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CLINICAL MEDICINE

I

TUESDAY CLINICS

AT THE JOHNS HOPKINS HOSPITAL

BY

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FOREWORD

AMERICAN medicine may well be proud of the advances made since the opening of the new century in the methods of clinical instruction in our medical schools. Formerly, except in a very few schools, the students were taught in the clinical subjects mainly through systematic lectures, quizzes on text-books, and amphitheater clinics. Occasionally a teacher made use of the British method of "ward walks," but, even then, the instruction was "didactic," the professor telling the student what was before him in the patient; the student passively received this knowledge, and though he might be permitted to verify parts of it, he played no personal part in the accumulation of the clinical data. At the present time practically all of our medical schools make use of an entirely different method, based upon the principle that "the way to learn is to do." The students, on entering upon their clinical studies, already trained in the methods and principles of the preclinical sciences, begin actually to *work with their teachers* in the study of the patients themselves. They become, in reality, assistants in the wards of the hospital, in the Out-patient Department, and in the clinical laboratories. They take histories, make physical examinations, perform various laboratory tests, and participate in the execution of therapeutic plans. The results of all of these activities, when adequately controlled and supplemented by hospital interns and by the junior and senior members of the teaching staff, can be made use of for the official hospital records. The students now really do a large part of the routine work of accumulating the facts that are made use of in diagnosis and therapy in the teaching hospitals, thus relieving the hospital physicians of burdens that would otherwise limit the amount of work of a higher order that they can do. The students themselves profit enormously by coming into direct contact with the objects of study. They secure an admirable training, under strict control, in the use of the apparatus and methods of clinical investigation through which the modern scientific physician seeks to unravel the mysteries of disease and to

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cure. Such a method of instruction presupposes large budgets for teaching hospitals, laboratory and library facilities, and paid scientific teaching clinicians who enthusiastically devote much time and energy to the work of the hospital, to the teaching of students, and to original research. These prerequisite conditions are rapidly being met and American clinical instruction has accordingly, during the past twenty-five years, undergone a truly wonderful development.

Movements toward reforms, however beneficial they may ultimately prove to be, are, nevertheless, prone, in the remedying of pre-existing conditions, to go to extremes. Those who conduct them are eager to better things, but they are apt, while clearing away rubbish, temporarily to discard some things that are valuable or even indispensable. Thus, the amphitheater clinic and the clinical lecture are at the present time looked upon askance, as remnants of a bygone period, scarcely desirable any longer, or not altogether reputable. In view of the excessive didacticism that prevailed formerly to the neglect of direct practical technical training, the attitude of suspicion assumed toward large clinics and the clinical lecturer is easily understandable. But is there not some danger of "throwing out the baby with the bath-water"? In securing all that we can of the new that is good, let us make sure also that we retain some of the best of what in method is old.

That, along with the newer forms of clinical instruction, the older forms of the amphitheater clinic and the clinical lecture, deserve places in the clinical curriculum, I feel sure. Properly co-ordinated with the practical technical training in the wards, dispensaries, and laboratories of the clinical institutes, these older forms of clinical teaching can be, in my opinion, of inestimable value both to the teachers and the taught. When properly used and not abused they afford desirable opportunities, on the one hand, for the excitation of interest and stimulation of the activities of the students, and, on the other, for the inspiration of gifted teachers, which cannot in any other way be made available.

Though the limits of this foreword preclude any full discussion of the matter of clinical teaching, it may be permissible for one who during the past eighteen years has been engaged in clinical teaching, making use of its several forms (large clinic, ward rounds, dispensary teaching, clinical laboratory teaching, recitations, conferences, seminars, use of text-books and handbooks, etc.), to mention some of the

advantages derivable from clinical lectures and amphitheater clinics that can be attended by a large number of students at one time. It is essential, of course, that the purpose of these methods of instruction be properly understood by both teacher and student, for many oppose them because they are unsuited to purposes that they should not be expected to fulfil. The main object of the amphitheater clinic should be the stimulation of the interest of a large number of students at one time in the formulation of clinical problems, in the methods of acquiring facts that will more clearly define the problems, in the arrangement of the data accumulated in ways that will suggest solutions of the problems, in the reasoning out of the bearings or implications of the various solutions that suggest themselves, in the comparison of these implications with the actual facts in a case, and in the methods of critical judgment that permit of arrival at a diagnosis and a plan of treatment. Now no text-book and no manual can accomplish this so well as can a clinic conducted by a living human personality. The influence of a respected living teacher in an amphitheater clinic can go farther toward arousing interest in clinical subjects, toward creating belief in the value of scientific methods of clinical work, toward emphasizing essential facts and problems, toward the inculcation of important principles, and toward bringing the student into active touch with the latest phases of a subject than can that of any inanimate encyclopedic handbook or text-book. As some one has said: "All faith is transmitted from person to person; lifeless objects do not create beliefs." The able clinical teacher, whose hearers respect him and have confidence in him, can in an amphitheater clinic impress students with the clinical realities, inspire them with belief in the importance of using the best methods, spur them to diligence and enthusiasm in work, and give them courage to strive to overcome obstacles in ways that will be of permanent influence in their lives. My own memories of the admirable clinics given by Alexander McPhedran, J. E. Graham, and I. E. Cameron in my student days at Toronto, and those of William Osler in Baltimore, of Friedrich Müller in Munich, of F. Kraus in Berlin, and of J. Déjerine in Paris during my postgraduate studies, are ineffaceable and precious. It is as true now as in Aristotle's time that "he who would learn must believe." To make students believe in the right things is a task in the performance of which the power of a text-book is far excelled by that of a living personality. *Vox viva docet.*

