining of pains all over the body, great weakness and nervousness. She cried a great deal. The physical examination showed: "Well-nourished woman, rather

pale, with a pulse of 90 and a normal temperature. There was a systolic murmur at the apex but the heart was not enlarged. The knee-jerks were exaggerated. The blood examination was limited to the estimation of hemoglobin, which showed 70 per cent. A diagnosis of hysteria and a mitral lesion of the heart was made. In the latter part of November of the same year the patient was suddenly seized with violent convulsions; she died shortly afterward."

CASE IV.—V. F., a girl, about five years old, a sister to the patient, was first seen by the physician on March 22, 1920. She complained of severe colicky cramps in the abdomen with vomiting. The past history was unimportant. Physical examination showed a poorly nourished, very anemic child, having a waxen appearance. The heart was slightly enlarged and there was a loud systolic murmur at the apex. The spleen was palpable. The urine was not examined. Blood examination showed about 70 per cent. hemoglobin with 3,000,000 erythrocytes. On March 28 the physician was again called. He found the child in convulsions, from which she died several hours later.

CASE V.—Mrs. F., the mother of the patient, took sick with symptoms similar to those of the others. The attending physician gave no details other than stating that she died in convulsions from an unknown cause under circumstances similar to the other two deaths in the family.

This information furnished by the father and subsequently amplified by the attending physician led to a conviction that there was a common etiology for all four cases, and, as has already been mentioned, the case in the hospital suggested lead poisoning.

In subsequent inquiries the matter of face-powder was mentioned and the father then recalled that the aunt had introduced into his household in the latter part of the year 1919 a variety of face-powder known as "Flake White." This powder had been used by the female members of his family since that time. The aunt had used it for a number of months previous to this. She recommended it as being both good and inexpensive. The method of applying it was to make a thin paste by mixing it with water and rubbing it between the hands and then to work it well into the skin, giving special attention to the wrinkles. The result at first would be a grayish-white surface, which on drying became pearly white. The feature for which this powder especially recommended itself to the users was the lasting quality of each application. The father stated that he himself had always purchased it for them in bulk at the local drug store.

A quantity of this powder was purchased by him at our request and turned over to us for chemical analysis. The heaviness of the powder impressed us at once. We examined it chemically and found

this powder, known as "Flake White," to be pure lead carbonate. On inquiring we not only found that it was commonly sold by all drug stores, including the very best recognized ones, but that it was freely admitted by the druggists to be lead carbonate, ground into an impalpable powder. It was dispensed to the trade for cosmetic purposes and was used principally in the form of lotions. The father said that to his knowledge this powder was quite generally used in his neighborhood.

CASE II (continued).—The patient died on September 5, 1920, just seven days after her entrance into the University Hospital. During this short stay several of the symptoms characteristic of lead poisoning appeared. Throughout this period she had involuntary urination and defecation. Her condition on the different days of her residence in hospital was as follows:

First Day. Patient was comatose but appeared very sensitive to touch. She did not answer when spoken to. The temperature was 98.6°, pulse 120, respiration 18.

Second Day. Periodic twitchings of the muscles of the face and extremities developed. Patient had difficulty in swallowing. She appeared more stuporous. She was fed by nasal gavage. Temperature 101.2°, pulse 140, respiration 24.

Third Day. Patient appeared somewhat brighter during the morning. She attempted to speak several times but uttered no intelligible sounds. She appeared to be more conscious of her surroundings and protruded her tongue on command. Temperature 100.2°, pulse 140, respiration 22.

Fourth Day. No special change from the previous day.

Fifth Day. Patient again attempted to speak. There were marked twitchings and tremors of the muscles of the face and hands. It was decided to start the administration of small doses of potassium iodide. She received two doses of three minims each of the saturated solution.

Sixth Day. Patient appeared more conscious and alert, but very irritable. With a little assistance she sat up in bed and drank a glass of eggnog, the first food she had swallowed by herself since her entrance. Both wrists showed marked weakness, which later in the day developed into mild wrist-drop. A faint bluish line appeared on the gum of the lower jaw. She received three doses of three minims each of potassium iodide solution. Temperature 102°, pulse 145, respiration 30.

Seventh Day. The bilateral wrist-drop became very pronounced and the blue line on the gums became plainly visible. The respirations were more rapid and the general condition of the patient was definitely less favorable. The potassium iodide solution was discontinued and stimulants were administered. In the morning the temperature rose to 103° and in the afternoon it reached 105°.

The pulse averaged about 150 and the respiration about 30. Crepitant and subcrepitant rales were elicited over both lungs posteriorly, but no evidences of consolidation were present. There developed a marked cyanosis. The pupils became unequal and extremely rapid spasmodic changes in the size of the pupils occurred. They contracted and dilated very suddenly, these variations not being due to any change in the intensity of the light in the room. She sank very rapidly and died on this day at 4.25 P.M.

Laboratory Examinations. Several examinations of the urine showed a faint trace of albumin with occasional granular casts and leukocytes. Because of the incontinence it was impossible to collect large quantities of urine for purposes of chemical analysis; however, about 300 c.c. were collected up to September 2. This was evaporated and tested for lead but the reaction proved negative. There is a possibility that if the urine voided after the administration of the potassium iodide had been tested for lead a positive reaction might have been obtained. Negative tests for lead in urine are not uncommonly encountered in cases of chronic lead poisoning.

Repeated examinations of blood smears stained with Wright's stain showed an average of 83 per cent. polymorphonuclears, 7 per cent. lymphocytes, 4 per cent. large mononuclears, 2 per cent. transitionals, 2 per cent. basophiles and 2 per cent. neutrophilic myelocytes. As previously mentioned the striking picture in the blood smears was the very marked basophilic granulation of the erythrocytes. Fig. 1 shows a drawing of an actual field of a smear as seen under the microscope with the oil-immersion lens. Fig. 2 shows a composite picture of various types of basophilic granulation and polychromatophilia encountered. The number of red blood cells involved varied with the quality of the staining as well as of the stain, which would indicate that the failure to find basophilic granulations in cases of lead poisoning is often due to faulty technic. Schnitter[9] calls attention to this fact when he states that in his early investigations of lead poisoning he rarely encountered basophilic granulations in the blood cells, but after he perfected his staining technic he was able to demonstrate the granulations in almost 100 per cent. of his cases. Well-stained smears in our case showed 3.2 per cent. of erythrocytes to be affected by the basophilic granulation, which represents the enormous figure of 32,000 in every million cells. When one considers Trautmann's[10] dictum that more than 100 affected cells per million generally means lead poisoning and that more than 300 affected cells per million is sufficient evidence of lead poisoning for forensic medicine, one can appreciate the significance of the above figures.

Besides the basophilic granulation there was also considerable diffuse polychromatophilia. This diffuse basophilia involved about an equal number of cells as the granular basophilia. The granules in the cells varied in size, shape and the number present in each

cell. Some of the granules are rather coarse, and, as a rule, are relatively few in number. Others are very fine and fairly numerous.
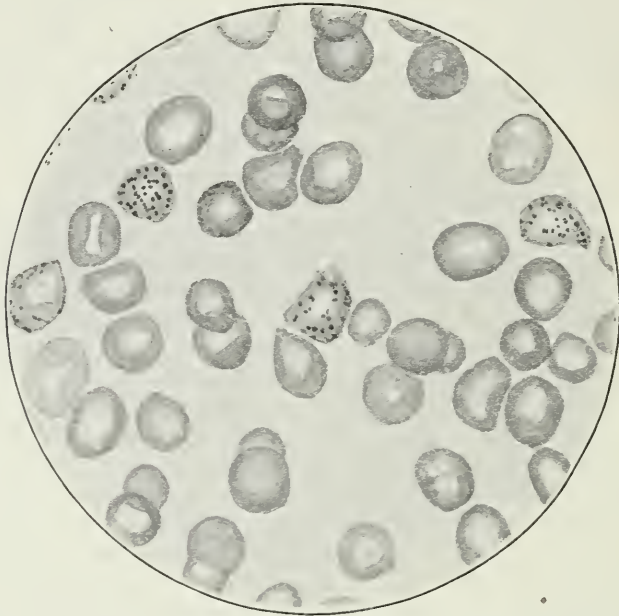
FIG. 1.*—Drawing of an actual microscopic field of a blood smear stained with Wright's stain stain, from Case II. (No. 10 ocular, oil-immersion objective.) Note the relatively large number of granular cells and the coarseness of the granules.

They are basic staining, round or angular, and occasionally appear like small rods resembling bacilli. The majority of the granules
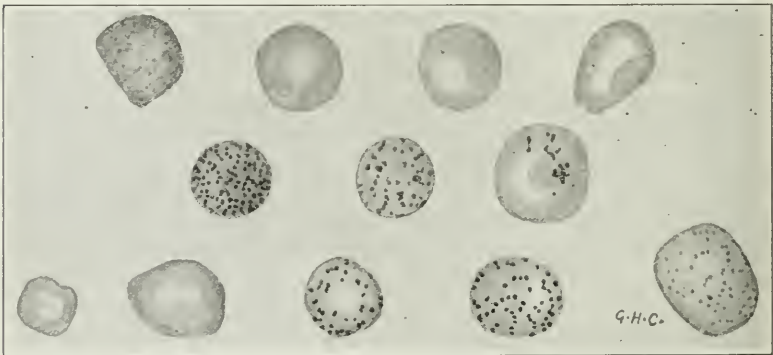
FIG. 2.*—A composite picture (drawing) of pathological cells encountered in the blood smears. Note the variations in size, shape and number of these granules.

* Figs. 1 and 2 are from drawings in color made by Mr. G. H. Childs, of the art department in the Department of Anatomy. All photomicrographs were made by Mr. Henry W. Morris, of the Department of Pathology.

are the shape of cocci, though somewhat smaller, and are often grouped in pairs like diplococci. The other changes in the red blood cells are not very marked. There is a moderate degree of anisocytosis and a slight degree of poikilocytosis present. There is no doubt but that the blood picture in this case is absolutely pathognomonic of lead poisoning. The surprising feature to us is that in spite of so definite and characteristic a blood picture the case had not been correctly diagnosed before entering the University Hospital.

Autopsy Protocol. An autopsy was performed on this case sixteen hours post mortem. As was to be expected in a case of lead poisoning there were few gross lesions present. The principal findings are as follows:

The body is that of a fairly well-developed but poorly nourished female, aged sixteen years. There is no edema and no jaundice. There is marked pallor and blanching of the skin and mucous membranes. There is a faint bluish line along the margin of the gum of the lower jaw. The heart has a yellowish-brown color and is flabby. The dependent portions of the lungs are slightly heavier than normal; droplets of mucopus can be expressed from the bronchioles. There are no areas of consolidation. The spleen is about twice the normal size; the pulp is soft. Liver and gastro-intestinal tract show no gross lesions. The left kidney weighs 75 grams, the right 100 grams. There is marked postmortem autolysis present. There are multiple nodules (abscesses), 1 to 3 mm. in diameter, scattered through the parenchyma of the right kidney. The intervening tissue between the nodules appears normal. The left kidney shows no gross lesions. In removing the brain a fairly large quantity of cerebrospinal fluid escapes. Examination of the brain reveals no gross lesion. The entire brain is preserved for histological study.

Lead was found in the liver and the left kidney by chemical analysis. For this we are indebted to Mr. J. P. Quigley, of the Department of Pharmacology. This final analysis established incontestably the diagnosis of lead poisoning in this case.

Microscopic examination of most of the tissues and organs revealed very little of interest and will therefore be omitted here. Only the tissues showing pathological changes will be considered.

A section of the heart stained with Sudan III shows a slight increase of interfibrillar fat within the muscle fibers. The lungs show slight congestion and a few minute patches of bronchopneumonia. The liver shows a moderate degree of fatty metamorphosis around the central veins and a slight round-cell infiltration into the periportal spaces. Sections of the right kidney show miliary abscesses in the cortex and a few also in the pyramids. There is extreme postmortem autolysis present throughout, and this greatly hampers a careful histological study. Sections from both kidneys stained with Sudan III reveal the presence of large
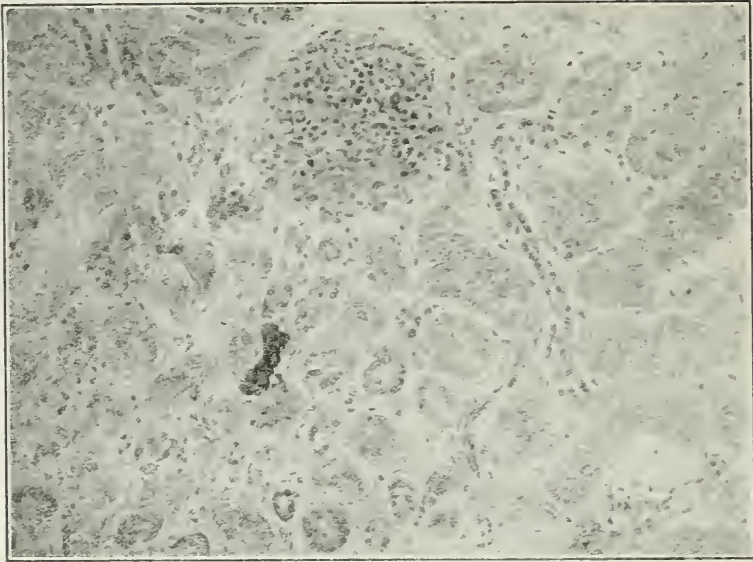
Fig. 3.—Photomicrograph of section of kidney. The postmortem autolysis is marked; this explains the peculiar appearance of the glomerulus. Closely packed rosette-shaped masses of lime salts are seen deposited in a degenerated tubule from Henle's loop.
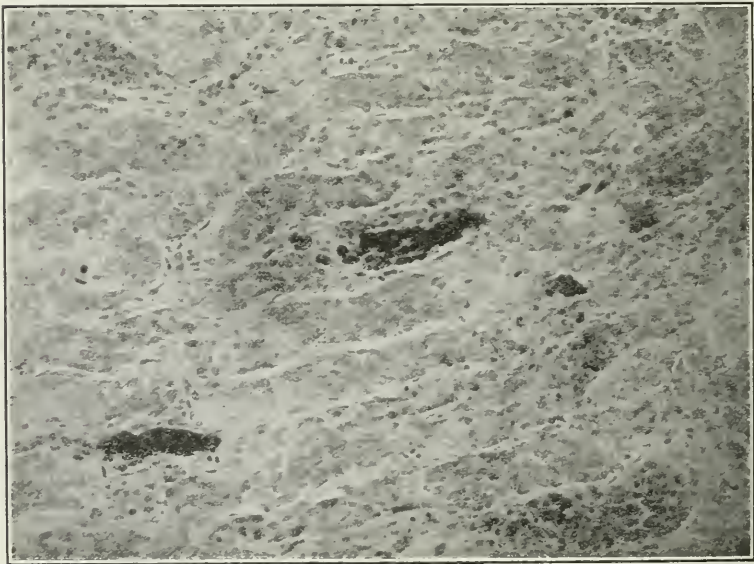
Fig. 4.—Photomicrograph of section of kidney showing several degenerated convoluted tubules filled with masses of lime salts.

and small fat droplets within the epithelial cells of segments of convoluted tubules. There are occasional large clumps of lime salts, some shaped like rosettes, filling up many degenerated collecting tubules and loops of Henle (Figs. 3 and 4). The amount of lime salt deposit is quite striking, and the changes in the kidney other than the accidental abscesses resemble very strongly the lesions produced by mercurial poisoning. The glomeruli show no definite lesion.

We are indebted to Dr. J. C. McKinley, of the Department of Neurology, for furnishing us with excellent sections from all of the different areas in the brain as well as for his assistance in the study
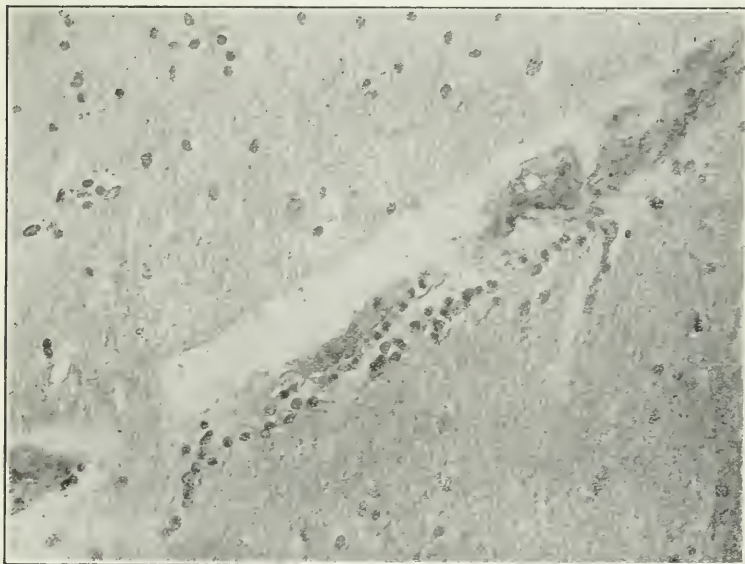
Fig. 5.—Photomicrograph of section from the midbrain. Note the narrow arteriole surrounded by several rows of lymphocytes, more marked on one side. Most of the sections show a clear space between the vessel wall and the surrounding tissues. This may be an artefact due to shrinking.

of these slides. Considering the intensity of the clinical symptoms the pathological lesions found in this brain are surprisingly meager compared with those of lethargic encephalitis, where the histological changes are often very profound, even in cases presenting mild clinical cerebral manifestations. The more intense lesions—and these are relatively insignificant—are in the sections from the thalamus, the lenticular nucleus and the midbrain. Here and there are seen slight perivascular round-cell infiltrations around the small arterioles. Sections from the midbrain (Fig. 5) and from the lenticular nucleus (Figs. 6 and 7) show the perivascular infiltration very plainly. In the lymph spaces surrounding many of these arterioles

are seen clumps of large phagocytic cells containing granules of bluish-green crystalline-appearing pigment. We do not know the
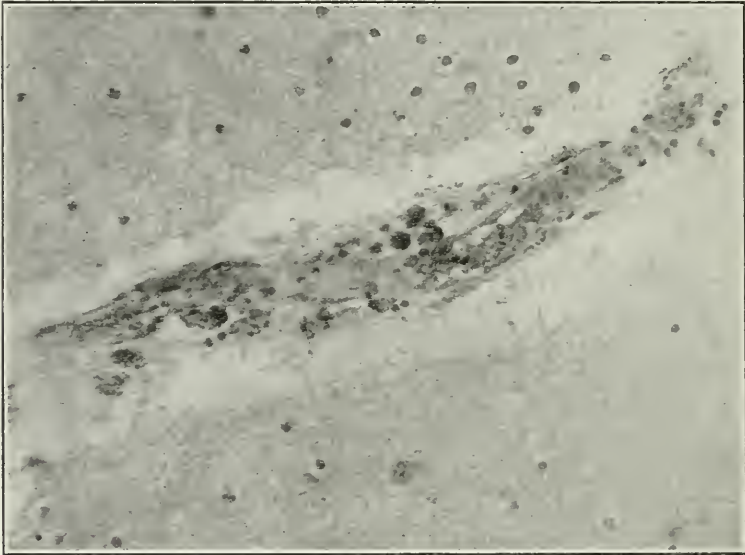
Fig. 6.—Photomicrograph of a vessel in a section from the lenticular nucleus. Note the large phagocytic cells containing a greenish crystalline pigment surrounding the vessel.
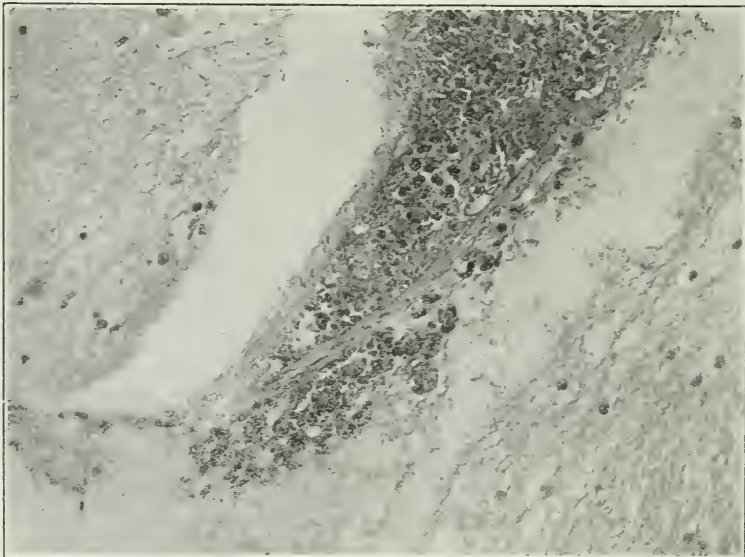
Fig. 7.—Photomicrograph of a larger vessel than in Fig. 6. The perivascular infiltration of large phagocytic cells containing the pigment granules is well shown.

character or the significance of these pigment granules. No microchemical tests were used for their identification. This pigment does not resemble the ordinary blood pigments, hemosiderin or hematoidin, nor is it opaque enough to represent particles of lead or its compounds. It may consist of phagocytized material of the basophilic granulation; if so it is fairly characteristic of the disease. Monakow[11] mentions a similar pigment. In the routine histological studies of brains in various other diseases we have not encountered this type of pigment. In the intima of some of the small arterioles there appears to be a proliferation of the endothelial cells.

Changes are also present, though slight, in the ganglionic cells themselves. Neuronophagia and satellitosis are occasionally encoun-

Fig. 8.—Photomicrograph of a section from the thalamus. Note the neuronophagia and satellitosis.

tered in some of the slides, but are most evident in sections from the thalamus (Fig. 8). It is difficult to determine whether the degenerations of the cells are due to the direct toxic action of the lead or are secondary to the changes in the bloodvessels. One of the bloodvessels in the thalamus (Fig. 9) shows complete occlusion by a mass of round cells, principally lymphocytes. The vessel is very thin-walled and there is considerable edema in the tissue immediately surrounding it. We do not know whether there is any significance in this type of lesion.

Discussion. The clinical evidence, the laboratory evidence and the evidence obtained at postmortem, supported· by chemical analysis of the organs, prove this case, beyond peradventure of a

doubt, to be one of lead poisoning, and that poisoning to be due to the use of a lead-containing cosmetic. It appears to be evident that the three other members of the family had been stricken during the course of the year by the same cause.

The aunt (Case III) had presented symptoms of weakness, nervousness and pains all over the body, anemia and frequent crying spells. The diagnosis in this case was hysteria. These symptoms are very common in lead poisoning. In fact, Charcot has given many characteristic examples of cases which he termed "hysterie saturnine." Oliver[15] states that some cases of encephalopathia saturnina begin like hysterical attacks with crying and laughing and death often follows within a few days of the onset.
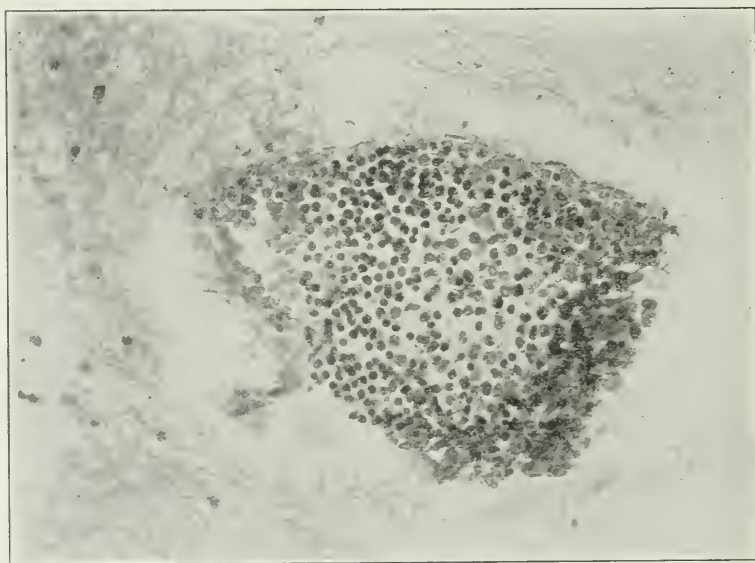
FIG. 9.—Photomicrograph of section from thalamus showing a cross-section of a fairly large thin-walled vessel completely filled with lymphocytes, a few endothelial cells and a few polymorphonuclears.

Case IV, that of the five-year-old girl, had also presented symptoms of lead poisoning, such as severe colicky cramps, vomiting and anemia. Death occurred in convulsions. This fact, together with the symptoms and the course of the disease, points very strongly to that conclusion, especially when considered in conjunction with the other cases. It is easy to assume that the exposure to the lead in this case probably occurred through the handling of the child by the other female members of the family at times when their hands were contaminated with powder, and we might also assume that, like other children, she had at different times dabbled

her face and hands with the powder of the women of the household. It is a well known fact that poisoning from lead does not depend upon the quantity ingested, inhaled or absorbed but upon the constant repetition of doses over a long period of time, however minute those doses may be.

The mother (Case V) died in convulsions. Although her symptoms are not given in detail either by the father or the attending physician, both stated that the circumstances of her sickness and death were entirely similar to those of the other affected members of the family.

We have thus far presented definite evidence of one case of non-fatal lead poisoning (Case I), one case of fatal lead poisoning (Case II), and three other cases of fatal poisoning in the same family as Case II, in which the presumptive evidence is so strong as to justify the conclusion that all five cases of poisoning were due to the use of a lead-containing cosmetic, dispensed in most if not all of the drug stores under the trade name of "Flake White." Besides these cases we have record in the literature of two similar cases in which the victims are reported to have used the very same powder. It was by mere chance that the true nature of these five cases was finally discovered. It requires therefore no great stretch of the imagination to realize, what cannot be too often repeated, that with the widespread dispensing of this powder for cosmetic purposes—without limitation—the number of persons suffering from the effects of this cosmetic whose condition remains unrecognized must be legion. The practice of using "Flake White" as a cosmetic is therefore definitely a menace to public health and demands attention of the health authorities.

Industrial and Miscellaneous Forms of Lead Poisoning. In connection with the study of these cases of poisoning from cosmetics it may be of interest to discuss lead poisoning in general, with special reference to the pathology associated with the various characteristic symptoms.

As has already been stated, lead is the commonest of all industrial poisons. Lead poisoning is encountered among painters, lead-smelters, paint manufacturers, plumbers, file-makers, linotypers, putty-makers and among workers of many other industries too numerous to mention. According to Oliver the causes of lead poisoning in painting, one of the occupations most commonly affected, are as follows:

1. Mixing of paint (dust).
2. Holding brush between the teeth.
3. Not washing the hands before eating.
4. Sandpapering of painted surfaces, which produces dust that is inhaled.
5. Burning off old paint, which produces fumes that are inhaled.

Accidental poisoning may come through drinking water which has passed through lead pipes or has been stored in lead-lined cisterns (Osler,[5] Oppenheim.[3]) Rosenau[1] states that this form of poisoning is more common than it is given credit for.

Lead poisoning may also occur from the solder in canned goods, from utensils lined with lead, various beverages, false teeth and thread and snuff containing lead. It has followed the use of lead and opium pills, lead ointment and in infants from the application of lead wash to the mothers' nipples. Osler reports an outbreak of lead poisoning in Philadelphia from the use of baking-powder containing lead chromate.

At this point it may be of interest to quote two cases cited in the literature of poisoning from unusual sources:

One case is reported by Stefanowicz[12] of a woman, aged thirty years, who developed lead poisoning from an apparently unexplainable source. She presented the characteristic blue line on the gums, bilateral radial palsies and complained of colic. Stefanowicz went out to her home in the country in order to investigate any possible sources of exposure. He observed a pile of kindling wood which had paint on one side lying near the house. This wood had come from an old painted building which had been torn down. Upon investigation it revealed that the woman baked her bread in a large open oven heated with this kindling wood and that the ashes were allowed to remain on the stones. The fact that a toothless old grandmother who could use only the soft part of the bread and a young child who preferred that part were both exempt from this poisoning, while the patient, who alone ate the crust, was affected, led to the conclusion that the bottoms of the loaves of bread became impregnated with the lead from the paint which had settled down as a fine heavy dust on the surface of the stones. Chemical analysis of this dust corroborated the presumption.

Rand[13] cites a case of the development of symptoms of lead poisoning in a dairyman who drove a milk wagon into town every morning. The water supply was neither pumped nor piped and therefore could not be considered a source of the poisoning. It was learned that the man had been drinking beer from bottles which had been cleansed with lead shot, and examination revealed the presence of some of the lead shot in the bottles which had not been removed after the cleaning.

Statistics. The number of deaths from lead poisoning is truly appalling. Hamilton[14] reports that in a period of sixteen months, from January, 1910, to April 3, 1911, there were 358 cases of lead poisoning with 23 deaths in twenty-three white-lead factories in the United States. Oliver[15] states that in ten years in England there were 1973 cases of poisoning reported in house painters and plumbers alone with 393 deaths. In Paris out of 300 patients admitted into the hospitals for lead poisoning 233 were house

painters. Osler reported 60 deaths in England and Wales during 1916. In the United States he reports 147 deaths in the registration areas during 1917.

All investigators mention the fact that females are more liable to plumbism than males. The proportion is given as four to one.[5] There is a special tendency among women to the cerebral encephalopathic forms. It is almost impossible for a pregnant woman working in a lead industry to give birth to a healthy child.[1][15] There occurs either abortion, miscarriage or the early death of the child from convulsions. Curiously enough this often happens in a high percentage of cases when only the father works in lead industries. This has also been found to be the case experimentally in animals.[16] Sterilization of the male is also not uncommon. That lead passes from the mother to the fetus is evident from the fact that it has been found chemically in the organs of the infants of lead-workers.

Women who take lead pills for producing abortion often die of the effects. The abortion is brought about by the killing of the fetus and by the stimulation of the uterine muscles to contraction.

Period of Exposure. There is no specified length of time for the development of lead poisoning. It is given as all the way from a week to ten years. The largest number of cases occurs during the first few months of exposure. Cases are reported in which the exposure was less than two weeks. Oliver reports a case of a woman dying of encephalopathia saturnina in three months. The length of time of exposure in the four fatal cases here discussed cannot be definitely given but can be safely stated to have been under one year.

Routes of Absorption. Lead gains entrance into the body by three routes: (1) Swallowing of minute particles of the substance; (2) by inhalation of lead dust or the fumes of lead in a molten state or the vapor of lead in a fused state, and (3) by absorption through the skin. It is the consensus of opinion of most investigators that the gastro-intestinal is the most common and the skin the relatively unimportant route. In the respiratory route the moisture, heat and carbon dioxide from the lungs help transform the insoluble carbonate into the soluble bicarbonate. In the gastro-intestinal route the saliva is supposed to have a slight solvent action on the carbonate in the mouth while the hydrochloric acid of the gastric juice changes the carbonate into soluble chlorides. The soluble lead compounds then combine with the proteins, forming an albuminate of lead. It has been found that the lead is more readily absorbed through an empty stomach, especially when there is hyperacidity or hypersecretion present. Absorption through the skin is facilitated by the fatty acids of the perspiration, which also help to transform the insoluble into soluble compounds. Oliver mentions the occurrence of cases of lead poisoning through the absorption of lead through the skin of the hands from the washing of painters'

overalls. In our series of cases as well as in the cases cited by Holland the entrance of the lead face powder into the system might have occurred through all three routes. However, it is very likely that in these cases absorption through the skin played an important part, since the perspiration which so frequently covers the face would assist this process of absorption.

Patterson[2] claims that the *inhalation* of dust or fumes is the chief source of industrial poisoning and that this method is more dangerous and produces symptoms earlier than the *ingestion* of larger quantities of the same compound.

Rand[13] mentions the discovery of lead in the blood plasma and believes this to be of the highest importance for purposes of diagnosis. This finding explains the manner in which lead is distributed through the body. It is thought that it exists in the plasma in the form of an albuminate.

From the plasma the lead is absorbed by the various organs and tissues of the body, chief among which is the liver. In the organs it may be stored for very long periods of time. Cases are reported in which lead has been eliminated from the body eighteen years after the patient has ceased working in lead industries. Grawitz[17] states that lead which is stored in the body may be liberated months afterward, causing symptoms such as optic atrophy, encephalopathia, etc. It has been found chemically in practically all of the organs and tissues of the body; glandular tissue (liver) and nerve tissue (brain) especially store large quantities of it.

Routes of Elimination. Lead is excreted through the kidneys, intestines, stomach and probably the sweat. During the acute stages of lead poisoning lead is frequently found in appreciable quantities excreted in the urine. This fact is often made use of in the diagnosis of this form of poisoning. Lewandowsky[4] states that the excretion takes place also through the milk and saliva. He states that the kidneys excrete it in quantities only when the body is saturated. In the later stages excretion is principally through the intestines, especially by means of migrating leukocytes. Because of this excretion through the digestive tract in severe cases hemorrhages and superficial ulceration may occur in the mucosa. That the stomach is also an important avenue for the excretion of lead is demonstrated by the fact that lead has been found in the vomitus (as well as in the urine and feces) as late as sixteen months after the subject has ceased to be exposed to lead. Unfortunately in our cases we did not test the feces for lead.

Susceptibility. Not all individuals are equally susceptible to the toxic effect of this metal. The sex predisposition has already been alluded to. There also appears to be a familial predisposition. Members of some families working under the same conditions as the individuals of other families who have been severely affected may show no evidence of ill-effects.

Patterson lists the conditions predisposing to lead poisoning, as alcoholism, defective teeth, gastro-intestinal disorders, constipation. Schnitter adds to the above diabetes and epilepsy. The number of hours of labor seems to be an important factor. In some factories in which there had been no record of poisoning there developed several cases following a change from six hours to eight hours per day.[15] Persons who have been previously affected appear to have an increased susceptibility. As has already been mentioned, individuals with gastric hyperacidity are especially prone to the effects of lead. Since it is known that an empty stomach exposes the laborer to intoxication, many establishments urge their employees to eat a heavy breakfast before coming to work.

The principal compounds of lead which produce poisoning are oxide, acetate and carbonate. It is the last which we found to be on the market under the trade name of "Flake White." For a time it was thought that the sulphate because of its greater stability should be substituted for the carbonate in the lead industries and thus decrease the possibility of poisoning; but on experimentation it was found that the sulphate was just as readily transformed into the soluble salt.[2]

Animal Experiments. Erlenmeyer[18] performed a number of experiments on cats to determine the relation of the quantity of lead to the degree of poisoning. He injected the cats subcutaneously with lead carbonate. They died with symptoms of cramps, colic and bulbar palsies in from forty-seven to one hundred and twelve days. The majority died within about sixty days. For the production of chronic poisoning he found that the question of time was more important than quantity, a finding well borne out clinically. He found that about 1 mg. of the lead salt per kilo per day over a period of about fifty to sixty days was sufficient to produce chronic poisoning. He concluded from his experiments that it is necessary to have a certain saturation of the body continued over a rather prolonged period of time in order to produce poisoning. This strongly suggests the possibility of the repeated entrance of the lead into the body in amounts so subminimal as to produce toxic effects unrecognizable as lead poisoning. Nevertheless the body undoubtedly suffers from the deleterious effects of even these small quantities. It is reasonable to assume that lead-containing face powder, because of the very nature of its application, may bring about just such results, multiple indeterminate symptoms of which the etiology remains unknown. Such cases would receive only symptomatic treatment; the true causative factor would remain untreated.

Symptoms. The symptoms of lead poisoning are variable. Among the earliest signs, according to Oliver, are pallor, loss of appetite and tendency to vomit. There may be associated sallowness and cachexia. The patient feels tired and often develops an obstinate constipation and the tongue becomes coated. In severe

forms there may develop convulsions without any previous com-
plaints. The emaciation and cachexia may appear very rapidly.
According to Apfelbach[19] the symptom complex depends upon
certain factors: (1) Dosage and rapidity of the dosage; (2) presence
of alloys in the metals ingested; (3) method of entrance, whether
through inhalation of fumes or through inhalation or swallowing of
lead dust; (4) individual susceptibility, such as sex, age, habits, etc.
The most common symptoms in the order of their importance are:
(1) Colic, (2) constipation, (3) pallor and anemia, (4) blue line on
the gums, (5) basophilic granulation, (6) tremor, (7) palsies. The
nervous symptoms sometimes predominate even in the acute forms,[4]
but are by far more common in the chronic. Headaches, dizziness,
ataxias, paralyses and disturbances of consciousness, such as coma,
delirium and confused excitement and stupor, often occur in this type
of cases. The effect upon the nervous system is generally primary
and only in a small percentage of cases is it secondary to disease
of other organs. Lewandowsky emphasizes the slowing of the pulse
during the attack. The pulse is full and of high tension.

Colic. The most common symptom—colic—is often the first
to appear. It generally manifests itself by a sudden development
of cramp-like, sharp, cutting pains which may be agonizing in
character at or above the umbilicus. Often the pains radiate into
the hypogastric and hypochondriac regions. Sometimes the pain
simulates appendicitis, and when this is associated with vomiting
and constipation it may be mistaken for intestinal obstruction.
Frequently the pain is relieved by pressure, and this is considered
by some to be especially characteristic of this type of colic. The
attacks rarely last more than fifteen minutes. Prodromes of nausea,
bad taste in the mouth, constipation and abdominal distress are
not uncommon. Even between the attacks the patient is not
entirely free from some distress. In contrast to hepatic or renal
colic there is rarely any perspiration associated with even the
severest of these attacks. The temperature is usually subnormal.

There are a number of theories advanced relative to the causa-
tion of colic. Frank[20] explains colic by the increased tonus or spasm
of the splanchnic vessels brought about by the action of the lead.
Oliver states that the colic is the result of strong tonic contractions
of segments of the intestine. The violent contraction of the muscle
fibers also forces the blood out of the splanchnics, raising the blood-
pressure, hardening the pulse and at the same time slowing the
pulse-rate. The cause of the spasm, he believes, is due to the
stimulation of the peripheral nerve-endings, as evidenced by the fact
that nitrates and atropin usually relieve the attack. Some investi-
gators claim that the colic is due to the direct action of the metal
on the muscle fibers of the intestine, while others state that it is
due to a stimulation of the vasoconstrictors. Lewandowsky believes
that the colic is the result of several factors acting simultaneously

upon the intestines. The symptoms are probably due to a stimulation of the motor nerve elements together with a direct stimulation of the smooth muscle fibers both in the wall of the intestine and of the bloodvessels. That lead acts toxically both on nerve elements and on non-striated muscle fibers is quite generally conceded and the production of abortions as well as palsies well illustrates that fact. Kussmaul and Maier[21] found sclerosis of the celiac axis in some cases. This is not a constant finding and is probably a secondary process.

Anemia. The pallor in cases of lead poisoning may be due to causes other than the degree of anemia present. According to Naegeli[22] the paleness of lead-workers is commonly due not to the anemia but to the contraction of the superficial bloodvessels. Only in the chronic cases of poisoning does a true anemia develop.

Grawitz[17] denies this. He and von Behrend showed in 1899 that lead was a peculiar blood poison which acted directly upon the red blood cells, affecting chemically the hemoglobin without producing hemolysis. The average blood picture in lead poisoning is about 50 per cent. hemoglobin, 2,500,000 erythrocytes and 12,000 leukocytes. There is generally moderate anisocytosis, mild poikilocytosis, moderate polychromatophilia and an occasional nucleated red blood cell. The striking feature in the blood picture is the presence of basophilic granules within many of the red blood cells. There is a great diversity of opinion as to the importance of this finding. Naegeli and his followers deny that this is very characteristic. Trautmann[10] believes it to be of great importance. He found that in less than 2 per cent. of cases other than lead poisoning there are involved more than 100 cells per million while in lead poisoning the figures may reach more than 100,000 per million. Schnitter[9] in his early studies of blood changes in lead poisoning found very many cases without any basophilic granulation. In his later studies, however, after he improved his staining technic with methylene blue stains, he found granules present in every case in a series of 88 cases. He could substantiate his presumptive diagnosis by a single examination of a blood smear. He supports Grawitz as to the extreme importance of this finding in cases of lead poisoning. From a prophylactic standpoint the examination of the blood of lead-workers for these granules is important, since not infrequently they will be present in the red blood cells before symptoms occur. The number of cells affected is generally proportional to the severity of the disease.

Basophilic granulation is found in conditions other than lead poisoning. They have been found occasionally in malaria, pernicious anemia, pseudoleukemia, chlorosis, posthemorrhagic anemia and tuberculosis, but practically never in excess of 300 per million cells.[10] Schnitter encountered less than 500 affected cells per million in only 5 per cent. of his series of 88 cases of lead poisoning. In 26 per cent. there were from 1000 to 5000; in 3 per cent. from 40,000

to 50,000; and in one case more than 100,000 per million. In our case (Case II) we found 32,000 per million. We must agree with Grawitz on the importance of basophilic granulation, for in two of our cases (Cases I and II) the diagnosis was made on this finding alone.

The origin of these granules is still a matter of controversy. Ehrlich, Askanazy, Schaumann, Naegeli and others considered the granules as nuclear remnants arising as an end-process from kary-olysis. Grawitz takes exception to this, stating that the granules are degenerating products as the result of a toxic effect upon the cytoplasm. This concept explains the term "granular degenera-tion," which is so commonly applied to these granules even in many text-books. He states that basophilic granulation is not found in normal blood either in the fetus, newborn or adult, nor is it to be found in the bone-marrow. He believes that the granules arise within the red blood cells of the circulating blood through the degenerative toxic action of various poisons upon the protoplasm. The most important of such poisons is lead. He bases his theory on the following reasons: (*a*) Granular degeneration is not found in the bone-marrow even in cases in which great numbers of affected cells are present in the circulating blood; (*b*) it is scarcely if ever found in normal blood; (*c*) the granules are usually fine and numerous while remnants of nuclei are usually coarse and few in number; (*d*) they are tinctorially different from nuclear remnants; (*e* they are found in erythroblasts with perfectly round intact nuclei; (*f*) they are not found in regeneration of blood following hemorrhage; (*g*) they are present in cases of lead poisoning in which no nucleated reds are present; (*h*) they are not demonstrable with ultraviolet light which shows the absence of nuclear material.

Askanazy and Pappenheim believe that the granules arise from the toxic effect of the lead-containing serum on the basophilic substance of unripe chromatophilic cells. This Grawitz holds as untenable, since often there are cases with extensive granular degeneration which present practically no polychromatophilia.

Naegeli disagrees with Grawitz on many points. He denies the frequency of this degeneration in lead poisoning, asserting that it is constant only in very severe anemias. He failed to find it even in cases in which there was a lead line present on the gums and when lead was found in the urine. He states that it runs parallel with polychromasia. He agrees with Ferrata that the origin of these granules is from nuclear remnants and therefore they are signs of regeneration. He gives as his reasons the following: (*a*) They are frequently present in the embryonic blood of animals; (*b*) they are absent in aplastic anemias; (*c*) they have been found in certain stages of human embryos; (*d*) they have been found in experimental anemias produced by hemorrhages.

Ferrata[23] has changed from his former view that the granules

are derived from parachromatin of the nucleus. He now agrees with Pappenheim and Askanazy that they are of cytoplasmic origin. He believes that the erythrocytes, which normally even in adults, pass through a polychromatophilic phase in order to reach the final acidophilic state, undergo "conglobation" of the basophilic substance under various pathological states and thus form the basophilic granules. These later studies tend to show that neither Grawitz nor Naegeli was technically correct and that basophilic granulation is evidence not of degeneration but of regeneration; this regeneration, however, is pathological.

Lead Line. The blue lead line on the gums is another important sign, though its absence does not preclude the diagnosis of lead poisoning. As already mentioned the lead which has been absorbed is carried in the blood stream as the soluble albuminate. Traces of this are often deposited as a grayish-black sulphide in the superficial layers of the mucous membrane of the gingiva by the action of hydrogen sulphide present in the tartar of the teeth. The line may form within a few days after exposure and may remain for weeks or months. The precipitate is located principally at the apices of the papillæ within endothelial cells of the capillaries and neighboring tissues. The deposit is most marked around the incisors and especially next to carious or ill-kept teeth. Patches are often deposited in the cheek where the mucous membrane lies in contact with decayed teeth and infrequently also in the lips.[24] Pyorrhea sometimes develops simultaneously with the lead line.

Tremor. Lewandowsky and Apfelbach speak of the early occurrence of a tremor of the tongue, fingers and hands. This tremor of the muscles may be fine, resembling that of hyperthyroidism or coarse like that in paralysis agitans. In Case II the tremor was rather fine and very pronounced in the latter part of the illness.

Palsy. Degenerative changes in the peripheral nerves are quite constant, producing the so-called "lead palsy." This affects principally the extensors of the hands and fingers and is usually bilateral.[24] The localization seems to be determined by the activity of the muscles. Some authors claim that the degeneration is in the anterior horns of the cord.[4] The little change found in the cord post mortem is explained by the supposition that the change in the ganglionic cells is only functional. However, the peripheral nerves show definite lesions. There is often an absence of the axis-cylinder and an increase in the connective tissue. Occasionally there is a multiplication of the nuclei of the sheath of Schwann. Seifert[25] states that the lead paralysis is the result of a combined degenerative peripheral neuritis and myositis. There are degeneration, atrophy and fatty changes in the contractile substance of the muscle fibers followed by fibrosis.

Arteriosclerosis. Lead workers are notoriously susceptible to arteriosclerosis, which in turn often results in contracted kidneys

and hypertrophied heart. Disturbances of vision and blindness may be due to hyaline degeneration of the arterioles and capillaries of the optic nerve, retina and choroid.[26] Seifert found atheromatous patches in the basilary artery. Kussmaul and Maier describe chronic inflammatory changes in the arterioles resulting in decreased elasticity of the vessels, which they believe is responsible for the cerebral apoplexies and encephalomalacias occasionally encountered in lead poisoning. According to these authors the lesion is chiefly a hyperplasia of the media.

Nephritis. The kidneys often suffer very severely in chronic plumbism. Kauffman places lead poisoning as foremost among the intoxications, producing chronic induration or the so-called chronic interstitial nephritis. From what has already been said about the toxic effect of lead on arterioles it is strongly suggestive that the lesion in the kidney is not really a true nephritis, but more probably an arteriosclerotic change. Those who study the histopathology of kidney lesions know that there is still great confusion in the identification of kidney conditions, and what is often diagnosed as chronic interstitial nephritis is in reality an arteriosclerotic kidney. Kauffman in discussing this type of lesion states that there is a gradual fibrosis of the glomeruli with atrophy of the associated tubules and a proliferation of the connective tissue together with a round-cell infiltration. Some glomeruli remain normal or are even hypertrophied. In Case II of our series the kidney changes were more degenerative than inflammatory and can best be classified under the toxic nephroses.

Arthralgias. A symptom often associated with lead colic, but quite distinct from it, is arthralgia. This consists of sharp, shooting pains in the flexor muscles of the lower or upper extremities which may extend into the joints and bones. Often the joints become swollen.

Encephalopathia Saturnina. One of the most interesting as well as the most serious manifestations of lead poisoning is the symptom-complex designated as encephalopathia saturnina, exhaustively described by Tanqueral des Planches[27] in 1836. Cases III, IV and V as well as Case II belong to this group of saturnism. The cerebral symptoms are numerous. The eyes may show ocular palsies, hemianopsia and amaurosis. Neuroretinitis and papilledema are frequent. The blindness is sometimes preceded by headache and convulsions. Retinal hemorrhages occur. Some of the general symptoms are apoplexy, delirium, convulsions, epilepsy and coma. Death often occurs in convulsions or coma.[3]

Of the psychoses, epilepsy is important. Acute psychoses which develop in the course of a month are relatively rare. In these cases there is a severe dulling of consciousness with motor changes. The symptoms sometimes set in suddenly but usually are preceded by prodromes of headache, dizziness, insomnia, hallucinations,

restlessness and fits of melancholy. The chronic psychoses are usually progressive in their course, passing finally into coma and ending in death.

The largest number of cases of encephalopathia saturnina occurs in workers employed in the white lead industry.[15] It may occur in young adults in whom the urine is free from albumin and the brain removed at autopsy is chemically free from lead. According to Oliver cerebral hemorrhage is a common cause of death in lead poisoning.

The pathology of this syndrome-complex has been studied by a number of investigators. The general findings closely correspond to those of Case II in the present study. One of the best discussions of encephalopathia saturnina is that of Westphal[28] in 1888. He gives a careful review of the subject and presents the histological studies of the brains of thirteen of his own cases. Many of the brains showed no demonstrable lesions; some, however, showed small areas of hemorrhage, softening and atrophy. He found that the most important change was an inflammatory reaction around the minute bloodvessels. He believes that lead has a direct toxic effect on the nerve cells, though it is usually undemonstrable. He summarizes the effect of lead on the central nervous system as follows: (*a*) The direct toxic action on the nerve cells; (*b*) the toxic effect on the vessels, producing hemorrhage and encephalomalacia; (*c*) the effect on the kidneys resulting in uremic manifestations; (*d*) combination forms of the above three. Kussmaul and Maier[21] made one of the first careful histological studies of the brain in a case of encephalopathia saturnina and found very little characteristic except a mild periarteritis of the cortical vessels together with a slight perivascular increase of connective tissue. Monakow[11] describes a widening of the adventitia of the arterioles with an infiltration of cells, oil droplets and pigment granules. It is probable that the pigment granules are of the same type which were found by us. The ganglionic cells appeared pale and swollen. There was some atrophy and gliosis present. Steidle[29] states that anemia of the brain is the most common finding. Otherwise there is very little present to explain the action of the lead. He believes that even mild circulatory disturbances resulting from the toxic action of lead upon the bloodvessels are sufficient to produce profound functional disturbances, since ganglionic cells are so very susceptible to stimulation. He also emphasizes the direct toxic action of lead upon brain cells, since more lead has been found deposited in the brain than in most other tissues of the body.

Prognosis. The prognosis of the minor manifestations, including lead colic, is good; that of convulsions and other forms of the encephalopathies is usually serious. Wrist-drop and other types of paralyses may persist.

Prophylaxis. The most essential requirement among the workers in lead industries is cleanliness. Frequent bathing and thorough cleansing of the hands and finger-nails, especially before every meal, should be made obligatory. The air should be kept free from lead fumes and dust by proper ventilation. If with all possible precautions prevention for the individual is impossible then a change of occupation is necessary.

The use of leaden cooking utensils, cheap enameled dishes and food wrapped in lead-foil should be discouraged. Lead shot should never be used for the cleansing of bottles. Rigid laws should be enacted prohibiting the sale of lead-containing face powder, hair dye, lotions or any cosmetic containing a compound of lead.

Treatment. In the acute form the stomach is to be emptied by lavage. Epsom salt has antidotal properties and is the cathartic of choice.

In the chronic forms the treatment is principally symptomatic. Most authorities agree that iodide of potassium in small doses (5 to 10 grains), administered three or four times a day, aids in the elimination of the lead from the system through the kidneys and intestinal tract by transforming the insoluble salt as deposited in the tissues into a more soluble compound. However, it is to be used cautiously in the more acute forms, as the rapid liberation of the lead from the tissues may increase the severity of the intoxication. Epsom salt, castor oil and enemata are to be used for the relief of constipation. For the colic, cathartics, hot applications to the abdomen, amyl nitrite, atropin and sometimes morphin are indicated. Special attention should be given to the mouth for the relief of gingivitis and pyorrhea. Iron is indicated for the anemia. The paralyses should be treated by strychnin, electricity and massage. For the relief of convulsions many authors advise the use of baths, amyl nitrite and spinal drainage.

Summary. 1. Lead is the most important of the industrial poisons.

2. Women are more susceptible to lead poisoning than men; abortions, miscarriages and early deaths of the infants are common.

3. Lead is deposited in the liver, kidneys, brain and other organs.

4. Lead is eliminated principally through the urine and feces, but it may be absent in either even in the very severe forms of poisoning.

5. The kidneys in some types of lead poisoning show deposits of lime salts in degenerating tubules similar to that found in acute mercurial poisoning.

6. The lesions in the brain in cases of encephalopathia saturnina are not very prominent. The principal microscopic findings are a mild perivascular round-cell infiltration, satellitosis, neuronophagia and the occurrence around some bloodvessels of phagocytic cells containing a greenish crystalline pigment.