The philosopher Paulsen in his book on universities said that "if the lecture system were not necessary for the students, it would be necessary for the sake of the teachers." Clinics and clinical lectures demand careful preparation by the lecturer and compel him to relate the concrete facts of a case to his knowledge of medicine as a whole. They make a teacher more systematic, and they lead him to consider the philosophy of his subject, for a lecture necessitates the directing of the attention constantly toward the essential and the universal, and so acts as a healthy corrective of the narrowing tendencies of specialism. Moreover, when lecturing, a wise teacher can tell immediately through his personal contact with his pupils whether or not what he gives them is living, effective, fruitful, and true. Students are less patient than paper; they grow restless under the mediocre, the barren, the dead, the unreal, or the inane; they demand that vocal teaching be vital, effective, and true; they exert a silent but perceptible influence upon those who teach. And, as Paulsen further emphasized, the effectiveness of the lecture is enhanced to some extent by the larger audience; "the many eyes that look up at the lecturer give wings to his thoughts, and lend his words such force and animation as cannot be attained within a narrower circle." In all these ways the teacher himself benefits by resorting at times to a form of instruction that involves speaking before a large group of students.

Many of my students have from time to time made the request that reports of my clinics at the Johns Hopkins Hospital be published. The present volume has been prepared in response to these requests. No clinic was, of course, given in precisely the form in which it here appears. From notes made at the time by stenographers and by Dr. Caroline Latimer and from my own outlines that I have preserved I have tried to reproduce these clinics in a form that more or less closely approximates the form in which they were given. As one object of the clinics was to encourage the clinical clerks to participate in the function, the dialogue form has been maintained to some extent in their reproduction. If these clinics as published serve to recall to my former students some of the interesting hours that we have spent together and give them pleasure I shall feel well repaid for the work done. Should they appeal to a still wider audience, I shall be all the more glad.

To my colleagues on the staff of the hospital and to the many clinical and laboratory assistants who have done the work upon which

these clinics are based, I desire to express my deep thanks. To Miss R. F. Reik, who has charge of the medical records of the hospital, I am indebted for many favors; and for painstaking work in the preparation of the manuscript I am grateful to my secretaries, Miss B. O. Humpton and Miss Jane Humpton.

LEWELLYS F. BARKER.

BALTIMORE, MD.,
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INTRODUCTORY CLINIC WITH DISCUSSION OF PRINCIPLES

I. CARCINOMA OF THE LEFT BRONCHUS

A BRIEF DISCUSSION OF THE LOGIC AND PROCEDURE OF MODERN CLINICAL DIAGNOSIS, ILLUSTRATED BY THE STUDY OF A PATIENT COMPLAINING OF A CHRONIC COUGH WITH SPUTUM, LOSS OF WEIGHT AND WEAKNESS, AND PRESENTING SIGNS OF OBSTRUCTION OF THE LEFT MAIN BRONCHUS.

ON beginning this course of clinical lectures I would call your attention to the fact that their chief aim is to help you in the clinical diagnosis of internal diseases.

The duty of the internist, as it appears to me, in making a general diagnostic survey is to study the patient, a psycho-physical organism, as a whole. Adequately to make such a study one must himself be expert in applying the methods of the internist and must know enough about the methods of all the medical and surgical specialities to realize their value and the need of applying them in any given case. When necessary the internist should, in the study of special domains, obtain the co-operation of skilled examiners whose objective observations he can rely upon, and he should have learned how to estimate, in relation to the patient's whole state, the relative importance or unimportance of the reports that they make. After a complete diagnosis has been reached the therapy to be instituted should be comprehensively planned. The carrying out of the therapy usually requires considerable expenditure of time and often, in certain complex cases, division of the work among experts in specialized domains may be desirable. Our attention in the present course must be directed, however, especially to the subject of diagnosis rather than to that of therapy, and I propose to bring before you at the outset the principles that I think should be followed in making a general diagnostic study.*

The making of a diagnosis, whether by a general practitioner, by an internist, or by a specialist, involves the application of the methods

* In what follows I have made free use (without quotation marks) of many phrases, sentences, and paragraphs from my articles published earlier on this subject.

of reflective thought to the solution of a problem, and in diagnostic thought, as in reflective thought in general, there are five main steps. Professor Dewey has given us a good description of these steps in his little book entitled *How We Think*. First, we must feel a difficulty; second, we must collect data that will localize and more clearly define our problem; third, we must brood over the facts and allow suggestions of solution of the difficulty to occur to us; fourth, we must reason out the implications of these suggestions; and, lastly, we must compare the actual facts with the implications of the suggestions to see if identity with some one of them exists, for only when identity has been demonstrated dare we accept a suggestion of solution of the problem as valid. Thus, and thus only, can we arrive at safe conclusions.