7. Basophilic granulation of the erythrocytes is a striking and characteristic feature of most cases of lead poisoning. With proper staining technic this finding is of inestimable value for diagnosis, and careful routine blood studies should be made as a prophylactic measure among the workers in industries using lead.

8. Besides being an industrial poison, lead is also the source of many miscellaneous forms of poisoning, chief among which is probably that resulting from the use of lead-containing cosmetics.

9. The use of lead-containing cosmetics over a prolonged period of time may result in death.

10. A face powder known as "Flake White" is lead carbonate ground to an impalpable powder. This powder is sold quite generally in drug stores for cosmetic purposes.

11. Mild degrees of poisoning from "Flake White" are probably widespread, but because the symptoms are often indefinite the true etiology remains undetected. Very severe cases probably also occur and remain undiagnosed.

12. The present study proves incontestably that death may occur from poisoning due to the use of "Flake White" as a cosmetic; it is very urgent, therefore, that rigid laws be enacted prohibiting the sale of any compound containing lead for cosmetic purposes.

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AN ANALYSIS OF ONE HUNDRED AND EIGHTY-TWO CASES OF CANCER OF THE STOMACH, WITH SPECIAL REFERENCE TO THE INCIDENCE OF PREËXISTING ULCER.

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Introduction. This study was undertaken with the idea of making available the data[1] that had accumulated during the last decade in this clinic on the subject of gastric carcinoma, and particularly in order to determine, in reference to the still unsettled question of the incidence of a preëxisting ulcer, the direction in which our evidence tended. Many of the facts brought out are already well established, and these will be passed over without special comment, although it is believed that they are of value in that they add something to the statistics of the subject; but on certain other matters that await their final solution we will refer to the literature and make such criticism as our findings seem to justify.

Preëxisting Ulcer. In presenting our data it will clarify matters to state at the outset that we have divided the cases into two groups: (1) Those giving a clinical history suggestive of a preëxisting ulcer, and (2) those of a progressive downward course without previous

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[1] Most of the cases were studied on the medical service of the hospital, but some were admitted directly to the surgical wards, and for the privilege of including the latter we are indebted to the various surgical chiefs.

gastric symptoms. In the latter group it was usual for the patient to state, even in answer to leading questions as to ulcer symptoms, that he had never before had any digestive troubles. In the former we have included not only those giving a definite story of gastric upsets with more or less symptomless intermissions, but also those with any previous disturbance of the stomach except vague childhood affections. If we have erred, therefore, we feel that it has been by including too many in the ulcer-before-cancer group. There were, however, few borderline cases, most falling readily into the one classification or the other.

With even this liberality in making up our ulcer group, only 31 patients (17 per cent) of our total of 182 were so classified. It is appreciated that the relationship of gastric ulcer to gastric cancer must finally be established on a morphological basis, but as yet the pathologists themselves are not agreed upon the criteria which indicate this relation. In 1909 Wilson and MacCarty,[2] from a study of 153 freshly resected tumors which they believed to be malignant, concluded that 71 per cent of them were secondary to ulcer; later MacCarty[3] contended that 68 per cent of their gastric ulcers were associated with carcinoma, and Wilson and McDowell,[4] in an even more recent communication, stated it as probable that gastric cancer rarely developed except at the site of a previous ulcerative lesion. There has never been, however, a general acceptance of these claims of the members of the Mayo staff for the reason that others have questioned their interpretation of the specimens. Ewing,[5] furthermore, in an exhaustive study of the subject, with special reference to the criteria on which a judgment should be based, concluded that the cancerous transformation of peptic ulcer was rather infrequent and probably did not exceed 5 per cent. Also, Wilensky and Thalhimer[6] in a microscopical study of a series of benign and malignant ulcerations failed to trace an etiological relationship between gastric ulcer and gastric cancer.

On purely clinical grounds a similar diversity of opinion has developed. In 953 cases of gastric cancer Smithies[7] secured a history suggestive of a preëxisting ulcer in 66 per cent and Moynihan[8]

[2] Wilson, L. B. and MacCarty, W. C.: The Pathological Relationships of Gastric Ulcer and Gastric Carcinoma, Tr. Assn. Am. Phys., 1909, xxiv, 593.

[3] MacCarty, W. C.: Pathology and Clinical Significance of Stomach Ulcer, Surg., Gynec. and Obst., 1910, x, 449.

[4] Wilson, L. B. and McDowell, J. E.: A Further Report of the Pathological Evidence of the Relationship of Gastric Ulcer and Gastric Carcinoma, Am. Jour. Med. Sci., 1914, cxlviii, 796.

[5] Ewing, J.: The Relation of Gastric Ulcer to Cancer, Ann. Surg., 1918, lxvii, 715.

[6] Wilensky, A. O. and Thalhimer, W.: The Etiological Relationship of Benign Ulcer to Carcinoma of the Stomach, Ann. Surg., 1918, lxvii, 215.

[7] Smithies, F.: The Etiological Relationship Existing between Gastric Ulcer and Gastric Cancer, Illinois Med. Jour., 1917, xxxi, 149.

[8] Moynihan, B. G. A.: The Pathology of the Living and Other Essays, 1910, p. 109.

believed that two of every three of his cancer cases gave such a history. Deaver[9] has stated that he believed one-half followed ulcer and Mayo[10] has contended that in at least 50 per cent clinical evidence of a precancerous lesion, probably not always ulcer, could be obtained. It should be noted, however, that with the exception of Smithies none of these authors presented an analysis of cases to support the contention. On the other hand, Friedenwald[11] in an analysis of 1000 cases discovered a definite ulcer history in only 7.3 per cent, and in only 23 per cent had there been symptoms of any digestive trouble. Finally, it may be pointed out that the infrequency of cancer in the duodenum, where ulcer is common, argues against the importance of a preëxisting ulcer, as does also the fact that only rarely have proved ulcer cases while under observation developed malignancy. Thus there seems to be good reason to believe that our finding in this series of cases of only a small percentage of preceding ulcers is approximately correct.

Age, Sex and Color. The ages for the total series ranged from twenty-four to eighty-six and were grouped by decades as shown in Table I. It will be noted that 156 (85.7 per cent) were between forty and sixty-nine years old, this percentage being also correct for the sexes separately, and that about one-third of them were in the sixth decade alone. The two patients in the third decade were twenty-four and twenty-seven years of age respectively, one male and one female, and both were proved at operation. The age and sex incidence for the ulcer group was practically the same as for the total series. There were 139 males and 43 females. They were all white except two, who were negroes.

TABLE I.—THE AGE INCIDENCE BY DECADES FOR THE TOTAL SERIES AND FOR THE ULCER GROUP.

Ages.		Total series.		Ulcer group.	
		Number.	Per cent.	Number.	Per cent.
20 to 29	. . . .	2	1.1	0	
30 to 39	. . . .	14	7.7	3	9.7
40 to 49	. . . .	46	25.2	9	29.0
50 to 59	. . . .	61	33.5	11	35.5
60 to 69	. . . .	49	26.9	7	22.6
70 to 79	. . . .	9	5.0	1	3.2
80 to 89	. . . .	1	0.6	0	
		182	100.0	31	100.0

[9] Deaver, J. B.: Early Recognition of Carcinoma of the Stomach, New York Med. Jour., 1919, cix, 749.

[10] Mayo, C. H.: Cancer of the Stomach and its Surgical Treatment (Collected Papers of the Mayo Clinic), 1919, xi, 41.

[11] Friedenwald, I.: A Clinical Study of One Thousand Cases of Cancer of the Stomach, Am. Jour. Med. Sci., 1914, cxlviii, 660.

Chief Complaint. Numerous chief complaints were stated by the patients, but by-far the most frequent was that of pain in the epigastric region, this occurring 100 times (55 per cent). The next most common was that of vomiting, which was given in 31 instances (17 per cent). Others in the order of frequency were "stomach trouble," loss of weight, "indigestion," belching, "lump" in the abdomen, weakness, constipation and pain in the back.

Symptoms. *Pain.* Although only 55 per cent gave pain as the chief complaint, 161, or 88.5 per cent, stated it as one of the prominent symptoms. Of this number 152 (94.4 per cent) complained of its being in the epigastric region, while in a few it was localized in the back, the umbilical area, the precordia or the right shoulder.

The character of the pain was variously described. It was most often referred to as being dull (18 per cent), and next in order as a soreness, a burning, a gnawing, a heaviness, a cramp, a discomfort, an ache or a hunger pain.

Reference of the pain from its original localization was mentioned in only 51 instances, and it is interesting that in 25 of these, or about one-half, it was to the back. Of the latter the tumor involved the pylorus 20 times (80 per cent), the lesser curvature 3 times, the greater curvature once and the cardia once. The 20 pyloric cases with reference to pain to the back constituted 29 per cent of the total number with pyloric involvement. Reference elsewhere of the epigastric pain was not common, although it occurred in the sternal region 6 times, the left shoulder 5, the right shoulder 4 and the chest generally 4 times.

Relief from pain was noted in the series as the result of various circumstances in 85 cases. Most often, in 51 (60 per cent), it was accomplished by vomiting, in 11 by eating, in 5 each by belching, bowel evacuations and the application of local heat, and even less frequently by such measures as lying on the left side, making local pressure and gastric lavage.

Other Symptoms. The bowels were noted as being constipated in 67 of 150 cases and as markedly constipated in 56 more, that is in a total of 82 per cent. In most instances the constipation began at the same time as the other symptoms. In only 23 cases were they normal in action; in but 1 was diarrhea alone present, while in 3 diarrhea and constipation alternated.

The appetite was impaired in 153 of the total number (84 per cent) and 89 per cent complained of gaseous eructations. Vomiting occurred in 127 instances (70 per cent). Only 3 times, however, was hematemesis commented upon, and 2 of these were in the ulcer-before-cancer group. Nausea was noted 116 times, or in 75 per cent of the records in which it was referred to. The loss of weight averaged thirty pounds.

Duration of Symptoms. In presenting the duration of symptoms it is necessary to refer to the two groups of cases separately. In the 31 ulcer-before-cancer cases the average period of all gastric symp-

toms was 10.5 years, this corresponding closely with Smithies's[7] finding in his larger series of 10.8 years, whereas in 29 of the patients the symptoms which we interpreted as being due to malignancy averaged only 4.5 months. In the other 2 the history did not suggest any change in the symptomatology which might be explained as corresponding with a change in the histological picture. The average period of cancer symptoms in our complete series was 8.6 months, this again agreeing fairly well with the 6.9 months found by Smithies.
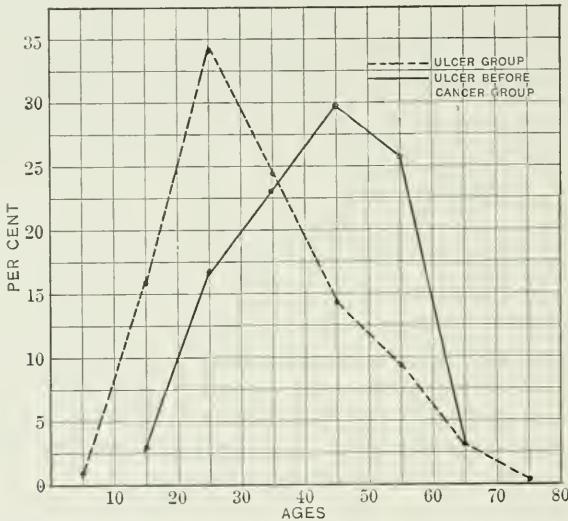
Chart I.—Age incidence for the beginning of "ulcer" symptoms in ulcer-before-cancer cases compared with that of ulcer cases at the time of applying for treatment. The latter is based on Friedenwald's findings in 1000 cases of gastric and duodenal ulcer.

Age Incidence for the Beginning of Symptoms. The age incidence for the beginning of symptoms in our ulcer-before-cancer cases (Table II) is noteworthy in that it shows that almost one-third of the total number fall in the fifth decade with as many in the sixth as in the fourth. No figures for the age incidence of the beginning of symptoms in benign ulcer are available in the literature, but even if comparison be made with the age incidence in such cases at the time of applying for treatment it will be seen that there is a wide difference. For instance, in Friedenwald's[12] series of 1000 cases, which is in agreement with other similar compilations, the acme of incidence, as shown in Chart I, occurs in the third decade. In his series the patients presented themselves at the clinic on the average of twelve years after the first symptoms were noted; thus the divergence of a curve that would represent the beginning of

[12] Friedenwald, J.: A Clinical Study of One Thousand Cases of Ulcer of the Stomach and the Duodenum, Am. Jour. Med. Sci., 1912, cxliv, 157.

symptoms in his group from that of our ulcer-before-cancer cases would be much greater than this diagram indicates.

TABLE II.—AGE INCIDENCE FOR THE BEGINNING OF "ULCER" SYMPTOMS IN 31 ULCER-BEFORE-CANCER CASES AND IN 79 BENIGN ULCER CASES.

Ages	Ulcer-before-cancer.		Benign ulcer.	
	Number.	Per cent.	Number.	Per cent.
10 to 19	1	3.2	8	10.1
20 to 29	5	16.1	36	45.6
30 to 39	7	22.6	21	26.6
40 to 49	9	29.1	6	7.6
50 to 59	8	25.8	7	8.8
60 to 69	1	3.2	1	1.3
	31	100.0	79	100.0
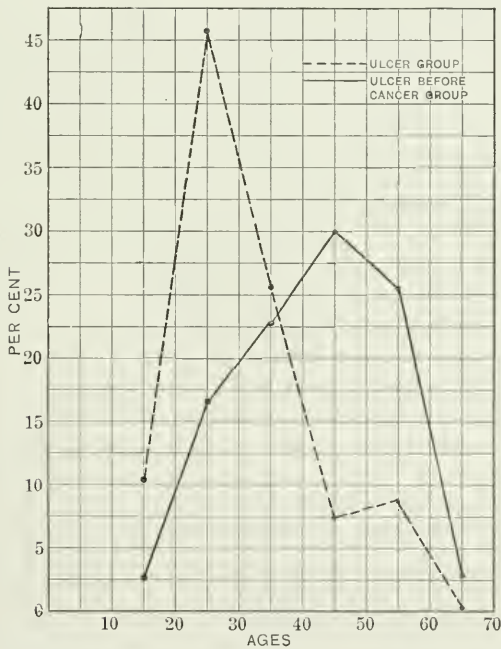
CHART II.—Age incidence for the beginning of "ulcer" symptoms in 31 ulcer-before-cancer cases and for the beginning of ulcer symptoms in 79 benign ulcer cases.

In order to secure accurate data on the age at the beginning of symptoms in ordinary ulcer cases we have gone over our benign gastric ulcer series (79 cases), and Table II shows, as would be expected, an even greater proportion of the cases between twenty

and thirty years of age. Comparison of the curve plotted from these cases with that of our ulcer-before-cancer group (Chart II) is consequently very striking. This suggests either that ulcers developing in later life have a greater likelihood of becoming malignant than do benign lesions generally or that the early symptoms are really those of a slowly developing malignancy.

Previous Medical History. The previous medical history of these patients, aside from gastric disease, seemed to have no bearing upon the diagnosis. Twenty-five had suffered from typhoid fever, 15 each from scarlet fever and pneumonia, 12 from gonococcal infection and lesser numbers from other infections. Six only (3 per cent) gave a history of trauma to the abdomen, this agreeing closely with Smithies's finding of 3.4 per cent., and being greater than Friedenwald's of 1.9 per cent.

Occupation. Likewise the occupation seemed unimportant. Thirty-three were housewives, all but 10 of the female patients, 19 were recorded simply as general laborers, 13 as farmers, 11 as miners, 8 as clerks and 7 as carpenters.

Family History of Cancer. The mother had suffered from cancer in only 8 instances: 1 in the breast and 1 each in the liver, face, bladder, uterus and stomach, and in 1 case the location was not stated. It had occurred in a sister three times (breast twice), a father twice (stomach) and a brother twice. This shows for our series a percentage of 8.8 for cancer in other members of the family, closely agreeing with the 9.4 in Friedenwald's group.

Physical Examination. A mass was palpated in the epigastrium in 95 patients of our series (52.2 per cent), and it was questionably felt in 16 others, making a total of 61 per cent. Emaciation was noted as being present in 151 cases (82.9 per cent), tenderness in 101 (55.5 per cent) and abdominal rigidity in 78 (43 per cent). Visible peristalsis was noted in only 30 instances. It is suspected that this finding does not represent the true occurrence of this interesting tell-tale phenomenon, since 42 per cent had pyloric involvement and 53.6 per cent of the 155 having gastric analyses showed evidence of gastric retention. Furthermore, this is a sign which requires close and patient observation and which is easily overlooked in a hasty inspection; but incidentally when found it is so significant as to repay the effort of careful examination. Enlargement of one or more lymph nodes above the clavicle on the left side was noted in 7 instances (3.8 per cent). In 3 of these the carcinoma was primary in the pyloric region, in 1 each along the lesser curvature and the cardia and in 2 it was described as being diffuse. In no patient were enlarged glands seen or palpated in the right supraclavicular area; such cases have, however, been reported and we have elsewhere encountered a few, though none happened to occur in this series.

Clinical Examinations. Most of the cases presented a moderate degree of secondary anemia, the extreme low figures being 20 per cent

of hemoglobin and 2,000,000 red blood cells. The average hemoglobin percentage was 61 (Fleischl) and the average red blood cell count 3,837,000. A leukocytosis (11,000 or more white blood cells) occurred in 31.2 per cent of the series while 11 per cent showed a leukopenia (under 6000), and 57.8 per cent had a count between 6000 and 11,000.

Urine and Feces. The urine showed albumin and casts in 86 cases (47.2 per cent). In 97 instances there were chemical studies upon the stools, but in only 52 of these (53.6 per cent) was there a positive reaction for occult blood. This is a smaller percentage than is given by some authors, and this is perhaps due to the fact that we were very careful to have our patients on a meat-free diet for several days before making the stool examination.

Stomach Analysis. The gastric analysis is of more importance. In the 155 of our patients who had one or more such tests the amount of the contents, removed forty-five minutes after an Ewald meal, was 100 c c or more in 53.6 per cent, 200 or more in 24.3 per cent, 300 or more in 13.6 per cent and 400 or more in 8.6 per cent. In 106 patients (68.4 per cent) there was no free hydrochloric acid, while in 7 (4.5 per cent) there was what generally has been considered a hyperchlorhydria (HCl above 40 $\frac{N}{10}$ NaOH). It was normal (20 to 40) in 22 (14.8 per cent) and there was a low hydrochloric acid content (0 to 20) in 20 (12.9 per cent).

Of the 27 cases that gave a history suggesting a previous gastric ulcer the figures were not notably different, 55.5 per cent showing achlorhydria, 7.4 per cent hyperchlorhydria, 18.5 per cent normal figures and 18.5 per cent hypochlorhydria.

The results of these analyses have also been grouped in reference to the position of the carcinoma and averaged as shown in Table III. The pyloric growths naturally gave rise to retention and coincident higher acid figures. When the cancer was situated at any other point the average content was about normal (except in lesser curvature involvement, which probably often produced some stenosis) and the acid figures decidedly and constantly subnormal.

TABLE III.—AVERAGE GASTRIC ANALYSIS FINDINGS ARRANGED
ACCORDING TO POSITION OF THE TUMOR.

Position of growth.	Amount in c c.	Total acidity.	Free HCl.
Pylorus	213	45	10.5
Lesser curvature	207	16	5.3
Fundus and cardia	71	15	1.0
Greater curvature	68	15	3.0
Extensive	89	18	2.0

Wassermann Reaction. Although 3 patients gave a history of chancre, of the 83 Wassermann tests performed only 1 was positive. This patient (H. B.), aged thirty-seven years, giving a vague luetic history, was admitted on account of symptoms which suggested pyloric obstruction. The serological test was reported as 4-plus,

but the roentgen-ray study showed marked obstruction, and it was not thought possible to overcome this by constitutional treatment even if it were syphilitic. He was therefore operated on, a clinical diagnosis of carcinoma was made and a pylorectomy with gastro-enterostomy done. Microscopic examination confirmed the diagnosis (adenocarcinoma). The patient rapidly improved, gained fifty pounds in weight and soon returned to his work as a gardener. Subsequently he was treated intensively with arsphenamin and mercury, but at the end of a year had a return of his obstructive symptoms. A second laparotomy revealed extensive abdominal metastasis.

Blood-pressure. Blood-pressure estimations were recorded in 119 of the patients, but in only 4 did the systolic reading exceed 160 mm. of mercury. The average systolic pressure was 118 and the diastolic 72. Curiously this is in complete variance with Friedenwald's finding of a systolic pressure above 170 mm. in 91 per cent of 132 cases.

Roentgen Studies. Roentgenographic reports were available in 125 of our cases and indicated that cancer was present in all but 4, thus giving the correct diagnosis in 96.8 per cent. In 3 the roentgenologist stated that the evidence he had was inconclusive, but suggestive of cancer; all of these proved to be inoperable when exposed by laparotomy. In a single case the roentgenological conclusion was incorrect, the operation showing carcinoma, whereas the diagnosis had been adhesions.

Operative Findings. Of the series 114 (62.6 per cent) were operated upon, but 3 of them at other hospitals. The percentage location of the tumors, as disclosed at operation, is presented in Table IV, and for comparison the location as determined by the roentgen-ray examinations. It will be noted that operation showed the pylorus and greater curvature involvements not to be so common as the roentgen-ray suggested, the excess being divided beween lesser curvature and diffuse lesions. This is about as would be expected, since when a lesion is on the lesser curvature the roentgen evidence of a filling defect is often on the greater curvature, and when extensive involvement is present only a part of it may be seen along the borders of the stomach.

TABLE IV.—PERCENTAGE LOCATION OF TUMOR AS DETERMINED BY
THE ROENTGEN RAY AND OPERATION.

Position of tumor.	By roentgen ray.	By operation.
Pylorus	61.4	51.4
Lesser curvature	5.7	14.3
Fundus and cardia	10.0	10.0
Greater curvature	18.6	11.4
Diffuse	4.3	12.9
	100.0	100.0

Nature of the Operations. In only 28 per cent of the operated cases was any attempt made at radical removal of the malignant process; in 31.5 per cent the diagnosis was confirmed, but the condition was too far advanced to justify any surgical treatment, and in the remainder (40.5 per cent) only such a palliative procedure as would aid temporarily in the nutrition of the patient was undertaken. Mayo[10] reports that of 2094 operations for gastric cancer performed in their clinic between 1897 and 1919 there were 736 resections (35.1 per cent), 746 explorations (35.7 per cent) and 612 palliative procedures (29.2 per cent). Roughly it may be said, therefore, that only about one-third of all gastric cancers that now reach the operating table can be given any hope of a cure, while a second third may be made more comfortable and perhaps given an increased period of life. The other third receive no benefit whatever.

If it were possible to determine beforehand that those of the last group were definitely inoperable they could be saved the discomfort of the exploratory procedure. Carman[13] has emphasized the value of the roentgen ray in this respect, and it would seem that the latter has now reached such a point of perfection that it can be depended upon in the future to spare from operation a larger percentage of this group. Of even greater practical importance, however, is it that the second third, those who receive only palliative treatment, be more promptly diagnosed and referred to the surgeon.

The Non-operated Cases. Of the 68 patients not operated upon 38 (55.9 per cent) were considered inoperable. If this number is added to the 35 found inoperable upon exploration it gives a group of 73 patients (47 per cent of all the patients willing to be operated upon) in whom surgical intervention could be of no benefit.

Conclusions. This analysis of 182 carefully studied cases of cancer of the stomach leads to the following conclusions:

1. A history suggestive of preëxisting ulcer was obtained in only 17 per cent, and it seems probable that the true incidence of such a preceding lesion does not exceed these figures.

2. Reference of epigastric pain to the back occurred in 29 per cent of the pyloric cancers, and of those with reference of pain to the back 80 per cent had involvement of the pylorus.

3. The age incidence for the beginning of "ulcer" symptoms in the ulcer-before-cancer cases had its apex two decades later than did a series of 79 ulcer cases. This suggests either that ulcers first giving rise to symptoms in middle life have a far greater likelihood of becoming malignant than do ulcers generally or that the ulcer-before-cancer cases are really malignant from the beginning. Either of these considerations justifies and indicates prompt and radical surgical treatment of all patients first developing symptoms suggestive of ulcer after forty years of age.

[13] Carman, R. D.: The Operability of Cancer of the Stomach as Determined by the Roentgen Ray (Colleeted Papers of the Mayo Clinic), 1919, xi, 31.

4. The average free hydrochloric acid and total acidity findings in the pyloric cancers was not abnormally low (15.5 and 45), but there was evidence of definite retention. There was also retention in some of those with lesser curvature involvement. When the cancer was situated elsewhere retention did not occur, but the acid figures were distinctly low.

5. Roentgen study gave a positive diagnosis in 96.8 per cent, and in but one case was it misleading.

6. At operation the tumors were shown to be somewhat more extensive and more often to involve the lesser curvature than the roentgen ray suggested.

7. Of the patients with gastric cancer who now come to the surgeon about one-third are given a chance of cure by radical operation, one-third are treated palliatively and for one-third nothing can be done.

THE RELATION BETWEEN POLIOMYELITIS AND EPIDEMIC (LETHARGIC) ENCEPHALITIS.[1]

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In considering the relation between epidemic (lethargic) encephalitis and acute anterior poliomyelitis, much depends upon whether the subject is studied from the purely clinical aspect or from exact comparisons made with postmortem material. In each disease, however, careful examinations by both methods should be made before conclusions are drawn.

It is a firmly established fact that several types of exudative inflammations of the brain are infectious in character. It is not possible, however, from microscopic examinations of tissue alone, to separate with precision the alterations produced in the nervous system by each of the different known agents. True, certain individual cases have been recorded from time to time in which characteristic differences seem to be present, but when these points are analyzed carefully it can generally be shown that they are based chiefly upon the situation of the lesions or are apparent variations caused by modifications in the intensity and duration of the disease. They cannot, therefore, be regarded as characteristically different tissue reactions corresponding strictly and precisely to various infectious agents.

This opinion has frequently been expressed by different authors, and especially in regard to the practical impossibility of separating

the lesions of acute anterior poliomyelitis from those of epidemic (lethargic) encephalitis when examined under the microscope.

It is not surprising, therefore, that the clinical phenomena produced by epidemic (lethargic) encephalitis may resemble those of acute anterior poliomyelitis.

Prodromal Symptoms and Onset. Like the onset of acute anterior poliomyelitis, that of epidemic (lethargic) encephalitis is an exceedingly irregular one. Classifications of each of these diseases have been based upon the location of the structures paralyzed by the lesions in the central nervous system. From the studies made during epidemics by Wickman and others we learn that an abortive type of poliomyelitis in which paralysis is absent is frequently encountered, and thus our present conception that acute anterior poliomyelitis is an infectious systemic disease in which paralysis may or may not occur has become established. The number of cases of acute anterior poliomyelitis in which paralysis is absent varies considerably in different epidemics, but most observers agree that the abortive types represent about 50 per cent of all cases of the disease.

Comparing the onset and development of epidemic (lethargic) encephalitis, almost all recent observations show that the condition is related to a previous attack of influenza. Epidemic (lethargic) encephalitis is not, as a rule, a part of an attack of typical influenza, but it is a well-known fact that epidemic (lethargic) encephalitis may follow an attack of influenza. For this reason premonitory symptoms, or those preceding the development of paralysis in epidemic (lethargic) encephalitis, may be those of an infection or merely incidents in the convalescence from that disease. This stage of the disease, therefore, in which the symptoms resemble those of a chronic influenzal infection, represents the general systemic phase, which is exactly analogous to the abortive or non-paralytic types of acute anterior poliomyelitis. It may, however, progress and become a specialized expression in the form of an affection of the central nervous system with paralysis. In this respect the diseases run closely similar courses, and it seems unnecessary to quote here the details of cases showing no paralysis. For present purposes it is quite sufficient to refer to the fact that the differentiation of non-paralytic cases of acute anterior poliomyelitis, and of non-paralytic cases in which influenzal infection of the nervous system is suspected, is dependent largely upon the knowledge of the occurrence of an epidemic of acute anterior poliomyelitis or the prevalence of influenza or of epidemic (lethargic) encephalitis in the community in which the cases are observed.

The Bulbar, Pontile and Midbrain Form. Considered topographically there are certain well-recognized forms of acute anterior poliomyelitis in which the inflammatory process is well localized and reaches its greatest intensity in the cerebral peduncles, pons or

medulla oblongata, the spinal cord and cerebral hemispheres being unaffected. These are the cases that show the strongest resemblance to epidemic (lethargic) encephalitis. The weight of opinion, moreover, strongly favors the view that the polioencephalitis superior and inferior or the polioencephalitis of Wernicke is true influenzal encephalitis and merely modifications in type of the same disease.

Epidemic poliomyelitis is generally believed to occur during hot weather, particularly in July and August. Most of the victims are children and the lower motor neuron type of paralysis is that most frequently encountered in cases with paralysis. The onset is sudden. Epidemic (lethargic) encephalitis is believed to occur chiefly during the winter months, the majority of cases having been met in adults. Not rarely a greater number of cases are seen in which only the cranial nerves are affected and there is prolonged lethargy, which is rare in acute anterior poliomyelitis. While such tendencies are important they are of no value in determining the nature of the disease in a given case.

Lethargy is not always present in cases of epidemic (lethargic) encephalitis; moreover, it occasionally occurs with acute anterior poliomyelitis. Tilney[2] has reported a case of acute anterior poliomyelitis in which it was severe and prolonged. Lethargy in various degrees, stupor or somnolence, frequently with delirium, may occur from intoxication in many different infectious processes, and while very common in epidemic (lethargic) encephalitis it is not in itself characteristic of the disease.

The clinical manifestations exhibited by lesions in the midbrain are most varied. Any extensive lesion in the bulb is almost invariably rapidly fatal, but the acute symptoms in both acute anterior poliomyelitis when it affects the bulb, as well as in epidemic (lethargic) encephalitis, may be severe. Nevertheless, they will often clear up, leaving a paralysis limited to one or more cranial nerves. In acute anterior poliomyelitis the seventh or facial nerve is said to be most frequently affected, whereas the third nerve is most often affected in epidemic (lethargic) encephalitis and also in Wernicke's polioencephalitis. Diplopia is therefore an early sign. However, any of the cranial nerves, as well as the limbs, may be paralyzed in each of these diseases from involvement of the pyramidal tracts from within the bulb. Neither the character of the paralysis of the individual cranial nerves nor combinations of types, such as unilateral, bilateral or multiple or single, have any significance in determining the etiology. These phenomena merely furnish indications of the locality of the inflammation and the direction and extent of its distribution.

In the cases recorded here, Case 1 was striking because of the slow onset, beginning with diplopia, due to involvement of the fourth

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[2] Neurol. Bull., New York, January, 1918, i, 7.

and third nerves; numbness of the left lower limb, extending at times to the left upper limb and a tendency to fall to the left; nystagmus and scotoma, running a prolonged course. These symptoms indicated diffuse foci within the brain-stem—a myeloencephalitis resembling multiple sclerosis. The exact cause could not be proved, but because of the character of the onset, the slow and prolonged course and the absence of an epidemic of poliomyelitis, it seemed probable that the case belonged to the group included under the head of epidemic (lethargic) encephalitis.

During the recent epidemic of lethargic encephalitis cases resembling multiple sclerosis have been observed. Furthermore, the microscopic findings in some cases of epidemic (lethargic) encephalitis are identical in appearance to those seen in early cases of multiple sclerosis.

In Cases 2 and 3 the onset was sudden or apoplectiform in character, resembling, in this respect, bulbar poliomyelitis. The cause of the objective signs in each of these cases indicated an inflammatory process, at first acute and later assuming a chronic character. The paralyses were those of the motor cranial nerves and involvement of the pyramidal tract within the pons. These cases occurred in adults without spinal involvement, during a period in which epidemic (lethargic) encephalitis was prevalent. An epidemic of acute anterior poliomyelitis was known, however, to have been raging in the vicinity (Boston) in which Case 2 developed. These are regarded as cases of bulbar encephalitis of the poliomyelitic type, but whether they were due to the poliomyelitis virus or to that of epidemic (lethargic) encephalitis cannot be proved, though the former view seems most probable.

Cases of so-called influenzal myelitis have been observed by Spiller[3] and others.

A somewhat rare manifestation of acute anterior poliomyelitis is a transverse lesion of the spinal cord, the patient exhibiting complete flaccid paralysis of both legs, loss of sphincter control and absence of sensation up to the level of the lesion. The latter may remain complete or may clear up, leaving the patient with spastic paraplegia, with increased knee-jerk, defective control of the bladder, etc. It must be admitted that positive proof that such cases are caused by the virus of acute anterior poliomyelitis is often lacking, yet Batten[4] observed such cases during an epidemic of acute anterior poliomyelitis. B. Sachs[5] recorded a case of acute anterior poliomyelitis in a girl, aged eighteen years, with sudden onset of complete flaccid paralysis and loss of sensation up to the xiphoid cartilage; there was complete recovery in two months. The cerebrospinal fluid showed a high lymphocytic count.

[3] Arch. Neurol. and Psychiat., June, 1919, No. 6, i, 799.
[4] Brain, 1916, xxxix, 1 and 2.
[5] Jour. Nerv. and Ment. Dis., 1912, xxxix, 757.

Netter and Levaditi[6] reported four cases presenting symptoms of transverse myelitis which they attribute to the virus of acute anterior poliomyelitis. These authors were able to show that the blood of a patient who had recovered possessed the property of neutralizing the virus of acute anterior poliomyelitis.

I recently observed a similar case in an adult:

Mrs. M., aged thirty-seven years, previously healthy, in August, 1920, gave birth to a healthy child. There were no complications and she seemed to be entirely well. On September 30, on awaking in the morning, she experienced considerable discomfort in the back between the shoulders. This was soon followed by numbness, tingling and burning sensations, which increased in severity. The condition became very painful, extending throughout the trunk and the lower limbs, below the costal margin. Simultaneously her lower limbs rapidly grew weak. The next day she was completely paralyzed, both for sensation and for motion, below the level of the costal border, and retention of urine and of feces occurred. The temperature was 99.4° F. Lumbar puncture showed 150 lymphocytes to the cubic millimeter. Leukocyte count of the blood showed 10,000. She had severe pain throughout the anesthetic area, which subsided rapidly after lumbar puncture. On the fourth day her condition was greatly improved; motion was returning rapidly in both lower limbs and sensation was nearly normal. During the next five weeks only gradual improvement was observed. At the present time her spinal fluid is normal; sensation is restored and motor power is almost but not quite normal. There was a history of an attack of influenza one year prior to the onset and a chronic cough and pharyngitis that had persisted until within a few months preceding the onset of the present condition.

By some observers this case might be regarded as belonging to the group of conditions described under the name of the meningitic type of poliomyelitis.

In cases of epidemic (lethargic) encephalitis the spinal cord is not, as a rule, believed to be affected. In acute anterior poliomyelitis the spinal cord is involved much more frequently than other portions of the nervous system. At a meeting of the Philadelphia Neurological Society held in November, 1920, Winckleman and Weisenburg reported a very important case of epidemic (lethargic) encephalitis which they had observed clinically and at postmortem and found the usual evidences of that disease in the basal ganglia, reaching the greatest intensity in the pons and medulla oblongata. They also found intense perivascular infiltration and edema limited to the gray matter of the cervical and upper thoracic portions of

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[6] Bull. et mém. soc. méd. des hôp. de Paris, 1914, xxxvii, 570.

the spinal cord. These alterations were identical in character and in location to those usually found in cases of acute anterior poliomyelitis, thus proving conclusively that in epidemic (lethargic) encephalitis the spinal cord may be affected.

A closely similar case is that reported by Harbitz:[7]

A woman, aged fifty-two years, following an attack of influenza, developed headache with partial loss of vision, first on one side and then on the other. The etiological factor was papillitis, resulting in complete blindness. Later both lower limbs became painful and weak and there was anesthesia as high as the axilla. The patient died of pneumonia. In the cervical cord segments so much congestion and edema were demonstrated that on cross-section the cord appeared grayish red in color, the boundaries between the gray and white matter being blurred. These changes were found with increasing distinctness in the first dorsal segment. Microscopic examination showed parenchymatous myelitis and neuritis, with degeneration of nerve fibers and ganglion cells in both the white and the gray matter. The resemblance of this case to the one referred to and reported by Winckleman and Weisenburg is very striking.

Local muscular atrophy is the one outstanding symptom of acute anterior poliomyelitis not observed in epidemic (lethargic) encephalitis, yet Grinker[8] refers to a curious case that he regards as a combination of acute anterior poliomyelitis and epidemic (lethargic) encephalitis. One year after having influenza the patient had an attack resembling apoplexy, with left-sided spastic hemiplegia. At first there were high leukocytosis and fever, transient sixth nerve palsy and strabismus, hyperemia of the optic nerves and muscular atrophy of the face and upper limb. Ten days later peripheral facial palsy followed the cerebral paralysis and there was atrophy of the muscles of the forearm and hand. The left thenar and hypothenar eminences resembled the Aran-Duchenne type of atrophy. Improvement occurred.

These observations tend to show that in epidemic (lethargic) encephalitis the extent of the inflammatory process is exceedingly variable and that the spinal cord may be affected. Spinal symptoms associated with bulbar signs do not therefore afford sufficient evidence on which to eliminate the possibility of epidemic (lethargic) encephalitis in diagnosis without consideration of the associated factors; neither does the absence of spinal-cord involvement lessen the probability of the bulbar symptoms being due to the virus of acute anterior poliomyelitis.

In concluding I would adduce the opinion that epidemic (lethargic) encephalitis is an infectious disease, having a separate

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[7] Norsk. Mag. for Laegevidenskaben, January, 1920.
[8] Jour. Nerv. and Ment. Dis., October, 1920, No. 4, iii, 323.

and distinct entity that is not to be confused with acute anterior poliomyelitis, from which it differs particularly in the long survival of the virus in the central nervous system. Its course may therefore be very irregular and be attended with remissions or exacerbations extending over months or years. (See Case I.) The differential diagnosis between acute anterior poliomyelitis and epidemic (lethargic) encephalitis will often be impossible to make if only the subjective and objective signs are considered. Much will depend on the knowledge of existing epidemics and the weighing of circumstantial evidence afforded by the associated phenomena at the onset of the illness as well as before it develops.

The following records of cases are presented because of their resemblance to the two diseases under discussion and to illustrate the difficulties encountered in clinical diagnosis.

I wish particularly to thank Dr. Shumway for permission to refer to his cases (No. 1) and Dr. Spiller for allowing me to refer to Cases 2 and 3.

CASE I.—Miss W. H. W., aged nineteen years. Seen by Dr. Shumway.

The family and previous medical history are unimportant. The patient stated that she had been perfectly well until October, 1914, when she noticed for the first time that her right eyeball turned inward and that she saw double. This condition persisted. She did not feel sick, but had frequent attacks of nausea and vomiting. In March, 1915, while walking, she fell; she attributed this accident to her visual disturbance, but admitted that at times she felt unsteady while walking. Examination at this time by Dr. Shumway showed: The pupils were equal and reacted to light. Diplopia in the horizontal meridian, the right image being below and increasing downward and to the left, due to weakness of the right superior oblique muscle. Moderate but distinct nystagmus. Ophthalmoscopic examination revealed low-grade optic neuritis. In walking and standing there was a decided tendency to fall toward the right. The tendon reflexes on the right side were slightly greater than those on the left. The plantar reflexes and the sinuses were normal. The blood count showed: Red cells, 5,560,000; white cells, 6600; hemoglobin, 90 per cent. The Wassermann test of the blood serum and spinal fluid was negative, but there were 20 lymphocytes to the cubic millimeter.

Her condition remained about the same, with some increase in the ataxia; but in September, 1915, Dr. Shumway found marked bilateral central scotoma and nystagmus, with almost complete disappearance of the diplopia. The scotomata remained about the same, but with slight variations in size. Dr. de Schweinitz confirmed these observations.

The following findings were recorded by Dr. Spiller in September,

1918: Patient has had tingling and numbness of the left lower limb since last winter, but rarely in the right lower limb. At times it extends upward on the left side and involves the left upper limb. Occasionally her left knee gives way in walking. During the last two or three days she has had marked vertigo; if she looks downward, objects seems to be rushing by her, on both sides, with the speed of an express train. This occurs chiefly when she is walking. Has had frequent attacks of nausea since and before 1915. Headache not marked. Menstrual periods have been very frequent—about two weeks apart, and normal in character.

Pupils are equal—prompt reaction to light and in convergence. Nystagmus on either lateral movement—greater on looking to right. Patient wrinkles the forehead, closes the eyelids, draws up the corners of the mouth, either together or separately, contracts the masseters, protrudes and moves the tongue and raises the soft palate, all in a normal manner.

Touch and pain sensations normal in the face. The grip in each hand is good. Finger-to-nose test well performed on each side. Diadokokinesia not so well done with the left as with the right hand. Biceps and triceps tendon reflexes unusually prompt on each side, but equal. Stereognosis normal in each hand. Sense of position, passive movement, normal in each hand. Touch and pain sensations normal in each upper limb. Grasp is good and equal in both hands. No local atrophies. Patellar tendon reflex distinctly exaggerated and equal on both sides. No impairment of motor power in the lower limbs. Very distinct Romberg symptom—falls toward the left each time. Gait very unsteady with eyes closed and slightly ataxic with eyes open. Achilles tendon reflex a trifle more prompt than normal on each side. Babinski reflex is attended with no movement of the toes on either side. Touch and pain sensibility normal in the legs below the knees and feet. Position normal in the toes of each foot. Abdominal reflex not obtained on either side; no trace of any movement, either on stroking or tapping.

The chief symptoms consist of numbness in the left lower limb, extending at times to the left upper limb; tendency to fall to the left with eyes closed; exaggeration of all tendon reflexes; vertigo, nystagmus and findings in optic nerves mentioned by Dr. Shumway.

CASE II.—August 23, 1920. Miss J. L. In perfect health previously; patient had returned shortly from a camp in Maine (?). On August 13, 1920, it was noticed that she was irritable and believed she was not well. That evening, at dinner, she suddenly declared that here eyes were "crossed"—she could not see properly —and complained of numbness in her right upper limb. She became profoundly stuporous, had a rectal temperature of $101\frac{3}{5}°$ and loss of control of the bowels and bladder, probably because of stupor. Doctor P. saw her about six days later. Her temperature

receded within a few days. About six or seven days after the onset the blood-pressure fell below 100; her breathing was of the Cheyne-Stokes type, but responded immediately to strychnin, which probably saved her life. Soon after the onset right hemiplegia was noticed.

"I found the patient stuporous, but she could be aroused and answered questions correctly, although a reply was secured with great difficulty. Her speech was very bulbar, not aphasic, and very difficult to understand. She had intense bilateral ptosis—could open the right lids slightly, but the left not at all. The left eyeball was entirely immobile; the pupil was widely dilated and did not react to light. The right eyeball had some downward and possibly a little upward movement, but no inward or upward movement could be detected. The left side of the face was normal. The right side was greatly but not completely paralyzed. She could draw up the right corner of the mouth in conjunction with the left, but probably not alone. The patient was too markedly stuporous to permit careful tests to be made. The wrinkles were somewhat fewer in the right forehead. The corrugator superciliæ functioned normally on each side. The soft palate moved normally. The tongue was red and coated, and when protruded, deviated markedly to the right. The right upper limb seemed completely paralyzed, but I was told that she had moved it slightly within a few days of my visit. The right biceps tendon reflex was nearly normal. A pin-prick caused discomfort in the right upper and lower limbs. A careful test of sensation could not be made because of the intense stupor. The right lower limb could be drawn up at the hip and the knees, but the patient had very little power. The right patellar jerk was feeble but the left was stronger. The Achilles tendon reflexes were uncertain. There was typical Babinski on the right side but not on left."

September 28, 1920. Patient keeps right eye wide open; no ptosis; right eyeball moves outward, downward, apparently inward, but not upward, but all movements except those of the upper lid are performed imperfectly. The right pupil contracts to light. Left ptosis complete—probably a little outward movement of the left eye, but no upward, downward or inward movement; no contraction of the left pupil to light. Innervates the right side of face a little when she shows her teeth. Does not speak a word. Frequent spasmodic movements, like those of crying, but there are no tears and no sounds. Right upper and lower limbs completely paralyzed. Right biceps and triceps reflexes a trifle more marked than the left. Right knee-jerks not very distinct but present, and not so good as the left; slight right ankle-clonus; distinct right Babinski but none on the left. Feels pin-prick in the right upper and lower limbs.

There is improvement in the general condition, marked by lessened stupor and increased appetite; no serious collapse has occurred for

three weeks; improvement in the right third nerve, but none in the left or right hemiplegia.

Considerable improvement subsequently occurred.

CASE III.—April 19, 1920. Professor H. Patient had been working very hard. Wife is tuberculous. She has had one pregnancy; no history of miscarriage obtainable. On March 31, while taking a shower-bath, the patient was discovered by his son leaning over, resting his head on the back of his hand, and seemed dazed. Dr. C. saw him an hour or so later; he stated that his face was much bruised, as though he had fallen. Both pupils dilated and left hemiplegia developed the same day. This has gradually improved.

The patient seemed unusually animated to Dr. P. a few days or possibly a week before the onset of the attack, and this fact was remarked on by Dr. P., but the patient's wife did not notice anything peculiar about her husband at that time. Examination showed bilateral ptosis equal on the two sides; palpebral fissures only about 2 mm.; right pupil dilated but not to the maximum; does not contract to light. Patient unable to look upward, inward or downward with the right eye; good outward motion and some slight fourth nerve action. Left eye impaired greatly in upward, inward and downward motion; left sixth nerve good. Complete right third nerve palsy; partial left third nerve palsy. Left pupil small but not excessively so; does not react to light. Weakness only of the lower part of the left side of the face; tongue protruded centrally; touch and pain sense in face normal. No rise of temperature at any time. Left upper limb freely movable at all parts, but distinctly weak; movements exceedingly incoördinate—more than the weakness justifies. Touch, pain, position and stereognosis normal on the left and right. Patient drags the left lower limb in walking and cannot walk without assistance. Left biceps and triceps reflexes diminished; left patellar and Achilles reflexes nearly normal. Typical Babinski on the left but not on the right. Touch, pain and position normal in the left foot.

Diagnosis: Vascular lesion or encephalitis of the right cerebral peduncle.

MENINGOCOCCUS SEPTICEMIA.

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THE occurrence of a septicemia caused by the meningococcus is becoming more frequently met with in recent years, and in the absence of a meningitis may easily be overlooked until the late

development of meningeal involvement gives the clue to the nature of the infection.

As a rule, these cases, particularly if left untreated, will eventually develop localizing signs either in the meninges, endocardium or joints, while if the character of the disease is recognized and specific serum treatment instituted at an early date these complications may frequently be avoided and a favorable outcome more often obtained.

Primary meningococcus septicemia is still comparatively infrequent, and despite the claims of some observers that all cases of epidemic cerebrospinal meningitis present an early bacteremia, the fact remains that when the case comes under the observation of the attending physician the signs of meningitic involvement are usually present.

Nevertheless, a primary meningococcemia may exist for weeks or even months, either with or without localizing signs, and, depending on the type of case, may closely simulate in its clinical course other acute infections, particularly malaria, acute rheumatic fever or endocarditis. The true nature of the infection may be revealed by the necropsy report, by the development of meningitis or by the demonstration of the organisms in the blood by means of blood cultures. The importance of keeping this fact in mind in atypical cases with doubtful etiology cannot be overestimated. The routine practice of taking blood cultures in these conditions should be insisted upon. The cultures should be taken repeatedly and over considerable periods, and should be incubated for at least seventy-two hours before being pronounced negative. Baeslack recommends that negative cultures be kept under observation for an additional five days before being discarded.

The Meningococcus intracellularis was identified in 1887 by Weichselbaum, who established its specific relation to epidemic meningitis.

The first case of meningococcus septicemia was reported in 1899 by Gwyn. This case was one of epidemic meningitis complicated by acute arthritis, and the meningococcus was isolated from the spinal fluid, the synovial fluid and the blood.

In 1901 the meningococcus was demonstrated in the blood of two meningitis patients by Cochez and Lemaire. Since that time meningococcus septicemia has been reported by Jakobitz, Martini and Rohde, Lenhartz, Marcovitch, Robinson and Duval. The meningococcemia in all of these cases was associated with meningitis.

In 1905 Elser, in examining the blood of 41 cases of cerebrospinal meningitis demonstrated the meningococcus in 10 of these cases. In most of these cases some form of extrameningeal lesion was present. The sites of these complicating lesions usually were the endothelial-lined cavities, such as the joints, the pleura, the pericardium and the endocardium,

Duval in his study of meningococcus septicemia makes the statement that no authentic cases are on record in which the meningococcus has produced lesions outside the meninges in the absence of preëxisting meningitis. However, we now know that the meningococcus may occur in the blood in cases in which there was no evidence whatever of preëxisting or accompanying meningitis.

The earliest case of primary meningococcus septicemia to be reported is that of Salomon, which occurred in 1902. This patient presented the symptom-complex of chills, fever and a profuse eruption resembling erythema exudativum. These symptoms continued for a period of about two months, at the end of which time the patient developed meningitis, the meningococcus being found in the spinal fluid. This patient finally recovered.

Andrewes, in 1906, reported a case of meningococcus septicemia who died in a few days and showed no evidence of meningitis either during the course of the disease or at autopsy.

Liebermeister, in 1908, reported a case of septicemia in which the meningococcus was demonstrated in blood cultures. This patient, after an illness of several months, finally recovered without ever having had any symptoms of meningitis.

Bovaird, in 1909, reported a case of meningococcus septicemia in which the spinal fluid was sterile. This patient's illness was complicated by severe iridocyclitis, but eventually ended in recovery after several injections of antimeningitis serum.

Cecil and Soper, in 1911, reported a case of meningococcus endocarditis and are inclined to favor the hematogenous route of infection in epidemic cerebrospinal meningitis.

Up to 1911 there appear to have been 5 cases of meningococcus septicemia reported in which there was no evidence of meningitis.

In 1915 Bray reported a case of meningococcus septicemia associated with pulmonary tuberculosis in which the patient recovered following the injection intravenously of antimeningococcus serum. He summarizes his case as follows: "The illness extended over a period of more than five months, with a known septicemia of three months' duration. The fifteen blood cultures yielded the meningococcus. The spinal fluid was sterile. The disease was characterized by a septic course, multiform eruption and cardiac murmurs, which later disappeared. The course of the infection was apparently not influenced by the administration of the serum." Bray's case received 260 cc of antimeningococcus serum intravenously during a period of twelve days. The initial dose was 20 cc and was gradually increased until the maximum of 40 cc was reached. He considered that the severity of the symptoms, together with the fact that the blood cultures still remained positive, suggested the advisability of discontinuing this form of treatment.

In 1917 Anderson reported 4 cases of meningococcus septicemia. These cases were apparently fulminating in type, showed a marked purpuric eruption and all resulted in death within a few days.

Sainton and Bosquet, in 1917, in discussing the clinical varieties of meningococcus septicemia, state that meningococcemia as well as meningitis may occur in such attenuated form that it may be unrecognized. They consider that one of the properties of the meningococcus is its ability to set up ephemeral disturbance in both the joints and the meninges.

In 1918 Sainton in discussing meningococcus infection of the blood describes seven different forms which this infection may assume, namely, the fulminating, the typhoid, the pseudomalarial, the eruptive, the articular, the metastatic and the abortive. He describes one case of meningococcemia in which meningitis developed on the sixty-ninth day. In the pseudomalarial form the patient may come and go freely during the period between attacks and thus sow the germ broadcast. Sainton considers intravenous injection of antimeningococcus serum to be the logical treatment, but recommends that great care be used in giving the serum intravenously, as this procedure occasionally proves fatal.

Netter in discussing intermittent fever of meningococcemia states that meningococcemia may assume the clinical appearance of typical intermittent fever, quartan or tertian. The attacks often coincide in such cases with the appearance of an eruption. In the majority of cases symptoms of cerebrospinal meningitis succeed these febrile attacks, but they may not appear for one or two months or more. Meningitis may even be absent altogether.

Krumbhaar and Cloud report three cases of fatal cerebrospinal meningitis with endocarditis. They emphasize the early occurrence of petechiæ as useful evidence in similar cases of septicemia.

Marino reports a case of meningococcus septicemia which died about nine hours after admittance to the hospital. He showed marked cyanosis and numerous hemorrhagic areas over the chest, the abdomen and the back, and blood cultures were positive for meningococcus.

Findlay, in 1919, reports a case of meningococcus septicemia without meningitis. The patient on admission presented a picture resembling the polyarticular type of gonorrheal rheumatism. He had a well-marked scarlatiniform rash on the thorax, the back, the face, the legs and the arms. Blood cultures were negative. Autopsy showed no evidence of meningitis, but smears from the serous exudate of the knee-joint and the pericardium showed the presence of the meningococcus.

Baeslack in a study of 25 patients suffering from meningitis demonstrated the meningococcus in the blood in 36.3 per cent of these cases. He concludes that systemic infection by the meningococcus is more frequent than previously suspected and that this systemic infection may occur without appreciable or with no localization. Also, he thinks that the systemic infection may be previous

to or coexistent with meningeal involvement, and therefore that the intravenous administration of antimeningococcus serum is rational and is indicated in conjunction with the intraspinal treatment.

Herrick believes that epidemic meningitis is preceded by a stage showing symptoms and signs of a generalized infection. This stage he considers lasts from a few hours to three days, averaging about forty-eight hours. A few patients with this meningococcus sepsis never develop meningitis. He states that these are usually either the abortive or the fulminating cases, rarely those with prolonged courses. He lays much emphasis on the skin manifestations in these cases. The milder types usually show a macular rash resembling early chicken-pox or large rose spots. The predominating skin sign is the petechial rash. Purpura is a feature of the fulminating cases.

Renault and Cain in discussing meningococcus septicemia believe that purpura is a manifestation of septicemia and that the diagnosis can be made by cultivating the serous fluid from the purpuric lesion or by histological examination of a scrap of tissue from it.

Sergent reports a case of meningococcus septicemia which recovered after the intravenous injection of a stock vaccine of meningococci.

Lereboullet and Cathala report a case of meningococcus septicemia which at first was regarded as simple rheumatoid purpura but which a few days later developed fulminating meningitis. They emphasize the necessity of seeking for the meningococcus in every case of primary purpura.

Ribierre in discussing meningococcemia emphasizes the importance of identifying the exact strain of the meningococcus causing the infection in order that specific antiserum may be used. He advises five injections at twenty-four-hour intervals, alternating subcutaneously and intramuscularly. If improvement is not observed he then gives the serum intravenously. He considers that the patient should be kept under observation for at least a month after the supposed cure, as there may be a tardy relapse.

Blackfan in discussing the treatment of epidemic meningitis states that the intravenous administration of serum is indicated theoretically by the occurrence of a primary blood infection before the onset of the meningeal infection. As a rule, however, this occurs early and is a transitory invasion. The diagnosis at this stage of the disease is difficult to make and the vast majority of the cases are not recognized before the development of the meningeal symptoms. He states that after this time there is usually no bacteremia.

The following case of meningococcus septicemia without meningitis or endocarditis is reported:

CASE HISTORY.—Male, aged twenty-one years, white, unmarried.

Complaint. Headache, fever, drowsiness, lassitude, loss of appetite.

Family History. Negative.

Personal History. Measles in childhood; influenza in 1918, mild case, good recovery; influenza again in March, 1920, duration three weeks, good recovery, no complications.

Present Illness. For a week prior to admission the patient felt tired and drowsy; had occasional headaches and poor appetite. Just prior to admission to the hospital the patient had a chill and severe headache.

Physical Examination. Upon admission to the hospital: Temperature 103.4°, pulse 104, respirations 24. The patient was well nourished and muscular. Color of skin and mucous membranes was good; no petechiæ. Lymphatic glands were not enlarged, spleen not palpable. Pupils were equal and reacted to light and accommodation; tongue slightly coated; tonsils somewhat hypertrophied but no angina present. Teeth in good condition; heart negative; lungs showed a few scattered rales at both bases. Abdomen soft; no tender areas or tumors; bones and extremities negative; reflexes, both superficial and deep, were normal. Eye-grounds negative; no muscular rigidity; no Kernig signs; no evidence of meningeal irritation.

Laboratory Data. Roentgen ray of chest negative; sputum negative for tubercle bacilli; throat cultures were repeatedly negative for Klebs-Loeffler bacilli and for meningococci. Blood smears were constantly negative for malarial parasites; blood cultures during the first two weeks of the disease were negative. The Noguchi reaction was negative. Stools normal and negative for ova or parasites. A complete record of the blood examinations is shown in the chart.

Clinical Course. On the day following admission the patient's temperature was normal and remained normal until the third day, when he had a chill and his temperature rose to 103.4°, followed by a profuse sweat and a return to normal temperature. Seventy-two hours later the patient had a similar chill, the temperature rising to 104.2°, returning to normal the next day. This quartan type of temperature continued during the first two weeks, following which the temperature assumed the septic type with a tendency to approach normal in the mornings and with an evening rise to 102° or 103°. The type of temperature in this case is shown in the chart. The leukocyte count during the first two weeks varied from twelve to eighteen thousand, with approximately 80 per cent of polymorphonuclears. Following the second chill on the fourth day after admission several spots appeared on the skin which were slightly raised, hyperemic, pale rose in color and irregularly distributed over the upper chest, the legs and the arms unaccompanied by itching, and which tended to disappear during the apyretic periods. This eruption resembled very much the rose spots of typhoid fever.

The eruption would sometimes persist for a day or two, then disappear completely and reappear again at irregular intervals. It was noticed first on the fourth day and persisted up to the third week. On the tenth day there was some swelling and tenderness of the right knee, which disappeared in twenty-four hours. On the twelfth day the patient complained of soreness of the fingers and the left wrist, which persisted for one day. On the days the temperature remained normal, the patient was much improved, had no discomfort, appetite was good and there was a general feeling of wellbeing. During the second week the patient developed marked
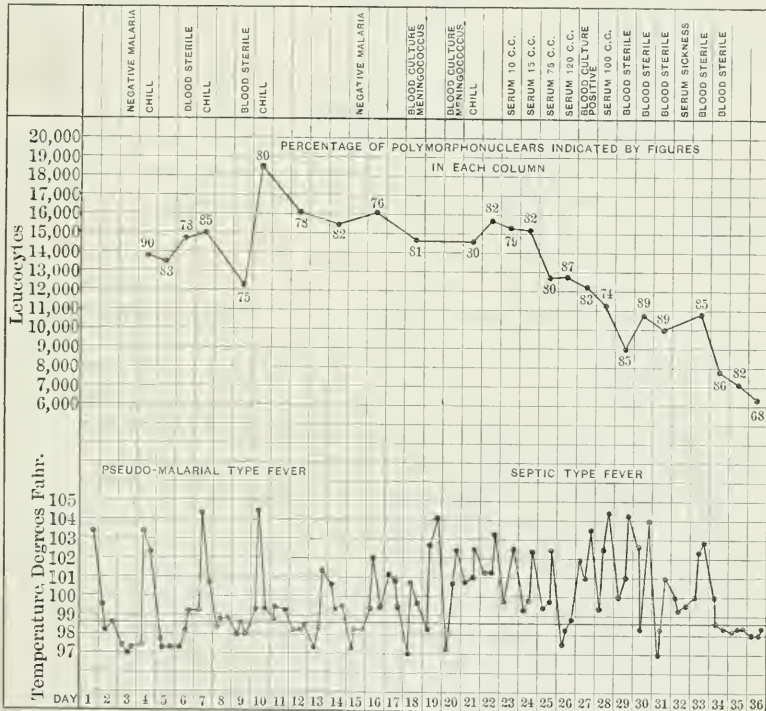
herpes labialis. There were no localizing signs or symptoms during the course of the disease, except the ephemeral joint disturbances, no evidence of meningeal irritation, and repeated blood cultures were negative up to the eighteenth day of the disease, when a Gram-negative diplococcus was discovered. The temperature chart, which strongly suggested a quartan malarial infection, led to repeated search for malarial parasites, although the blood picture, showing a moderate leukocytosis and an increase in the polymorphonuclear cells, was distinctly against a malarial infection. However, on the ninth day quinin was administered by the mouth in ten-grain doses, three times a day for a period of five days, without noticeable effect.

On the eighteenth, twentieth and twenty-first days blood cultures showed the presence of a Gram-negative diplococcus which conformed in all respects to the meningococcus, both culturally and serologically. This organism was agglutinated by polyvalent antimeningococcus serum and by Type IV Gordon serum. It was also identified as a meningococcus by the Naval Medical School and the Public Health Laboratories at Washington, D. C.

On the twenty-third day serum treatment was commenced, $\frac{1}{2}$ cc of polyvalent antimeningitis serum being given subcutaneously, and two hours following this 7 cc were given intravenously. At this point the patient became slightly cyanotic, the pulse became rapid and small and there was evident dyspnea. The intravenous injection was stopped at this time.

On the twenty-fourth day 15 cc of polyvalent serum was given intravenously without any untoward effect.

On the twenty-fifth day a total of 75 cc of serum were given intravenously in doses of 15 cc each, at intervals of from one to two hours, depending on the patient's condition. These injections were well tolerated.

On the twenty-sixth day a total of 120 cc of serum were given intravenously at intervals of one hour or two. These injections produced no alarming symptoms. The serum given up to this time agglutinated the meningococci isolated from the patient's blood in dilutions of 1 to 50.

On the following day blood cultures still showed the presence of the meningococcus and an effort was made to secure serum possessing higher agglutination qualities. A serum was finally obtained which agglutinated this particular strain of meningococcus in a dilution of 1 to 400. On the twenty-eighth day 100 cc of this serum was given intravenously by the gravity method after diluting three times with a normal saline solution. An hour and a half was allowed to complete this injection. The patient showed no alarming symptoms immediately following this injection, but eighteen hours later became markedly cyanotic, developed a purpuric rash, the pulse became rapid and feeble, the temperature subnormal, the heart dilated and the condition distinctly alarming. Following the use of atropin and digitalin hypodermically these alarming symptoms gradually subsided, the temperature rose to 101° and the patient about six hours later was in good condition.

On the thirtieth day the temperature was 103°, the pulse 112 and the respirations 24, and it was not considered advisable to continue the further use of serum at this time, particularly as blood cultures following the last injection of serum were negative.

On the thirty-first day the temperature remained normal, the pulse 92 and the respirations 20. The leukocyte count was normal at this time and the blood culture was negative. From this point on the patient made constant gains and repeated blood cultures were negative.

On the thirty-second day the patient developed serum sickness, nine days following the first administration of the serum. He showed the typical urticarial lesions of serum sickness, which persisted for about twenty-four hours and then disappeared. From this point on the patient made a rapid and uneventful recovery and two months later showed no evidence of his former illness.

There was no evidence of an endocarditis at any time during the course of the disease, and with the exception of the evanescent arthritis of the knee and wrist there was nothing to indicate a localizing lesion. At no time during his illness did the patient show evidence of meningitis or meningeal irritation. A spinal puncture was not performed for two reasons: the first being the absence of all signs pointing to meningitis, and the second the danger of introducing the meningococcus into the spinal canal while the patient showed the presence of the organism in the blood stream. Although it has been urged by some observers that a prophylactic injection of anti-meningitis serum into the spinal canal might prevent the development of meningitis, it was considered that the intravenous method of administration, while more directly combating the septicemia, would at the same time act as a prophylactic against meningeal infection.

During the acute course of the disease the patient showed evidence of renal irritation, as evidenced by the presence of albumin and occasional hyalin and granular casts in the urine. These, however, disappeared following the return of the temperature to normal, and the urine one month later was negative.

As to the best method of administering serum in meningococcus septicemia it would appear that the frequent intravenous injection of small amounts of serum, say 15 cc to a dose and repeated at intervals of an hour or two, depending on the patient's condition, are preferable to the single injection of a large amount of serum, as the alarming symptoms following the injection by the intravenous method may frequently be delayed, whereas if the injection be given in small doses, waiting a few hours between each injection, the chances of overwhelming the patient before the serum injections can be stopped are greatly lessened.

It is believed that this principle would apply with equal force in the administration of other specific sera and that many of the untoward effects could be avoided by this procedure.

This case may be summarized as follows:

It began as an acute febrile condition with a temperature chart typical of quartan malaria but with a moderate leukocytosis and an increase in the percentage of polymorphonuclears, and at the end of the second week the temperature became distinctly septic in type. A maculopapular eruption, resembling the rose spots of typhoid fever, appeared on the fourth day and persisted up to the third week. There were no localizing signs at any time during the course of the

disease except the transient joint symptoms. Blood cultures were negative up to the eighteenth day when the meningococcus was identified. He received a total of 320 cc of antimeningococcus serum intravenously over a period of six days, following which the temperature became normal and the blood cultures sterile. Recovery was uneventful from this point. The prompt termination of the febrile course, the marked improvement in the general condition of the patient and the negative blood cultures following the specific serum therapy leave no room for doubt regarding the efficacy of this form of treatment.

It would appear that cases of meningococcus septicemia are becoming more frequent, or at least more frequently recognized, and that it is well to be on the alert for such cases in order that the diagnosis may be made and treatment instituted before the development of meningitis or endocarditis. The appearance in an acute febrile case of petechiæ or a maculopapular eruption resembling at times the rose spots of typhoid fever, together with a moderate leukocytosis and a temperature chart, which may either be of the septic type or may resemble markedly the chart of malarial fever, should raise the suspicion of meningococcus sepsis and should lead to repeated blood cultures being made in an effort to identify the meningococcus. The skin lesions of meningococcus sepsis are particularly striking. The eruption may be purpuric, hemorrhagic or maculopapular. In the acute fulminating cases, which usually die within the first few days, a purpuric generalized eruption is the rule. These cases are quickly overwhelmed and die frequently before the development of meningitic symptoms. In the protracted cases of meningococcus sepsis the character of eruption shows more of a tendency to assume the maculopapular or hyperemic type.

Some observers lay great stress on the intravenous administration of serum in acute meningitis and are of the opinion that the organism gains entrance to the meninges through the blood stream, thereby inferring that all cases of meningitis are primarily bacteremias. While it is true that positive blood cultures can be obtained in a fairly large percentage of cases of meningitis the fact also remains that the average case of cerebrospinal meningitis has well-developed meningitic symptoms at the time he comes under the observation of the physician. Acute primary meningococcus sepsis without involvement of the meninges is still a rare condition, and while these cases, if untreated, as a rule, will develop a meningitis in the course of a few weeks or months, their early recognition by means of blood cultures will usually serve to prevent the development of meningitis by the early administration of adequate serum therapy.

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THE MORPHOLOGY OF THE HEART IN RELATION TO HABITUS AND A NEW METHOD OF ESTIMATING MORPHOLOGICAL CHANGES.   A ROENTGEN STUDY. [1]

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The older teaching of visceral morphology based on the anatomical findings in the cadaver have given way to a newer and truer conception based on the roentgen examination of the living.

Roentgenology has demonstrated that there exists no one type of organ as regards morphological characteristics, and as far as morphology influences function, there is no one type of physiological normal.

It was the organs of the gastro-intestinal tract which were first considered in the light of this conception, for the roentgen examinations soon demonstrate that in contrast to the previous anatomical teaching there was no one type of stomach as regards its form, shape, outline, axis, mobility and physiological activity, but that the morphological and to a certain extent the physiological characteristics depended very greatly on the body cavity which housed them.   In other words the morphological normalcy of an organ depends on its conformation to the type of organ which belongs to the particular habitus.   This from a modern viewpoint is the basis for the establishment of the normal.

The organs of the thorax must also be studied in the light of this conception of the variation in visceral morphology with bodily habitus.

In the roentgen-ray department of Bellevue Hospital the classification of Mills of the four major types of general physique has been adopted and in use for several years.   These major types are the hypersthenic, the sthenic, the hyposthenic and the asthenic.

Characteristics of the Major Types.   The asthenic habitus is one which presents the following anatomical thoracic characteristics: The thorax is long, shallow and narrow.   The subcostal angle is very acute.   The ensiform is usually absent.   The pulmonic fields are relatively broad in the upper part and narrow in the lower, with large apices which extend well above the clavicle.   The diaphragm slopes sharply downward.   The relationship of downward inspira-

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[1] Read before the New York Academy of Medicine, December 21, 1920.

tory movement to upward expiratory movement in forced respiration is as 1 : 5. The abdomen is relatively short. The diaphragms are flat. They are at the level of the eleventh rib. The transverse pelvic diameter is much greater than the chest transverse diameter at the base of the thorax.

In the hyposthenic habitus the thorax is only moderately long but somewhat broader than in the above type. The subcostal angle is wider, being about 40 degrees. The pulmonic fields are not so narrow at their bases. The domes of the diaphragm slope downward. They are at the level of the tenth rib. The relationship of downward inspiratory movement to upward expiratory movement in forced respiration is as 1 : 3. The disproportion between the pelvic diameter and that through the base of the thorax is not so great, but the pelvic diameter is still wider.

In the sthenic habitus the thorax is shorter and wider. The subcostal angle is about 90 degrees. The pulmonic fields are relatively wide at the base and narrow in the upper zone. The diaphragmatic domes show even convexity. They are at the level of the ninth rib. The relationship of downward inspiratory movement to upward expiratory movement in forced respiration is as 1 : 2. The pelvic and thoracic diameters are approximately equal.

In the hypersthenic habitus the thorax is short, its anteroposterior diameter is great and the subcostal angle is very obtuse. The pulmonic fields are very broad in their lower zones. The apices scarcely show above the clavicles. The diaphragmatic domes are convex and high. The right is at the level of the eighth rib. The downward inspiratory movement is to the upward expiratory movement in forced respiration as 1 : 1. The transverse thoracic diameter is greater than the transverse pelvic diameter.

Heart Morphology in Relation to Habitus. In the roentgen study of the heart in the light of habitus the cardiac shadow must be studied in relation to the pulmonic fields in which it is located. The pulmonic fields are two triangular areas shaped like Gothic windows, bounded below by the curve of the diaphragm and above and laterally by the convergence of the ribs, and correspond to the areas occupied by the lungs.

The characteristics of the pulmonic fields—namely, the altitude, the transverse diameter at the level of the domes and the degree of curvature of the diaphragmatic domes—are expressions of the habitus, for each habitus possesses characteristics as regards the transverse diameter, altitude and basal curve, which are peculiar to it. So, also, the changes which are produced in these factors during the respiratory phase are peculiar to the particular habitus. For instance the altitude of the pulmonic field increases during inspiration. It increases more in the hypersthenic and scarcely changes at all in the asthenic even in forced inspiration. Thus in the sthenic, in the vertical posture the diaphragm moves twice as

far upward in expiration as it does downward during inspiration; in the hypersthenic the relation of upward to downward displacement during respiration is equal and in the asthenic there is five times as much upward displacement during expiration as there is downward displacement during inspiration, but the sum total of movement is less than in the higher types.

There is also a similar variation in the transverse measurement during respiration and the degree of variation differs in the different habiti.

The most striking changes during respiration, however, are in the position, the degree of curvature and in the variation in shape of the diaphragmatic domes. And these changes differ in the various forms of bodily habitus. The intimacy of the anatomical relationship of the heart to the diaphragm is such that in the morphological study of the heart, the diaphragm becomes perhaps the most important factor to be considered.

Position of the Heart. There exists an intimate relationship between position of the diaphragm and the position of the heart. In order, therefore, to study the position of the heart in the particular habitus it is essential that the study be made with the diaphragm in a certain standard position. It is, of course, impossible to obtain by a maneuver a relatively similar position of the diaphragm in the various habiti. It is, however, essential for the purpose of comparison that the variation in the different types be as little as possible. To that end the position of the heart in all the types, except the asthenic, is studied in deep inspiration. In the latter type the heart is studied in deep expiration.

In the asthenic type, where the diaphragm is low, the heart position differs strikingly from that in the hypersthenic type, where the diaphragm is high. In the hypersthenic the heart lies "transversely," the axis being relatively horizontal, about 33 degrees (the angle formed by the intersection of the transverse and long diameters). In the sthenic type the heart lies "somewhat obliquely," the axis having an obliquity of 37 degrees. In the hyposthenic type the heart is "markedly oblique," the angle of the heart axis being 43 degrees and in the asthenic type the heart is "vertical," the angle of the heart axis being 48 degrees, but may be as much as 55 degrees.

It is thus seen that so far as the axis is the expression of position, the heart varies in its position according to habitus.

Form of the Heart. The heart is generally described in the anatomies as being conical in form. The roentgenological studies of the living have shown that grossly the heart shape varies distinctly. This variation in heart form is due primarily to the developmental factors which produce the habitus, but is undoubtedly also influenced in some degree by the physiological requirements of the body activity which includes degree of nutrition and skeletal muscular development. Nevertheless, the predominating factor is habitus.

The heart shape in the hypersthenic habitus is broad transversely, relatively short vertically and generally oval. The cardiovascular angle is obtuse, 135 degrees, and distinct. The left ventricular curve shows considerable convexity. The apex is broad and points outward (Fig. 1).

The heart shape of the sthenic habitus is triangular. The cardiovascular angle is distinct, having a value of 150 degrees. The curves of the right auricle and left ventricle are only moderately convex (Fig. 2).
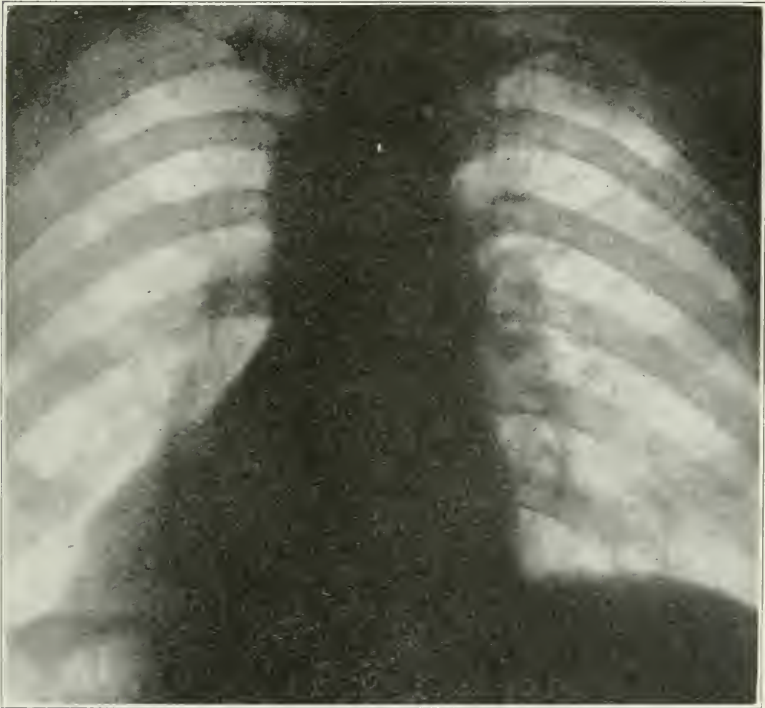
Fig. 1.—Radiograph—the chest of the hypersthenic habitus.

The heart shape of the hyposthenic habitus shows a tendency to circular form. The cardiovascular angle is about 165 degrees and is displaced to the upper part of the median shadow. The curves, particularly the left ventricular, are less convex than the sthenic (Fig. 3).

The heart shape of the asthenic habitus is long and narrow, approaching a circular form. The cardiovascular angle is obliterated, so that the upper half of the left heart border is almost a straight line. The curves of the right auricle and left ventricle show comparatively little convexity. The apex points downward and is

sharp (Fig. 4). It is thus apparent that the convexity of the various curves which constitute the heart silhouette varies with the habitus and that the heart shape as a whole varies in form with the habitus.

Size of the Heart. The most commonly utilized measurement of the heart is the transverse diameter. This is obtained by drawing perpendiculars from the median line to the point of maximum deviation of the heart shadow to the right and to the left, the sum total

FIG. 2.—Radiograph—the chest of the sthenic habitus.

of which is spoken of as the maximum transverse diameter. Numerous tables of this sort have been devised, by Groedel, Moritz, Otten, Dietlen, Bouchard, Guillemont, Claytor and Merrill, for the upright, sitting and horizontal postures, and the posture, age, height, weight, sex and occupation have been utilized as factors in the estimation of the size of the cardiac shadow, and normal limits have been tabulated.

The analysis of these tables and our own studies would indicate that age, sex and height are relatively unimportant factors in the estimation of the heart size.

For instance, take the compilation according to height. For a heighth of 66 to 69.6 inches the variations (horizontal) of the trans-

verse diameter (Dietlen) are 11.3, 13.1, 15.3, a variation of 4 cm. Sitting (Groedel), 11.4, 13.2, 14.6, a variation of 3.2 cm.

Thus the heart in an individual of this height might if his transverse diameter were 13.3 be either 2 cm. too small or too large and if 15.3 might be 4 cm. too large or normal (Haudek).

Further, in Groedel's tables a male individual of 58 to 61.6 inches may have a transverse diameter of 12, 13.1, 14.4 while a male of 70 to 74 inches (a foot higher) may have 12, 13.2, 13.6, the average measurement increasing 1 mm. while the maximum is less for the
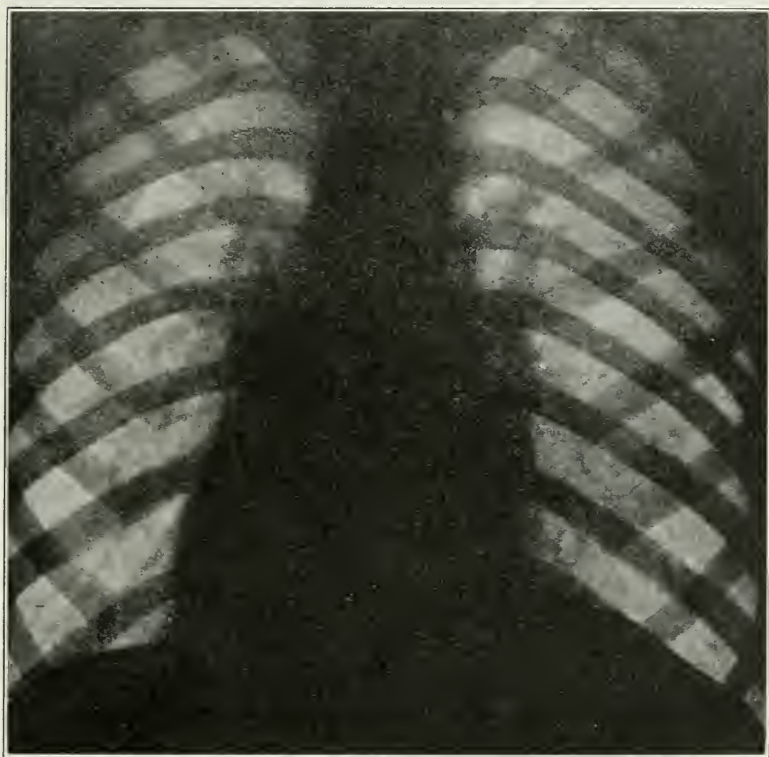
Fig. 3.—Radiograph—the chest of the hyposthenic habitus.

taller man. There is still less variation in the measurements made in the standing position. So, also, in Smith's figures the difference in transverse diameter measurement between a man 60.2 and 72.2 inches is but 7 mm.

To still less a degree does sex and age vary the transverse measurements. Weight better than any of the other factors permits a classification in which the differences appear to be more consecutive in the average. This is because weight is in a sense a characteristic of habitus, for the weight averages highest in the hypersthenic and lowest in the asthenic, yet in Claytor and Merrill's tables, arranged

according to weight, the minimum T. R. of a man weighing 120 to 129 pounds is given as 10.7 and the minimum T. R. of a man weighing 180 to 200 pounds is given as 11.0, a difference of 3 mm.

There is another and more weighty criticism of these standard measurements, and this is that, depending on the axis of ovals of identical shape and size, there will be a variation in the maximum transverse diameter as obtained in the usual method of measurement of this diameter (Fig. 5). It is therefore possible for two indi-
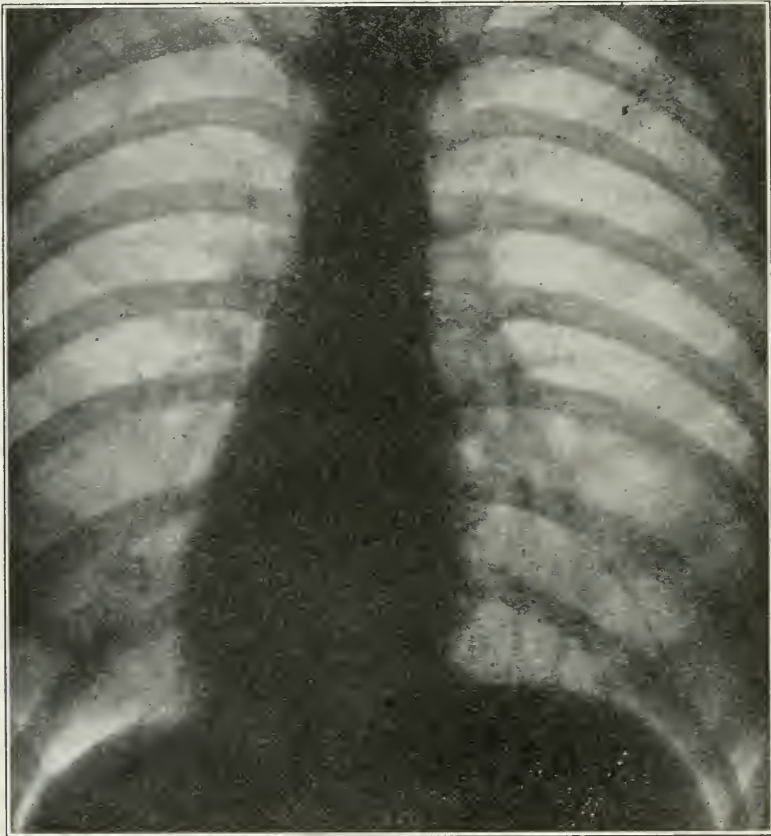
Fig. 4.—Radiograph—the chest of the asthenic habitus.

viduals to possess the same-sized hearts, but in one case, if housed by a hypersthenic thorax, the maximum transverse diameter will be greater than if the same heart were housed in an asthenic thorax.

This transverse measurement, therefore, must be balanced against the angle of obliquity of the heart axis to be of any clinical value, and as a further check the other expressions of habitus, the altitude and the width of pulmonic field must also be taken into consideration, and still further the possible influences which variations in weight may exert must be noted. It is therefore logical to deduce

that the transverse or for that matter any of the standard measurements are only of value when considered in the light of habitus.[2]

Taking the factors given, the value of the angle of obliquity of the axis, size of pulmonic field and weight, in consideration, it is
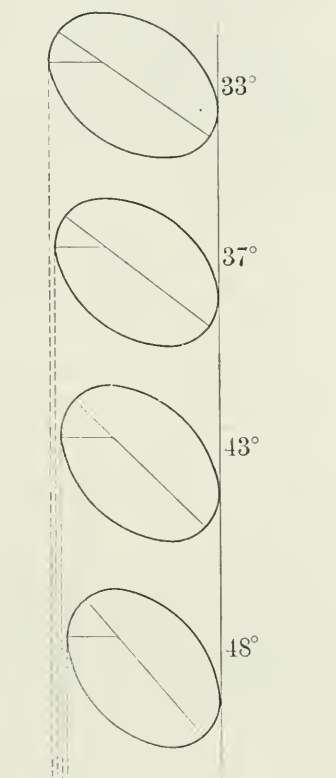
Fig. 5.—Showing the variations in transverse measurement of the same oval in various degrees of obliquity.

possible to establish sets of figures which express heart size in a fairly rational manner (Table I). Haudek has established tables in which there is a decided increase in the various subdivisions of the average values from 2 to 2.2 cm., but he does not consider them from the standpoint of habitus and its dominant types.

TABLE I.—AVERAGE STANDARD MEASUREMENTS IN RELATION TO HABITUS.

	Transverse diameter.	Long.	Broad.	Aortic arch.
Asthenic	8.8	11.4	9.9	3.9
Hyposthenic	11.1	13.1	10.6	4.8
Sthenic	12.4	14.1	10.6	5.1
Hypersthenic	13.8	14.7	10.7	5.7

[2] The clinician, then, when he maps out the heart in relationship to the nipple and midclavicular line, and in reference to the interspaces and ribs, is correct, for he is determining the relationship of the heart to the habitus. But he must view the estimation from this standpoint.

But when all is said and done, when the figures are studied, even with the checks enumerated, one is driven to the conclusion that though the roentgen estimation of the cardiac diameters can be made with more actual accuracy than by clinical methods, nevertheless its greatest value is not so much as an absolute measurement, but that it serves as a check on the percussion findings of the clinician rather than as an anatomical determination of cardiac size. Dietlen examined 231 patients with finger percussion, medium stroke and firm pressure of the pleximeter and compared his findings to the orthodiagrammatic measurements. His conclusions are that in three-quarters of all the cases the percussion findings correspond to the orthodiagram, allowing 0.5 cm. difference. De la Count finds percussion correct in estimating the right border in 85 per cent. of cases and the left border in 70 per cent of cases, allowing 0.5 difference between percussion and orthodiagram. It must therefore be concluded that in about 75 per cent of the cases the heart can be correctly mapped out, allowing an error of 0.5 to 0.75 cm.

The main general objection to all these standard diameters is that they do not indicate, except in very advanced lesions, the changes which take place in the chambers of the heart. A thickening of the heart wall and an enlargement of a heart chamber may occur without any change in the numerical value of the diameters. But such changes will at once produce a change in contour and shape, and the determination of this seems to be more important than the numerical values obtained from the various diameters.

Now the various chambers of the heart produce curves in the contour of the heart shadow. Below, on the right side, we have the right auricular curve springing from the diaphragmatic shadow and extending to the junction of the curve of the ascending arch of the aorta. On the left side we have four curves. The uppermost is the curve of the arcus and a small portion of the descending arch. This is overlapped by the arc of the pulmonary artery, which is overlapped below by the curve of the left auricle, the latter two curves being located in a valley, situated between the high points of the arcus above and the left ventricular curve below, which extends from the left auricular curve to the diaphragm where it merges with the right ventricular curve.[3]

An estimation of the relative size of the heart chambers can be obtained with a fair degree of accuracy by the determination of the convexity of the curve which constitutes the profile of the chamber and actual measurements indicate that the values of the curves vary with the habitus.

[3] Radiographically the determination of some of the points of division of the cardiac shadow corresponding to the junction of certain chambers of the heart is simple, as in the right auricular curve or in the pulmonic curve, but at other points, as for instance between the right and left ventricles and between the left auricle and ventricle, recourse must very frequently be had to ortho- or telefluoroscopic methods. It is important to determine this latter point, which marks out the base of the heart, at which ventricular contractions cease—a point of no motion.

The cases used for the study were patients from the wards of the third surgical division, Bellevue Hospital, and medical students from the University and Bellevue Hospital Medical College. They were regarded as normal, following a careful history and a thorough physical examination, particularly as regards their abdominal and thoracic viscera and peripheral circulation.

The relationship of cardiac size, form, position and function to each type of habitus was then studied by all the roentgen methods.

The following technic and routine were employed in fluoroscopy. The examination was made in all positions and postures with fluoro-
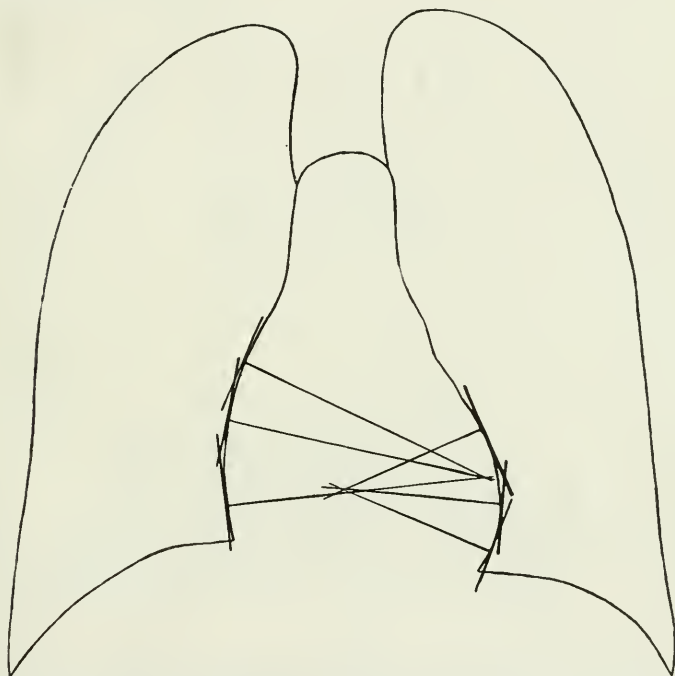
FIG. 6.—Diagram illustrating methods of drawing radii. Three lines are drawn tangent to the curve of the right auricle. At these tangential points perpendiculars are erected. The point of intersection of the perpendiculars is the center of the circle of which the curve is an arc. Each of these perpendiculars present a radius which is measured in centimeters. A similar procedure is followed with the curve of the left ventricle.

scopic devices in which the tube and screen were movable independently of each other, thus making it possible to examine both by the centric and excentric methods. Besides this telefluoroscopic examinations and orthofluoroscopic examinations by a simplified method for the purpose of determining the position of the apex and the points of junction of the chambers were made.

In studying the relationship of cardiac function to habitus, comparative observations were made as accurately as is possible with regard to the following points: First, the rate and regularity per minute of ventricular contraction; secondly, the sequence, force and amplitude roughly of the pulsations of the curves of the right and particularly the left side of the heart. It cannot as yet be stated with any degree of accuracy just what the variation in cardiac function according to habitus is. Perhaps with more thorough investigations with an electrocardiograph or kimoroentgenograph habitus may be found to be associated with certain types of cardiac
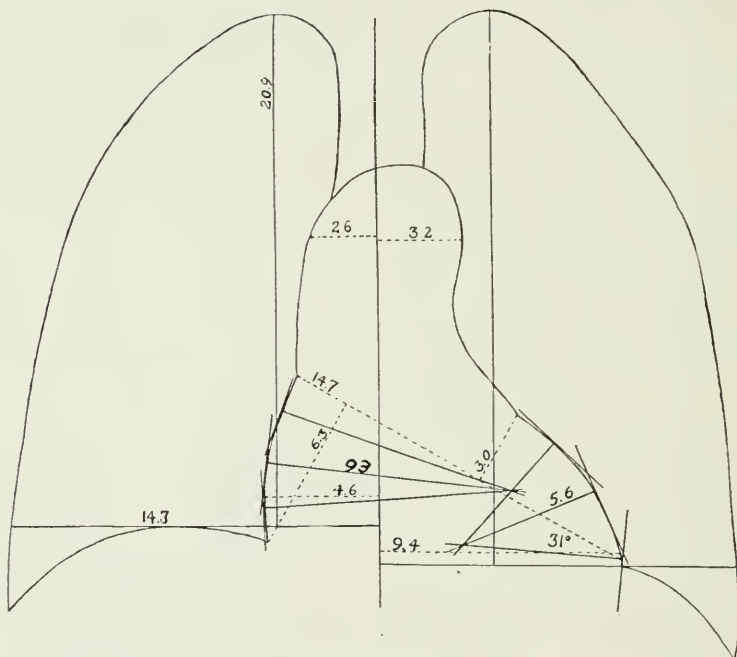
Fig. 7.—Diagram indicating the standard measurements and radial values of the heart of the hyperstenic habitus.

function, especially as regards cardiac muscle tonus, exactly as tone, peristalsis and motility vary in the gastro-intestinal tract according to the habitus.

The actual measurements were made from teleroentgenograms. The technic of teleroentgenography is important not only from the standpoint of individual accuracy but also from the urgent necessity for standardization of this form of radiography, so that the results of all investigators may be truly comparable. The uprights of the tube and screen stands are on scaled tracks, with the upright of the former movable and that of the latter fixed. The screen and tube

are movable in uprights which are correspondingly scaled in one-quarter inch divisions. In this way tube centering, alignment and tube-screen distance are accurately obtained. A target-screen distance of 7 feet 1 inch (85 inches or 215 cm.) is utilized. Schmincke has shown that at this distance the cardiac outline obtained may be regarded as corresponding accurately with the actual anatomical outline. The tube was centered at the level of the sixth thoracic vertebræ. Albers-Schonberg has shown that the greatest transverse diameter of the heart lies in a plane parallel to this level. Bardeen has confirmed this observation on numerous cadavers and on cross-sections of the trunk.
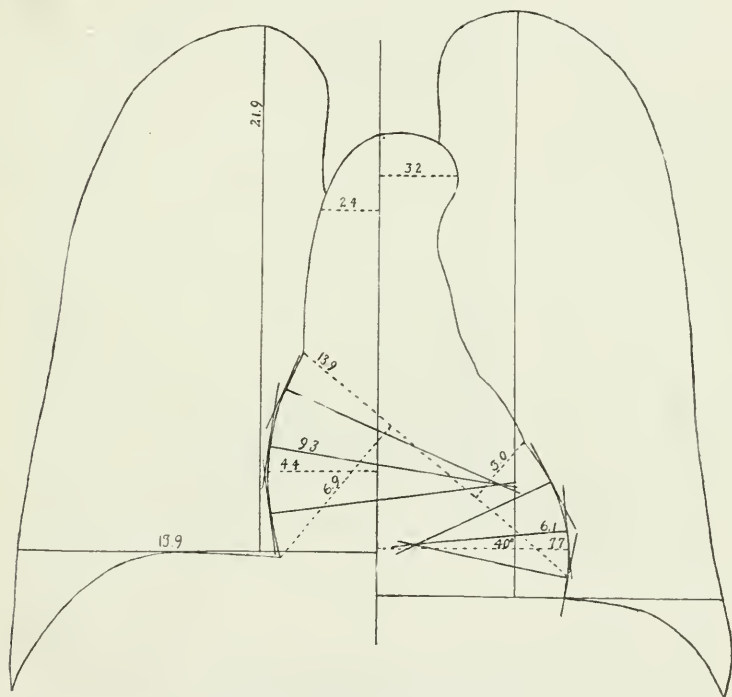
Fig. 8.—Diagram indicating the standard measurements and radial values of the heart of the sthenic habitus.

The exposure was made in the upright position with the anterior chest wall against and parallel to the plate. Depending on the thickness of the chest wall the time of exposure varied from one to three seconds' duration. Exposures were made in full inspiration except in the asthenic type, where they were taken in complete expiration.[4]

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[4] The purpose of this procedure is to get the various obliquities of the heart shadows as nearly identical as possible and as small a variation in angle as possible, the averages in our examinations extending from 33 to 48, a variation of but 15 degrees.

Tracings were drawn from the radiographs obtained in this way and the following measurements of the cardiac shadow were made:

1. Transverse diameter—obtained by adding:

     (a) Maximum deviation to the right from the midline;

     (b) Maximum deviation to the left from the midline.

2. Total length measured from the junction of the right auricle and aorta to the apex.

3. Diameter of the base measured at right angles from the long diameter to the most distant point below on the right and to the junction of the auricle and ventricle above on the left.
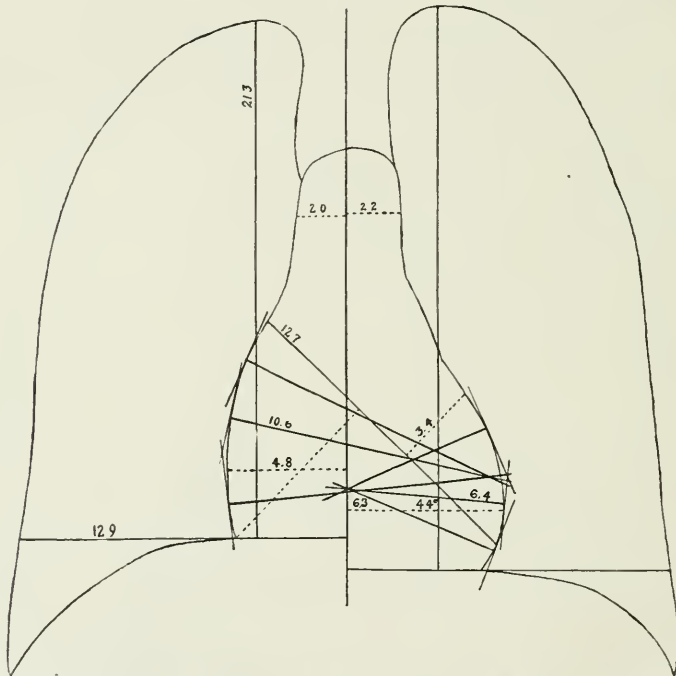
FIG. 9.—Diagram indicating the standard measurements and radial values of the heart of the hyposthenic habitus.

4. The angle formed by the intersection of the transverse and long diameters.

5. Maximum width of the aortic arch at the second rib.

6. Width of the pulmonic fields measured at the level of the diaphragm.

7. Length of the pulmonic fields measured from the apex above to the highest point of the diaphragmatic curve.

8. Radius of the right auricle.

9. Radius of the left ventricle.

Measurements Nos. 1 to 7 inclusive are called the standard

measurements to which it is desired to add measurements Nos. 8 and 9, a measurement hitherto not described. To obtain the radius, for example, of the right auricle three tangents are first drawn to the right auricular curve (Fig. 6). Then perpendiculars drawn from the points where these tangents touch the curve meet at a point which is approximately equidistant to any point on the curve, and a line drawn from this intersection point to any point on the curve constitutes a radius. In a similar manner by drawing
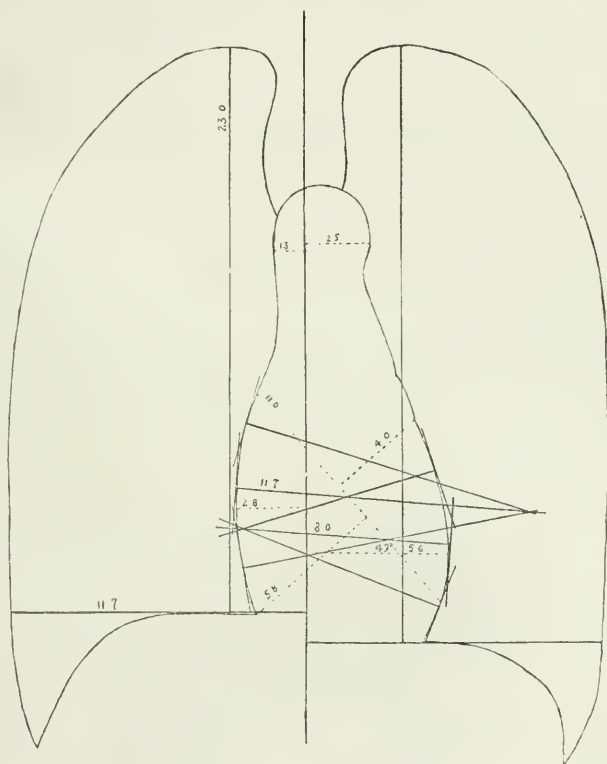
Fig. 10.—Diagram indicating the standard measurements and radial values of the heart of the asthenic habitus.

tangents and perpendiculars to the left ventricular curve its radius may be obtained.[5]

The radius of the curve is utilized as an expression of the size of the chamber.

As yet only the right auricular and left ventricular curves have been studied for the great majority of changes in the normal and

[5] Rarely the lines so drawn do not intersect at a single point. The error is less than three millimeters and negligible.

pathological heart are shown here, and it is the changes in these contours which are the most difficult to read.

It has been found that the radius of the curve varies with the habitus in a certain definite way, and that there is for each habitus a certain definite radius (Table II). When these curves do not conform in their radial value to the habitus the cause of the deviation must be sought for in intra- or extracardiac disease.

TABLE II.—SHOWING RELATION OF RADIUS OF RIGHT AURICLE AND LEFT VENTRICLE TO THE WIDTH AND LENGTH OF THE PULMONIC FIELDS, ANGLE OF OBLIQUITY, CHEST CIRCUMFERENCE AND WEIGHT.

Habitus.	Radius for right auricle, cm.	Radius for left ventricle, cm.	Width of pulmonic field, cm.	Height of pulmonic field, cm.	Angle in degrees.	Chest circumference, cm.	Weight in kg.
Asthenic . .	11.5	8.3	11.6	23.1	48	70.2	45.5
Hyposthenic	10.0	7.7	13.2	23.8	43	78.7	57.8
Sthenic . .	8.9	6.9	14.2	23.0	37	86.9	68.0
Hypersthenic	7.9	6.8	14.4	22.5	33	93.2	72.0

TABLE III.— TABLE SHOWING RELATION OF RADII TO WEIGHT FOR HYPERSTHENIC HABITUS.

Weight in kg.	Radius for right auricle, cm.	Radius for left ventricle, cm.	Angle in degrees.
40 to 50 (rare)	8.5 to 8.0	6.6 to 6.2	30 to 34
51 to 60	8.0 to 7.6	6.2 to 5.9	30 to 34
61 to 70	7.8 to 7.3	6.0 to 5.7	30 to 34
71 to 80	7.6 to 7.0	5.8 to 5.5	30 to 34

NOTE.—A radius for right auricle below 7.0 cm. is considered abnormal. A radius for left ventricle below 5.5 cm. is considered abnormal.

TABLE IV.—TABLE SHOWING RELATION OF RADII TO WEIGHT FOR STHENIC HABITUS.

Weight in kg.	Radius for right auricle, cm.	Radius for left ventricle, cm.	Angle in degrees.
40 to 50	9.5 to 8.8	7.5 to 7.0	35 to 39
51 to 60	9.0 to 8.6	7.2 to 6.8	35 to 39
61 to 70	8.8 to 8.4	7.0 to 6.6	35 to 39
71 to 80	8.6 to 8.0	6.8 to 6.2	35 to 39

NOTE —A radius for right auricle below 8.0 is considered abnormal. A radius for left ventricle below 6.0 is considered abnormal.

TABLE V.— TABLE SHOWING RELATION TO RADII TO WEIGHT FOR HYPOSTHENIC HABITUS.

Weight in kg.	Radius for right auricle, cm.	Radius for left ventricle, cm.	Angle in degrees.
40 to 50	11.0 to 10.5	8.4 to 8.0	40 to 45
51 to 60	10.5 to 10.0	8.2 to 7.6	40 to 45
61 to 70	10.0 to 9.5	8.0 to 7.4	40 to 45
71 to 80	9.5 to 9.0	7.8 to 7.2	40 to 45

NOTE.—A radius for right auricle below 9.0 cm. is considered abnormal. A radius for left ventricle below 7.0 cm. is considered abnormal.

TABLE VI.—TABLE SHOWING RELATION OF RADII TO WEIGHT FOR
ASTHENIC HABITUS.

Weight in kg.	Radius for right auricle, cm.	Radius for left ventricle, cm.	Angle in degrees
40 to 50	11.7	8.6	46 to 56
51 to 60	11.5	8.4	46 to 56
61 to 70	11.3	8.2	46 to 56
71 to 80 (rare)	11.2	8.0	46 to 56

NOTE.—A radius for right auricle below 11.0 cm. is considered abnormal. A radius for left ventricle below 8.0 cm. is considered abnormal.

The first deviation which occurs in the heart shape as a result of pathological changes in the walls of the heart manifests itself roentgenographically by a change in the contour of the cardiac profile. Such changes cannot be determined by the change in size. Only when well-marked do they produce the characteristic heart shapes, as, for instance, the rounded mitral heart and the oval heart of aortic valvular disease.

The distinct bulging of the pulmonic and auricular curves in well-marked cases of mitral stenosis or patent ductus is sufficiently characteristic to be recognized at a glance, but the beginning enlargement of the auricles as a result of obstruction of the pulmonary circulation, or beginning enlargement in the early stages of valvular disease, or the beginning change in the ventricular walls in arterio-nephritic disease can only be determined by an accurate measurement of the radii of the curves which constitute the profile of the heart shape.

Conclusions. 1. The position of the heart varies with the habitus.

2. The shape of the heart varies with the habitus.

3. That habitus must be taken into consideration in estimating cardiac size.

4. That reasoning by analogy the cardiac function, particularly as regards muscular tonus, may perhaps vary with the habitus.

5. That only by actual measurement of the curves of the heart can the changes in contour be made out in early cases.

6. That the value of the curves varies with the habitus.

7. That the radial value of the curves of the left ventricle and right auricle vary with the habitus.

8. That the radii measurements are a more accurate and valuable expression of impending or established change in the architecture of the heart chambers than the so-called standard measurements.

REVIEWS.

DISEASES OF CHILDREN. By HERMAN B. SHEFFIELD, M.D., formerly Instructor in Diseases of Children, New York Postgraduate Medical School. Pp. 798; 238 illustrations. St. Louis: C. V. Mosby Company, 1921.

THE arrangement of this book is somewhat different from most of the standard works dealing with the subject. There is a division into fourteen chapters which on examination are found to be sections rather than chapters. For example in the first chapter, which is on the Control and Prevention of Disease, the following subheadings are present: Nutrition and Infant-feeding; Hygiene and Sanitation; Immunization; Therapy.

In any book dealing with the period of infancy it is of first interest to turn to the pages on infant-feeding. It is there that the individuality of the author can be discovered. There is not much space devoted to nutrition in Dr. Sheffield's book, but probably as much as the size of the book warrants. After a theoretical discussion of the digestion of protein, carbohydrate and fat, breast-feeding is very briefly considered. It is to be noted here that some pediatrists would take exception to the statement that it may be necessary to remove the baby from the breast because of high fat content in the milk. Such high fat percentage is almost always a temporary matter, and even then rarely disturbs the baby to any great extent. Under artificial feeding of babies it is seen that the author evidently believes in low protein in his mixtures, as all the formulas given are made from top milk when the infant is under three months of age. A rather ingenious arrangement is given for calculating the mixtures required, the calculation being made on age rather than on weight. The necessity for individualization in feeding is recognized. In the tables for feeding older children only the nature of the foods selected is mentioned—the amounts are not stated.

The rest of the book takes up in order the usual diseases of the newborn, the infant and the older child. Subjects of recent interest are given mention, such, for example, as the Schick test, the toxin-antitoxin immunization in diphtheria and the vitamines. Certain lapses are noted in bringing some of the chapters up to date. Thus in spasmophilia the statement is made that it (spasmophilia) is still shrouded in mystery, and no reference is made to the question of a disturbance of the mineral metabolism in its causation.

The illustrations in the book are fair and show a rather large number of unusual conditions. A. G. M.

TRANSACTIONS OF THE AMERICAN UROLOGICAL ASSOCIATION. Vol. XII, 1920. Pp. 353; 83 illustrations. Baltimore: Williams & Wilkins Company, 1921.

THESE *Transactions* contain many valuable and progressive papers. Notable among the thirty-six herein published is Eisendrath's study of "The Relation of Variations in the Renal Vessels to Pyelotomy and Nephrectomy;" Barringer's presentation of "Newer Methods of Radium Treatment of Carcinoma of the Bladder and Prostate;" Smith's "Spinal Anesthesia in Urology."

<div align="right">A. R.</div>

PRINCIPLES OF HYGIENE: A PRACTICAL MANUAL FOR STUDENTS PHYSICIANS AND HEALTH OFFICERS. By D. H. BERGEY, M.D., DR. P.H., Assistant Professor of Hygiene and Bacteriology, University of Pennsylvania. Seventh edition, thoroughly revised. Pp. 556; 63 illustrations. Philadelphia and London: W. B. Saunders Company, 1921.

THIS seventh edition brings Dr. Bergey's well-known manual thoroughly up to date. Into it are incorporated many valuable public-health lessons learned during the World War. The general arrangement and the subjects presented are in the main the same as in the previous editions.

The book has not been prepared merely for medical students and practitioners, but also to aid students in architecture in comprehending the sanitary requirements in ventilation, heating, water-supply and sewage-disposal. Its chief value, however, lies in its simple and accurate presentation of the general principles upon which the health officer and the physician work in their respective capacities in dealing with conditions which are detrimental to health or which tend to improve health. Furthermore, certain chapters, especially those dealing with personal hygiene, food and dieting, exercise and clothing will be of considerable interest and much value to the layman.

It is a pleasure to note that throughout the treatise the metric system of weights and measures is used. This is far simpler than the English system, and although it has been legal in the United States, according to Dr. Bergey, since 1866, it is only now coming into fairly frequent use in the medical profession. Its adoption by such text-books as this will make for its more general use.

In the appendix are included the United States quarantine laws and certain state regulations, and these add considerably to the reference value of the work. On the whole the book deserves the hearty welcome which has been accorded previous editions.

<div align="right">T. G. M.</div>

OPERATIVE SURGERY. By J. SHELTON HORSLEY, M.D., F.A.C.S.,
Attending Surgeon, St. Elizabeth's Hospital, Richmond, Va.
Pp. 721; 613 illustrations. St. Louis: C. V. Mosby Company,
1921.

THE many years' experience of the author has been crystallized
in this masterful book on operative surgery. Throughout the text
the keynote is the relation of physiology to surgery and the preser-
vation of the functional ability of an organ when its anatomy is
necessarily modified by operation. The author lays great stress
on a proper conception of the biological phenomena as being of as
great importance as the mere knowledge of surgical technic or the
ability to perform an anatomically perfect operation.

The volume does not purport to be an encyclopedia of all surgical
procedures, but is a selection of those personally found to be of the
greatest value, although in many instances several operations
appropriate for different aspects of the same underlying affection
will be found. Especially, in view of their excellence, mention must
be made of the chapters on plastic surgery and the surgery of the
bloodvessel system, in which the author is a recognized master and
authority. Systemic surgery is described in the various chapters
in a style easily readable, with the description clear and quickly
comprehensible and with sufficient discussion of the variations of
conditions and complications to be met. In addition to the chapters
on systemic surgery there are sections dealing with technic, compli-
cations, drainage, transfusion, incisions and the general principles
of operative surgery. The book is splendidly and profusely illus-
trated. The volume will take its place at once in the front rank
of the text-books on operative surgery.   P. F. W.

DISEASES OF THE SKIN. By J. M. H. MACLEOD, M.D., Physician
for Diseases of the Skin, Charing Cross Hospital; Physician for
Diseases of the Skin, London Hospital for Tropical Diseases;
Physician to the Skin Department, Victoria Hospital for Children;
Lecturer on Dermatology, Charing Cross Medical College and
London School of Tropical Medicine; formerly editor of the
British Journal of Dermatology; Vice-President, Dermatological
Section of the Royal Society of Medicine; Membre de la Société
Française de Dermatologie; Corresponding Member of the
American Dermatological Association. Pp. 1307; 23 illustrations
in color and 435 figures in black and white. New York: Paul
B. Hoeber, 1921.

MACLEOD, after a thorough and complete understanding of the
normal histology and pathological changes that occur in the skin,

has completed an excellent text-book on dermatology. It is unusual for one author to have written extensively in book form on the pathology of the skin, and in addition a text-book on dermatology covering all phases of this important subject.

MacLeod's work both as to illustration and text is monumental, as very few books on dermatology have attained this proportion and completeness.

The preliminary portion of the subject is unusually well covered—158 pages of text help the reader in the elucidation of the individual diseases. Classification of the various diseases has again, as in other text-books on the subject, proved difficult, as the etiology of so many dermatological conditions is as yet unfathomed.

The diseases of the skin are described under the following headings: Congenital affections of the skin; cutaneous affections due to cold; cutaneous affections due to heat; cutaneous affections due to sunlight; dermatitis due to electricity, roentgen rays and radium; dermatitis due to local irritants; cutaneous affections due to streptococci, to staphylococci, to fungi, to bacilli, to protozoa (syphilis), to animal parasites; pruritus; erythemata; urticaria and allied conditions; drug eruptions; lichen; eczema and rosacea; scaly affections; vesicular and bullous affections; lupus erythematosus; mycosis fungoides; affections of the cutaneous bloodvessels; anomalies of pigmentation; atrophies of the skin; affections of the hair, of the hair follicles, of the sebaceous glands, of the sweat apparatus, of the nails, of the lips and mouth; benign neoplasms of the skin; malignant neoplasms of the skin; pseudoneoplasms of the skin and tropical affections of the skin.

The photographs are excellent, the illustrations in color good, but some are of a rather vivid hue.

The volume is a credit to the author and the publisher, and can be thoroughly recommended as one of the best works on dermatology extant.   F. C. K.

THE TREATMENT OF ACUTE INFECTIOUS DISEASES. By FRANK SHERMAN MEARA, M.D., PH.D., Professor of Clinical Medicine, Cornell University Medical College; Consulting Physician to Bellevue Hospital, New York; to the Mountainside Hospital, Montclair, N. J.; to the Morristown Memorial Hospital, Morristown, N. J., etc. Second edition, revised. Pp. 806. New York: The Macmillan Company, 1921.

A REVISION of the original text has been made to accommodate the many changes necessitated by the increase in the knowledge of certain of the acute infectious diseases, such as measles, streptococcus pneumonia and meningitis. The results of epidemics in the military camps have added to the literature much information of value.

The author has added in addition descriptions of the more common acute infections of the upper respiratory tract, such as coryza, tonsillitis, laryngitis and tracheobronchitis and a chapter on acute pleurisy. Encephalitis lethargica and trench fever have been added and rat-bite fever and Rocky Mountain spotted fever have been revised. It was thought advisable to retain the chapter on grip, although a new chapter was devoted to epidemic influenza. The book is well written, well arranged and convenient for reference. The references to the literature are given in footnotes on each page as they occur. There are at times direct quotations of the original reference. A complete, systematic summary is added to each chapter. Containing as it does the essence of the text set forth in the briefest form, but still containing the most important points of information, the book becomes an invaluable, handy reference for the busy practitioner, while the completeness of the text renders it an important addition to the library as a source of more detailed and recent information. The reproduction of many prescriptions and the descriptions of non-medicinal methods contribute to its value as a therapeutic guide.   A. E. S.

GEORGE MILLER STERNBERG: A BIOGRAPHY. By his Wife, MARTHA L. STERNBERG. Pp. 331. American Medical Association, 1920.

THE American Medical Association is to be congratulated in a departure from policy when it published Sternberg's *Biography*. In this volume is reviewed, by his widow, the life of a man who helped in a large measure to make American medicine and its history. The story is intensely interesting, because Dr. Sternberg's career was full of hard work and achievement. Mrs. Sternberg tells entertainingly of his days spent at military posts combating cholera and yellow fever; of his pioneer bacteriological work, and of his activities as Surgeon-General during the Spanish-American War. The conquest of yellow fever is one of the great episodes in medicine. Three names are suggested in this connection: Sternberg, Reed and Gorgas. It is fortunate to have such an excellent biography of the first member of this illustrous trio.   T. G. S.

PROGRESS

OF

MEDICAL SCIENCE

SURGERY

UNDER THE CHARGE OF

T. TURNER THOMAS, M.D.,

ASSOCIATE PROFESSOR OF APPLIED ANATOMY AND ASSOCIATE IN SURGERY IN THE
UNIVERSITY OF PENNSYLVANIA; SURGEON TO THE PHILADELPHIA GENERAL
AND NORTHEASTERN HOSPITALS AND ASSISTANT SURGEON
TO THE UNIVERSITY HOSPITAL.

Manipulation of Stiff Joints.—JONES (*Jour. Orthop. Surg.*, 1921, iii, 385) says that one of the difficult problems presented to a surgeon is the decision as to when a stiff joint is to be moved and when it is to be rested. A painful joint which is rigid in all directions is the seat of an arthritis, while a painful joint which is rigid in certain directions only, movement being normal in others, is free from arthritis but subject to adhesions. Adhesions may be divided into two groups—intra-articular and extra-articular. Adhesions are avoided by the early and safe resort to active and passive movements. These movements should be practically painless and should consist mainly in assisting the patient to move his own joints. Light adhesions may be broken down under gas; if strong and resistant, full anaesthesia is best. The joints should be moved through the full anatomical range unless adhesions are very firm. The pump-handle method as applied to the breaking of adhesions or the practice of passive movements is to be avoided. Voluntary efforts, however, can be repeated with advantage as often as the patient can be persuaded to make them. If effusion should take place in a joint after manipulation, it is strongly suggestive of the rupture of intra-articular adhesions. If the range of movement is diminished by use and exercise the joint requires rest. If even in the presence of pain the range of movement is increased by exercise, rest is contraindicated.

Some Aspects of the Mechanism of the Human Foot in Walking.—GIBSON (*Jour. Orthop. Surg.*, 1921, iii, 158) says that the foot is essentially a kinetic mechanism and that the term "arches" applied to the various parts of it is not so accurate nor so significant as the term "springs." Without entering deeply into the mechanics of springs it is evident that the more flexible the material the greater will be the power of the spring to convert a vertical impulse into a horizontal deformation—the larger it is the greater the amount of such conversion. One other quality is a prime necessity in a spring, namely, strength.

In the human foot there are two springs but not with independent action. The outer spring is made up of the following bones: os calcis, cuboid, fourth and fifth metatarsals. The inner spring is made up of the os calcis, scaphoid, the three cuneiforms and the first three metatarsals, especially the first. In both cases the point of maximum convexity of the spring is supported by a tendinous sling whose upper attachment is to the bones of the leg. The peroneus longus is on the outer side, the tibialis posticus on the inner side.

Fractures of the Elbow in Children.—STONE (*Jour. Orthop. Surg.*, 1921, iii, 395) says that reduction should be attempted with the elbow fully extended if necessary. The elbow is then held flexed midway between pronation and supination by strapping the wrist to the shoulder with adhesive plaster and adding the support of a sling. The flexed position should be maintained for two weeks. Then a change to a right-angled splint for at least three weeks then, finally, a sling for a week as a safeguard against accident before natural use in play. Passive movement is either useless or harmful, or not only the synovial cartilage but the large masses of epiphyseal cartilage tend to prevent rought jagged ends from traumatizing the delicate synovial membrane. The two causes of limitation of motion after elbow fracture in children are spasm and deformity. Spasm indicates one thing, that motion would cause pain—nature demands rest till spasm is gone. In deformity the limitation is clean-cut—definite, comparable to the stopping of a door by an obstruction. Primarily the deformity is bony, in part the result of imperfect reposition of the fragments, in part of callus formation. Secondarily there may be all sorts of ligamentous and muscular readjustments which limit motion. In overcoming deformity the decrease in the size of the callus, the gradual absorption of bony projections and adaptive changes are the essential factors. One group of cases requires open reduction, namely, those in which the epiphysis of the external condyle has been detached and has turned turtle. The slightly concave fractured surface points upward, outward and backward. The articular surface lies in contact with the fracture line at the lower end of the shaft. In epiphyseal separations about the elbow joint the roentgen-ray may often be wholly negative. The diagnosis must be made by history, the disturbed function and local tenderness. Volkmann's ischemic contracture is one of the most serious and distressing complications of elbow fractures. Any muscle deprived of its blood supply for a period of six hours undergoes degenerative changes from complicated muscle cell to low-grade scar tissue. Contraction of the scar causes flexion of the muscles.

Reconstructive Surgery of Traumatic Foot and Ankle Deformities.—COTTON (*Jour. Orthop. Surg.*, 1921, iii, 196) says that the functions of the foot in order of their importance are to support the body weight, to give attachment to the muscles of the legs and foot, to act as a lever in progression, to furnish the spring movements in walking by permitting lateral and up-and-down movements. Traumatic deformities of the foot and ankle which interfere with the normal function may be caused by injury or infection of the bones of the leg or ankle joint, bones and joints of the tarsus; injury or infection of the muscles or tendons, injury to nerves supplying motor function to muscles of the leg and foot. The

most common cause of traumatic weak foot is unreduced Pott's fracture —the most common variety is fracture of the fibula about three inches above the external malleolus. This type when unreduced gives us the typical traumatic flat foot. It is necessary to restore the alignment of the foot to the leg, to put the foot back in gear with the leg. This can be brought about by osteotomy of the tibia and fibula above the old fracture or by refracturing the bones at the site of the old fracture. Another type of deformity is due to unreduced fracture of the lower end of the tibia extending into the ankle joint an acquired talipes equino-varus. The simplest method of treatment is by tenotomy of the tendo Achillis and other resisting tendons or fascia and wrenching, combined with osteotomy of the tibia and fibula above the ankle joint. Another common cause of deformity and prolonged disability of the foot is fracture of the os calcis. The lateral deformity of the fracture with the shortening of the tissues on the outer side of the ankle and of the peroneal tendons furnishes the pathology for the clinical condition of rigid weak foot. The prophylactic treatment is the reduction of the fractured os calcis by manipulation with furnishing of proper support to the foot when weight-bearing is begun. When the condition has developed the treatment is practically the same as that of rigid weak foot. The principles used in the treatment of osteomyelitis with deformity are, first, the thorough operative removal of the diseased bone by the cone method with correction of the deformity by osteotomy, followed by frequent cleansing of the wound and prevention of pocketing. The weight-bearing function is the first object of all treatment. Unnecessary risks and fanciful operations should be tabooed.

Non-operative Treatment of Scoliosis.—Traslow (*Jour. Orthop. Surg.*, 1921, iii, 228) says that successful treatment of structural scoliosis must depend upon a clear understanding of the elements of deformity and the lessening, if not complete elimination, of all of them. Uniform and regular measurement and numerical record of the elements of deformity are important as guides to continuance of treatment and as indicating elements most needing correction. A balanced use of corrective plaster-of-Paris jackets, of retention braces and of internal exercises is essential in satisfactory results. The position of the patient when the plaster jacket is applied is responsible for improving body posture and shoulder carriage; the successive paddings are for care of the spinal deviation and rotation. The essentials of a retention brace are ability to hold correction attained, application by the patient with reasonable accuracy, extensibility and lateral compressibility to meet normal growth and progressive deformity decrease; mechanical self-correction by the brace seems possible but not yet fully attained. Gymnastic exercises must be progressive, intensive and with a minimum of erect weight-bearing. They must aim to correct all of the elements of deformity, especially that of rotation. Starting positions other than standing facilitate these ends. Retention of deformity correction attained must be maintained while exercise is developing natural muscular support. Artificial support may gradually give way to natural support. The paralytic scoliotic must receive a larger proportion of artificial support than will be required for those not paralyzed in trunk muscles. Internal splinting by operative bone fixation may also be necessary in severe paralytic cases.

THERAPEUTICS

UNDER THE CHARGE OF

SAMUEL W. LAMBERT, M.D.,

NEW YORK,

AND

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Etiology of an Outbreak of Infectious Diarrhea.—WEISS (*Arch. Int. Med.*, 1921, xxviii, 37) states that out of 422 cases of diarrhea occurring in the autumn of 1918 in the A. E. F. at the St. Anne Barracks, Nantes, only 15 required hospital care. Eight of these were available for study and from 7 a Gram-positive micrococcus was isolated from one or more sources—in 4 cases from the feces, in 6 cases from the urine and in 1 case from the blood. The eighth case, the only negative one, was convalescent. The author describes the organism carefully and shows the identical manner in which the various strains react on fermentation mediums and with serum agglutination tests. He was able, also, to produce diarrhea in Macacus rhesus monkeys by feeding them the organism, and in a number of these cases the disease proved fatal and the organism was recovered at postmortem. A monkey actively immunized by a polyvalent vaccine made from these cultures was subsequently resistant to infection. The author concludes that the evidence presented suggests the etiological relationship of the organism described to infectious diarrhea in the outbreak studied.

Modern Methods in Handling Hospital Statistics.—PEARL (*Bull. Johns Hopkins Hosp.*, 1921, xxxii, 184) shows the value of and need for careful statistical investigation of medical data in a modern hospital. He gives the functions of a statistical department: (*a*) Assembling and tabulating routine statistical data; (*b*) organization of special department records; (*c*) consultant service (of expert statistician to persons publishing papers); (*d*) research (special biometrical investigations). He discusses the hospital records and points out the commonest defects: "The advantages of this method of preserving histories (the so-called 'unit system' of case histories) over the far more common system of binding them in great volumes in numerical or temporal sequence are so obvious as not to need detailed exposition. Such a method is really essential." The modern system of mechanical tabulating and indexing is described whereby records are transferred, by means of a machine called a "key punch," to cards, the record on the card appearing as a series of punch holes. Then by means of another machine, known as a "sorter," the punched cards can be mechanically sorted at a rate of 250 cards per minute into any desired arrangement. The pertinent cards thus sorted need only be run again through another machine, known as a "tabulator" and the results relative to any desired category of information will be mechanically

counted and tabulated. The organization of the card forms is shown and fac-similes are produced of (*a*) the primary card, (*b*) the secondary card, and of (*c*) five special cards (now in use in the Brady Urological Clinic of the Johns Hopkins Hospital). The statistical department in a modern hospital should consist of a chief statistician, an assistant statistician and four clerks. He details the material equipment needed.

The Intravenous Administration of Calcium Acetyl Salicylate.— CAMPBELL (*British Med. Jour.*, July 9, 1921, p. 37) states that acetyl salicylic acid is in part decomposed into salicylic acid and absorbed as salicylate—that part is taken into the blood stream unchanged. The salicylate formed from it exercises its usual antipyretic action on the tissues. The undecomposed molecule is responsible for the analgesic action in headache, neuralgia, etc. It occurred to Campbell that the analgesic action could be greatly increased if the drug were injected directly into the blood stream, thus avoiding decomposition in the alimentary tract. Since acetyl salicylic acid is only slightly soluble, calcium acetyl salicylate was used. The results more than fulfilled expectations; the pain is relieved in one-half to three-quarters of an hour and the effect persists for several hours and in some cases for days. Among the painful conditions that yielded to this new therapy were sciatica, acute rheumatism, tabes dorsalis, interstitial keratitis, acute iritis, arsenical neuritis, dysmenorrhea, etc. It is noteworthy that one patient who was unable to take sodium salicylate or acetyl salicylic acid by mouth was promptly relieved by calcium acetyl salicylate by vein.

The Salicylates. XIII. The Liberation of Free Salicylic Acid from Salicylate in the Circulation.— It has been claimed that the absence of a right-sided valvular endocarditis is due to the antiseptic qualities of free salicylic acid liberated in the right heart by virtue of the greater carbon dioxide content of the venous blood; that the occurrence of initial endocarditis is associated with the greater alkalinity of the arterial blood, which cannot liberate free salicylic acid and consequently does not possess antiseptic qualities. Although HANZLIK (*Jour. Pharm. Exp. Therap.*, 1921, xvii, 385) admits that this view is not compatible with the modern conceptions of the mechanism of neutrality regulation of the blood, he thought it desirable to put it to a test. Animals were injected with salicylate and were subjected to the most favorable conditions for reduction of the alkalinity of the blood, mainly by means of fatal asphyxia. But first it was necessary to determine the degree of acidity necessary for the liberation of free salicylic acid from salicylate *in vitro*. It was found that free salicylic acid is demonstrably liberated from the sodium salt at a low degree of acidity, one whose hydrogen-ion concentration corresponds to pH $=6.7$; more definitely at pH $=6.5$. The presence of 25 per cent serum or plasma in salicylate "buffer" mixtures prevents the liberation of free salicylic acid at the high degree of acidity of pH $=5.9$. Therefore it is improbable that free salicylic acid could be demonstrated in the circulation during life. This was fully confirmed on animals subjected to fatal asphyxia whose cardiac and arterial bloods were rendered very slightly acid (pH $=6.8$ or 6.9). Consequently the theory that free

salicylic acid liberated by virtue of the greater CO_2 content of the venous blood of the right heart exerts an antiseptic action and prevents the development of a right-sided auriculoventricular (tricuspid) endocarditis in rheumatic fever is untenable. An explanation of the phenomenon must be sought elsewhere.

The Action of Drugs in Infection.—I. The Influence of Morphin in Experimental Septicemia.—KRAFT and LEITCH, (*Jour. Pharm. Exp. Therap.*, 1921, xvii, 377) report that morphin lowers the resistance of rabbits toward septicemia produced by Streptococcus hemolyticus. Just how this decreased resistance is brought about they fail to determine, but suggest that the harmful influence of morphin is due to several factors: Inhibition of phagocytosis, increase in intestinal stasis and a depression of body temperature, of metabolism and of the body defence. While there can be no doubt of the value of the sedative action of morphin in certain non-inflammatory conditions the authors are convinced that opium and its derivatives must be prescribed with great caution to those patients who are suffering from diseases associated with inflammation.

PEDIATRICS

UNDER THE CHARGE OF

THOMPSON S. WESTCOTT, M.D., AND ALVIN E. SIEGEL, M.D.,

OF PHILADELPHIA.

Feeble-mindedness in Hereditary Neurosyphilis.—RAEDER (*Am. Jour. Dis. Children*, March, 1921) studied thirty children ranging in age from two to sixteen years. In either one or both parents there was a positive Wassermann reaction on the blood serum. Most of the parents had neurosyphilis usually of the paretic type. Either blood serum or blood serum and spinal fluid Wassermanns were made, in all thirty cases. Of these nineteen showed a definitely positive Wassermann reaction. With few exceptions the older children or those born nearest the time of the parental infection showed a positive Wassermann, while the younger and farthest removed showed a negative Wassermann. On twenty-two of the thirty children spinal fluid was obtained and in four of these a positive Wassermann reaction was returned. Psychometric examination of these children showed psychic steps corresponding to the grades of physical defects. Mental deficiency in congenitally syphilitic children of not feeble-minded parents is usually due to syphilis.

The Electrocardiogram in Normal Children.—SEHAM (*Am. Jour. Dis. Children*, March, 1921) found that in the premature in the first three months of life the normal electrocardiogram indicates that there is a right ventricular preponderance. At about the fourth month the $R1$ becomes longer than the $S1$, and from then on the ventricular com-

plex approaches the adult type of curve. In general the average height of deflections in children are greater than in the adult. Except in the premature satisfactory records showing all the deflections seen in the normal adult electrocardiogram can be obtained during any period of childhood. The P is higher in childhood than in the adult in all three leads except in the premature. It was absent in only two cases of this series. It was found electronegative in eight records. The Q plays a prominent part in the electrocardiogram of childhood. It is larger in Leads II and III. Altogether it adds confirmatory evidence that there is a right ventricular preponderance in the first few months of life. The R in Lead I during the first few months of life is lower than at any other period, but in Leads II and III it averages higher than in the adult. The increase of $R1$ corresponding with the decrease of S in Lead I is also an indication of a right ventricular preponderance during the earliest periods of life. The S deflection is the most characteristic and distinctive of the ventricular complex in childhood. In Lead I it is both relatively and absolutely higher in the first three months than in any other period of life and in the other leads it is relatively higher than in the adult. The T is very susceptible to external influences in the child and therefore its height is unreliable. In the first ten days it is quite frequently absent. After that it is quite constant. It was found inverted but only during the latter part of childhood in 15 per cent of the readings. The general impression that the younger the child the more frequent the arrhythmias was not confirmed by the electrocardiograph. The younger the child the faster the pulse and the faster the pulse the less frequent the arrhythmia. In the newborn the average difference between the highest and the lowest pulse periods was $\frac{2}{50}$ second. Whereas in the older children from six to thirteen years of age the average difference was $4 \frac{3}{50}$ seconds. In the period of infancy no sinus arrhythmia occurred, while in the school age 47 per cent showed it. The transmission time in children is, on the whole, of shorter duration than in the adult. In the newborn the auricular activity occupies an average of 0.18 second, whereas in the last period of childhood it consumes an average of 0.19 second. In the adult the R interval averages 0.18 second. In the newborn it averages 0.21 second and gradually increases until at the school age it averages 0.34 second. In the adult the average for RT phase is 0.36 second.

Safety-pins in the Stomach.—JACKSON and SPENCER (*Jour. Am. Med. Assn.*, February 26, 1921) report two cases in which the pins were removed by mouth without anesthesia. Discussing foreign bodies in the alimentary canal they say that in most cases foreign bodies that have reached the stomach without having been pushed down will pass harmlessly through the intestinal tract. Enough exceptions arise that make it necessary to watch the foreign body at frequent intervals by fluoroscopy until the foreign body is passed. During this time no change should be made in the diet and laxatives are not to be given. Open safety-pins have been passed by rectum, but removal from the stomach by mouth is advisable where the pin is so large relatively to the size of the patient that there is some doubt that it will pass, and also when waiting for from three to eight weeks has demonstrated that the pin will probably not pass. There is little likelihood that a foreign body

will be regurgitated. The safest and best method is by peroral gastroscopy. When a skilled endoscopist is not available external operation by a skilled surgeon is safer and more successful. When a number of bodies is in the stomach, as frequently happens in the insane, external operation is the best procedure.

Physical Defects in Children.—EMERSON (*Am. Jour. Dis. Children*, March, 1921) examined 607 children. He found that children reported to be sufficiently well to attend school and to engage in the activities of normal children were found to average 5.2 physical defects of all kinds and 2.5 of nasopharyngeal defects. Children brought to a hospital clinic for examination and treatment showed an average of 6.8 general defects and 3.5 nasopharyngeal defects. The distribution of defects according to age was remarkably uniform. In each group studied the largest number of children were between the ages of seven and nine years. These years showed the greatest average number of defects in the Massachusetts General Hospital group as 7.2, but in the Little Wanderers' Home group the highest average number of defects, 6.0, was found from ten to twelve years. Only nine children in the 602 were free from defects. The nasopharyngeal defects appeared in a large number of cases and also totaled a greater number of defects than any other group.

Stigmata of Predisposition to Bone and Joint Tubercle.—RIVERS (*British Jour. Dis. Children*, October to December, 1920) says that denial or neglect of intrinsic predisposition to bone and joint tubercle betokens not only the lack of clinical insight but an unfamiliarity with the literature. It would seem that a part of such a predisposition is not due to a single undefined susceptibility but was multiform and made up of several abnormalities acting probably by mechanical facilitation of infection or else associated with other undiscovered abnormalities acting in a like manner. For the facts and findings concerning pigmentation, ichthyosis, nasal defect and mental unsoundness they are best explained in the light of intrinsic contributory causes. There are obviously several practical bearings, diagnostic, prophylactic and others. There is also a eugenic aspect which is rather important. The author feels that no tuberculous ichthyotic, unless of great intellectual attainments, and no tuberculous mental defective, should be allowed to reproduce.

Roentgen-ray and Tuberculosis in Infants and Children.—O'BRIEN and AMES (*Jour. Am. Med. Assn.*, May 28, 1921) studied forty-four infants and children. They found that the von Pirquet and intracutaneous skin reactions were reliable tests of infection with the tubercle bacillus and the number of positive reactions increases from infancy up to childhood, all their patients over ten years of age reacting. In twenty-six of thirty-six positive skin reactions the roentgen-ray disclosed the site of infection to be intrathoracic. D'Espine's sign as a clinical index of tuberculosis of the bronchial lymph glands is of relative value, being elicited only eleven times as against roentgen-ray evidence of tuberculosis in twenty-eight cases. Three cases of positive sputum were found in fourteen diagnoses of chronic pulmonary tubercu-

losis. Fourteen cases of chronic pulmonary tuberculosis of the adult type were found. Fifteen cases that were negative clinically showed definite roentgen-ray evidence of structural changes of tuberculous infection. This raises the question as to whether these children are not liable to develop clinical tuberculosis, and they should be watched carefully and roentgen-rayed frequently.

Exercise Tolerance of Children with Heart Disease as Determined by Standardized Test Exercises.—WILSON (*Jour. Am. Med. Assn.*, June 11, 1921) found that the circulatory reactions after test exercises in 45 normal children and in 116 children with heart disease confirmed the results of the study of a previously reported group of 20 normal children. A working table was formulated of standardized test exercises followed by normal systolic blood-pressure curves without symptoms of dyspnea and fatigue. It was standardized from an analysis of the reactions of an average group of 65 normal children according to age, weight and height. The degree of distress and type of systolic blood-pressure curve following the standardized test exercises was used as a gauge in estimating the exercise tolerance of children with heart disease. Of the 71 children having definite organic heart disease without symptoms of insufficiency, 69 per cent had a normal tolerance for standardized test exercises, 29 per cent had fair tolerance and 2 per cent had a poor tolerance. In children with chronic organic heart disease, exercise tolerance tests give important and useful information which may be utilized as a scientific basis for intelligent regulation of the child's activities. The observations resulting from this investigation would seem to indicate that the fear of exercise is unwarranted and that a wider latitude may be permitted with safety.

OBSTETRICS

UNDER THE CHARGE OF

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Pregnancy Complicated by Pyelitis.—BAUGHMAN (*Am. Jour. Obst.*, February, 1921, p. 436) reports three cases of pregnancy complicated by pyelitis. These patients were under observation for a considerable time, were treated by lavage of the pelvis of the kidney and pyelograms were taken from time to time as the pelvic size changed. They were private patients treated in a private hospital. The first was a multipara who, during her second pregnancy, had slight nausea at first, which later became severe, with persistent vomiting. There was pain over the abdomen and back, with the greatest tenderness over the right kidney. There was no elevation of temperature and the urine obtained by the catheter was acid, with a few pus cells. The Bacillus coli communis was found on examining the urinary tract, and the patient was treated by irrigation of the pelvis of the kidney. This was followed by increased appetite and improved general condition, and at the fifth irrigation a pyelogram of the kidney was taken. This showed great

distention of the right kidney, pelvis and ureter; moderate distention of the left pelvis and ureter. Both ureters were kinked and tortuous. At the sixth irrigation the patient suffered considerably; her appetite was impaired and she was nauseated. Labor was accordingly induced, and after the birth of the child five irrigations were given, the first fourteen days after delivery. The patient passed through an attack of cystitis, which was treated by daily irrigation of the bladder, followed by instillations of mercurochrome. The patient ultimately made a complete and satisfactory recovery. The second case was that of a primipara who had severe pain in the back and right side and a temperature as high as 104° F. There was frequent urination followed by burning sensation. Three chills occurred in one day. The leukocytes were 16,000; the urine was acid, with a trace of albumin and some pus cells. During the acute attack the patient suffered from nausea. After three irrigations of the bladder the patient seemed better, but after the fourth there was much nausea for two days. The fifth irrigation was given with mercurochrome, which seemed very little irritating, and it was then possible to make a picture of the kidneys. This showed the left pelvis and ureter moderately distended, the right pelvis and ureter more dilated than the left, the kink in the ureter below the pelvis, but below that point there was dilatation. The vertebral column of the fetus was shown in such a position as probably to interfere with the emptying of the pelvis of the kidney on that side. The patient seemed to improve until the ninth irrigation, when it was found that the pelvis of the right kidney was not draining. A pyelogram taken showed moderate dilatation of both kidney pelves, especially marked on the right side. The ureters in the upper part were distorted. After the twelfth irrigation, of 2 per cent. of nitrate of silver solution, against the advice of the physician the patient went home immediately after the irrigation. She suffered considerable pain and had a restless night. Labor began, the child was born asphyxiated, was resuscitated with difficulty, but died a few hours later. Eleven days after delivery irrigation was again resumed with a fairly good result. A pyelogram showed ureters normal, the left pelvis in good condition, the right pelvis of the kidney only partially filled, with accumulation of solution in the calyces. It was thought that possibly the right kidney was smaller than the left. The patient's general condition was good. His third case was that of a multipara who suffered from severe nausea and vomiting for a period of ten days. There was pain in the back and abdomen and great tenderness over both kidneys, especially the right. The urine was acid, with pus and red blood cells; there was moderate elevation of temperature and mucus in the discharges from the bowel. On examination the blood leukocytes were 8000. The patient was considerably improved by three irrigations, when she began to have attacks of sweating. After the fifth irrigation it was possible to take a pyelogram, when the right pelvis and ureter were found greatly distended. The left was normal. The patient was treated with several irrigations, which seemed to produce benefit. Following the taking of a pyelogram, vomiting, headache and nausea returned to a considerable extent and the catheter was left in the pelvis of the right kidney for two hours after one of the irrigations. The patient seemed better for the treatment, and as the child was viable and the pelvis of the left kidney showed signs of becoming involved, labor was induced. The birth of the child was normal and fourteen days

after delivery the mother again received irrigation, and a pyelogram was made. There had been some improvement in the condition of the pelvis of the right kidney, and there was a kink in the right ureter near the pelvis. The patient finally went to her home and another examination made later showed a slow but definite improvement. Repeated examinations during the next few weeks showed that the patient's condition had reached a point where it was almost normal. These cases illustrated the fact that the pelvis of the right kidney is more often involved. In two of these patients the bladder was very constantly involved; in one case inflammation of the bladder was occasionally present. In two of the cases the colon bacillus was the exciting cause and in one the Staphylococcus albus. The pelves of the kidneys were almost of the same size as regards right and left. Irrigation seemed uniformly useful. Apparently the ureters had been obstructed by the pressure of the pregnant uterus because there was marked improvement after delivery. It was interesting to observe that the right kidney in one case was congenitally small and that there was a compensatory increase in the function of the other kidney. In the puerperal period irrigation was well borne as early as two weeks after the birth of the child. Fever was absent with these patients, which seemed unusual in view of the severity of some of the symptoms. Apparently the pelvis of the kidney may become greatly distended and yet resume its normal condition. In one case 100 cc of urine were obtained from the pelvis of one kidney. It is interesting to note that when labor was induced at a selected time, when the condition of the mother was good, that the children were born living. When labor developed without induction the child was stillborn. In discussion it was stated that, owing to the mechanical conditions in pregnancy, there was frequently stasis, followed by lowered resistance, migration of bacteria and infection of the kidney. The last usually comes directly from the colon and the bacteria found are colon bacilli. A mixed infection sometimes occurs. When the colon bacillus and staphylococci are both present there is more resistance to treatment. Good results have been obtained by the introduction of the ureteral catheter, leaving it twelve hours at a time. This apparently gives better results than irrigation, as irrigation seems to increase the dilatation of the damaged kidney. It is valuable to vary the position of the patient in treating and studying these cases. After recovery has apparently occurred, if the patient has slight disturbance in the functions of the kidneys and bladder bacteria will often be found in the urine. An important cause in the development of infection of the urinary tract is retention of urine in the bladder, and in these cases care must be taken to avoid that. In local treatment nitrate of silver is especially valuable, following thorough irrigation with boric acid to clear away the urine. If this is not done the silver will not be precipitated by the chlorides. In these cases the ureters, where they go into the bladder, are intensely congested, and this is also true to a lesser extent throughout their entire course. Nitrate of silver is not only a good antiseptic but a valuable astringent. After a severe labor cystitis and infection of the kidney may develop, because of mechanical injury during labor. Retention of urine and bad drainage from the kidney are usually the important factors in such a case. These patients often improve very slowly, and it may be necessary to carry out treatment energetically and for some time.

The Mortality of Parturition.—DAVIS (*Jour. Am. Med. Assn.,* February 21, 1920, p. 523) contributes a paper upon this subject. Much of his data is obtained from applications for insurance in life insurance companies. He draws attention to the lack of suitable hospital accommodations for parturient women. He considers the midwife a menace and believes that obstetric surgery and practice should be done in the homes of patients only under the most favorable conditions. Mortality statistics show that for women of the child-bearing age, fifteen to forty-five, childbirth is the second greatest cause of death. Life insurance records show that, for all women insured under forty-five years of age, the diseases of pregnancy and of the puerperal state constitute the second greatest cause of death. Nephritis and so-called Bright's disease and childbirth occupy the fifth place as to causes of death among insured women. A study of 10,000 family histories given by applicants for insurance shows that 1 in every 17.3 associates the death of a mother or sister or both with childbirth, 1 in 28.3 with tuberculosis, 1 in 45 with cancer. It is known that a considerable percentage of these deaths are inaccurately recollected, hence these records are often not accurate in showing the frequency with which childbirth is the contributary cause of death.

GYNECOLOGY

UNDER THE CHARGE OF

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New Uterine Suspension Operation.—A review of gynecological literature for any given year would not be complete if mention were not made of at least one of the dozen or so new operations for suspension of the uterus which are thrust upon the profession every year. One of these new operations has been described by GRAD (*Am. Jour. Obst., and Gynec.,* 1921, I, 411), and consists essentially of a subperitoneal shortening of the round ligaments. He has performed several hundred of these operations during a period of eight years, and from a review of one hundred cases in which a follow-up study was made, he is convinced that his operation eclipses all its predecessors. Such a feeling, however, is rather common among inventors of operations. In brief, the technic of the operation consists of grasping the round ligament midway between its cornual insertion and the internal ring and putting the ligament on tension. Immediately below the grasp of the forceps the operator picks up the anterior layer of the broad ligament with a thumb forceps and nips it with a scissors. Beginning at this point, with the scissors, the incision in the anterior layer of the broad ligament is extended along the edge of the round ligament, until the internal

ring of the inguinal canal is reached. In this manner the entire round ligament is divested of its peritoneum and the broad ligaments are separated. A stitch of linen is then taken in the pillars of the ring, which also picks up half of the round ligament as it enters the ring, and then with the same suture the round ligament is picked up, inside of its denuded area, about one inch from its uterine end and the two points of the ligament are brought together by tying the suture. The uterine end of the ligament is then sutured to the pillars of the internal ring with a few linen sutures and the intervening redundant portion of the round ligament is sutured together and then buried between the layers of the broad ligament, all of this being accomplished with the original suture. The anterior layer of the broad ligament is then sutured with catgut to the posterior surface of the round ligament, burying the redundant round ligament and covering all raw surfaces. After the procedure is performed on both sides the operation is frequently supplemented by shortening the uterosacral ligaments or by a ventro-suspension by means of a single catgut stitch, so as to be only temporary in nature. As a result of the author's investigation into this subject he concludes that every case of retroversion of the uterus with symptoms requires an abdominal section, and for this purpose the above operation is readily performed and is not time-consuming, creates no abnormal conditions in the pelvis, tunnels no holes through the abdominal parietes, causes no intraperitoneal complications, does not interfere with pregnancy or labor, is devoid of mortality and morbidity, and the final results of the operation show 95 per cent of successes which should be a very high recommendation.

Stem Pessary.—The stem pessary is up again for discussion after a peaceful slumber for a few years. This time Rawls (*Am. Jour. Obst. and Gynec.*, 1921, I, 499) has studied the end results in 117 cases in which a stem pessary was used for one reason or another in the Woman's Hospital of New York and has come to fairly definite conclusions. He states that the intra-uterine stem pessary has a limited field of usefulness in gynecology. It is applicable to 51.7 per cent of cases suffering from either dysmenorrhea, sterility, amenorrhea, ante-flexion of the uterus, stenosis of the cervix or congenital malformation of the uterus. As an operative measure it is applicable to 2.3 per cent of patients treated and 1.3 per cent of operations performed in a gyneco-logical ward. From its use sequelæ other than a temporary rise of temperature occur in from 17.6 per cent to 21.8 per cent of the cases, with a permanent morbidity of from 5.8 per cent to 9.8 per cent. As a therapeutic measure for dysmenorrhea there is improvement in 77.8 per cent with relief in 61.1 per cent, and for sterility there is relief in 23.4 per cent. The intra-uterine stem pessary gives as good end-results as other operative procedures for like indications, and from its use there is less primary invalidism and no more liability to sequelæ or morbidity. The stem pessary should never be used except in care-fully studied and selected cases, and then the minimum of sequelæ and morbidity with the maximum of result will be obtained, as evidenced by the careful study which the author has made.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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Gonococcus Types I.—HERMANIES (*Jour. Infect. Dis.*, 1921, xxviii, 133) performed absorption tests on 85 strains of gonococci. Forty-nine of these were isolated from cases of urethritis, vulvovaginitis and ophthalmia by growing on ascites agar under the conditions of partial tension. The remaining strains were obtained from other laboratories and included the "so-called Torrey strains." It was found that the 85 strains fell into six very distinct serological types, by far the largest number of strains belonging to either type I or II. The agglutinins of a serum produced in rabbits by one type could not be absorbed by any of the strains forming the other types no matter how highly the serum was diluted and how much of the growth was used. The Torrey strains from three laboratories established themselves as members of type I, while of the ten strains received from another laboratory only four fell into this type. The remaining six formed the C race of type II. Believing that it would lead to mere assumptions the author makes no attempt at all to explain the differences in types of the Torrey strains. In a second communication (*Jour. Infect. Dis.*, 1921, xxix, 11) the same author further studied, by similar methods, the thirty-six strains forming type II in the original investigation. It was noted that these thirty-six strains grouped themselves into four fairly distinct subtypes or races. By means of a genealogical table the author shows graphically the antigen complex of the four races of type II, along with their interrelationships and their probable path of evolution. "Judging from analogy the six distinct and separate gonococci types discussed in the previous paper may have sometimes been merely races of one or two types. In the course of evolution the common connecting bond was eliminated and the races became new species. As the process of variation is still going on, and will continue as long as their living conditions are secured, there is no limit to further differentiation. A single clear-cut type may, by molecular rearrangement, acquire new antigenic characteristics and split into several races. Finally, by elimination, these may be differentiated into species."

Studies on the Pneumonic Exudate.—Having previously demonstrated in cellular material from the pneumonic lung a proteolytic enzyme active in eroding the surface of Loeffler's blood serum at P_h 7.3 to 6.7, LORD and NYE (*Jour. Exper. Med.*, 1921, xxxiv, pp. 199, 201, 207 and 211), in a series of four articles, further investigated the physical and biological properties of enzyme. It was found that the

enzyme remains active after preservation in the ice-box mixed with chloroform and toluene for eighteen months as well as at incubator temperature before and after heating to 65° C. for one hour, although it is only slightly active at room temperature and inactive after heating at 75° C. for one hour. The activity persisted when the enzyme was mixed with concentrations of sodium chloride varying from normal to 32 times normal. No dialysis of the enzyme could be demonstrated. The bile in which type I pneumococci had been dissolved caused no erosion of the blood serum. The purulent sputum obtained during life and the exudate at autopsy from the later stages of lobar pneumonia commonly eroded the Loeffler blood serum, while the cellular material obtained from the pneumonic lung in an early stage of lobar pneumonia failed to erode the surface until washed with normal saline solution. Mixtures of washed pneumococcic cellular material and normal human serum failed to erode the blood serum when the amount of cellular material was less than one part of cells to approximately three parts of serum, whereas erosion did occur when the cellular material exceeded this amount in the ratio. The authors believe that these observations point to a local ferment-antiferment balance between the pneumonic exudate and the human serum *in vivo*. By washing blocks of pneumonic lung and testing the supernatant fluid with the homologous antipneumococcus serum it was found that in those cases of lobar pneumonia due to the fixed types of pneumococcus (I, II, III) a specific precipitin reaction was obtained. On the other hand specific agglutinins for the homologous pneumococcus were wanting or present only in small quantity in the pneumonic exudate. The authors conclude that the pneumonic lung contains a soluble substance inhibiting agglutination of the fixed types of pneumococci by the homologous antipneumococcus serum.

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Mononuclear Phagocytes of the Lung.—PERMAR (*Jour. Med. Res.*, 1920–21, xlii, 147) gives a more detailed account of the development of the mononuclear phagocyte of the lung. The same experimental method was followed as in his first paper on these cells—that is the administration of carmine powder in salt solution intratracheally and along with this the use of a vital stain to mark the endothelial cells. Pyrrhol blue and isamine blue were the dyes used. He found that the proliferating cell first enlarged in all dimensions, without greatly altering its shape, and at this stage it had a great avidity for the dye, which at this stage appears in granules in the cytoplasm. The cell then becomes polypoid in outline and retains only a narrow attachment to the vascular lining. Then by ameboid motion the cell passes outward through this point of attachment and comes to lie outside the vessel wall, and by further migration eventually reaches the air spaces of the lung. Its passage through the alveolar lining is effected in the same way as its original exit from the capillary wall. The free cells found in the alveoli were nearly always considerably larger than those just developed and in process of migration toward the air sacs. Mitosis was very difficult to make out in the preparations studied, but there was every evidence that the process described and photographed by Mallory in his work on the skin lesions in measles is identical with what goes on in the capillaries of the lung in response to the presence of

foreign particulate material. In the latter instance, however, the process is less active than that developing in an acute infection such as measles. Nothing could be adduced to show there is any specialization of the endothelium lining the capillaries. The proliferative reaction was localized to the capillaries in the vicinity of the irritating masses (carmine) lying in the alveoli. In no instance was there observed proliferative activity on the part of endothelium lining the lymphatics of the lung. The migration and fate of the mononuclear phagocytes of the lung formed the subject of the third paper of this series (PERMAR, *Jour. Med. Res.*, 1920–21, xlii, 209). This constituted a study of what was virtually an acute experimental anthracosis in which the red granules of carmine powder replaced the familiar black granules of airborne carbon. The vital stain was useful here, as in the preceding experiments, to enable the newly proliferated endothelial phagocytes to be identified. They could thus be traced to the air spaces, where they phagocyted the free carmine granules, and thence to the terminal lymphatics. It is of interest that the cells do not manifest the same indifference regarding their point of exit from the air spaces as they do to the point of entrance. They showed a tendency to pass into and through the somewhat heavier walls of the atria from which they have easy access to the finest pulmonary lymph channels. They were then traced along the lymphatics to the hilus, and were found in the lymph nodes here in small numbers as early as twenty-four hours after the introduction of carmine into the lung. It is worthy of note that the sudden flooding of the air sacs by the carmine powder in suspension is dealt with by the same mechanism as is the gradually insufflated carbon in anthracosis.

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

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Making Morbidity Reports Aid the Epidemiologist.—KELLY and STEVENS (*Public Health Reports*, 1921, xxxvi, 1219), of the California State Health Department, describe the method they use for securing the greatest aid from morbidity records furnished to the health officer. There is constructed for each county a cumulative curve showing the average of each disease for each geographical unit for the preceding five years, and a similar cumulative curve is plotted for each disease each week and at once shows where the current curve deviates from the average or normal. Index maps show by different colored

pins the prevalence above the five-year average and an incidence above the preceding year; again a separate map for each disease. Spot maps for each disease show all cases for any given quarter of the year. A card record is used for comparison over larger periods and gives the precise location where control measures are necessary.

Modern Steam Laundry Processes as a Means of Destroying Vermin.—PIERCE, HUTCHINSON and MOSCOWITZ (*Public Health Reports*, 1921, xxxvi, 710) studied this subject with special reference to the utility of laundry methods for the destruction of body lice, and conclude their report with the following recommendations: "In view of the foregoing tests there is proposed as a measure in disinsection of woolens a process which not only will disinsect but also will cleanse the garment and return it to the owner in good form, without undue shrinkage. This process consists of the following measures: (1a) In the washer run a current of live steam for fifteen minutes, revolving the cylinder every five minutes, and discharging water of condensation every five minutes. Remove the garments and shake until almost dry. This requires only a few shakes. (1b) Submerge in water at 165° F. for twenty minutes, without motion, except a few revolutions every five minutes; (2) wash fifteen minutes at 131° F. in heavy suds and light load; (3) rinse three times, three minutes each, at 131° F.; (4) extract; (5) run in tumbler for fifteen minutes, at a minimum of 140° F. Live steam (1a) or very hot soaking (1b) are advised only in cases in which there is no heated tumbler (5) available, or where the garments are suspected of being contaminated with very resistant spore-bearing bacteria. In other words, the usual laundry methods for the disinfection and disinfestation are recommended because of their added value of cleansing. There can be no doubt that the ordinary processes of the laundry will kill all lice and their eggs, and probably all insect life. It is proved that woolens can be treated at a temperature which will kill lice and bacteria, without undue shrinkage—that is 131° F. Washing in heavy suds, with motion; 165° F. soaking, without motion; live steam, without motion, and occasionally removing the water of condensation; or dry tumbling of wet garments; these do not cause undue shrinkage of woolens."

Botulism and Spoiled Canned Food.—The U. S. Public Health Service (*Public Health Reports*, 1921, xxxvi 751) reviews a fatality from eating home-canned stringbeans which were canned by an approved process but which were obviously unfit for consumption. A warning is given that danger is incurred by the use of canned goods that are not entirely sound.

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