The *first of these steps*, as I have said, is the *feeling of a diagnostic difficulty*—the recognition that we are confronted by a problematic situation. I deliberately emphasize this feeling of difficulty at the outset of a diagnostic study in order to arrest your attention, for I am convinced that one of the main causes of insufficient diagnosis is the failure to recognize how difficult it is to make a comprehensive diagnostic study, or even to realize that such a study in a given case with a marked presenting symptom involves any difficulty at all. To be a good diagnostician one should be endowed with a strong instinct of curiosity with its emotion of wonder and its accompanying impulse to approach and examine more closely the object that has excited it. One must not be satisfied with detecting some one feature that seems prominent, accepting it as an explanation. It is not so very long since a single symptom, generally that most complained of by the patient, sufficed for the making of a diagnosis by certain physicians. If a patient complained of headache, of itching, of a cough, or of a pain in the back no diagnostic perplexity was felt; the diagnosis—"headache," or "pruritus," or "cough," or "lumbago"—was made without further ado, and therapy was undertaken at once in accordance with some supposedly universal principle or dogma. Even now, I fear, men educated in modern medical schools sometimes fail to appreciate the extent of the investigation necessary for a complete diagnosis in obscure cases. I would have you always bear in mind that a condition appearing simple at first sight may, in reality, be so complex as to require a thorough-going analysis before the exact nature of the diagnostic problem can be satisfactorily discussed. Unless the feeling of

diagnostic difficulty to which I have referred be adequate, diagnostic investigation is all too prone to be detrimentally curtailed.

The *second step* toward the solution of a diagnostic problem is the *collection of data* that will make its formulation more precise. Suspension of judgment pending this investigation is essential for good diagnosis and, with this end in view, you are taught as students to follow some systematic plan of questioning and of examining the patient in order to locate and define your diagnostic problem. Suggestions of solution are apt to occur to your minds as you go along, but no matter how plausible they may be, you will do well not to yield assent to them too easily in the earlier stages of your diagnostic study, though you may make use of them as an aid in determining the directions in which the examination should be especially extended, or in deciding that in the particular case before you certain methods of collecting facts need not be applied. Although a systematic plan of studying a patient is desirable, students and physicians must take care that curiosity does not become fibrosed by too rigid adherence to a routine process of examination. This is one of the dangers to which the instinct is subject, and physicians must safeguard themselves against it, especially as they grow busier in practice.

For convenience, the methods of collecting the facts necessary to a general diagnostic survey may be considered under the following heads:

- (1) The anamnesis.
- (2) The general physical and psychical examination.
- (3) The application of certain laboratory tests.
- (4) x -Ray examinations.
- (5) Examinations in special domains.

“Anamnesis” is the term covering the data obtained from the patient or his friends concerning himself, his family, and his previous environment and experiences. It includes also the record of any abnormal sensations, moods, or acts that have been observed by the patient himself or by others, with the dates of their appearance and duration, as well as any modifications that have resulted from treatment. It is surprising how often a precise chronology of the appearance of the different symptoms in a given case throws light upon the diagnosis; I need only remind you of the temporal sequence of the symptoms of a tumor of the cerebellopontile angle to convince you of this fact. When asking about the presence or absence of symptoms

it is well to proceed systematically, including all the commoner symptoms that occur in different diseases of the several anatomical systems of the body, for by so doing we throw out a drag-net likely to enclose self-observed phenomena of the patient that may be serviceable in directing the further course of diagnostic observation. An experienced questioner can elicit such an anamnesis in a far shorter time than the tyro would think possible. If the anamnestic net be carefully drawn the information gathered by it will go far toward enabling the examiner to appraise the physical, psychological, and social status of the patient under study.

After the anamnesis has been carefully recorded the student may go on to the systematic objective examination of the patient's body and mind. This general physical and psychological examination, as at present conducted, includes so many details that its results should never be trusted to the memory. They ought to be written down or, preferably, dictated as the examiner proceeds. It is usually most convenient to begin by noting certain general points and then to examine the body by regions (head, neck, thorax, abdomen, pelvis, extremities). I prefer to have you begin the objective exploration by examining regions rather than systems, for at this stage of the diagnostic inquiry it is desirable to suppress, as far as possible, explicit diagnostic inferences and to confine the attention strictly to the accumulation of facts in a systematic way, without too much regard to their bearings upon the conclusions toward which the examination as a whole is directed. Examination by regions rather than by systems helps to maintain that preliminary suspension of judgment regarding the nature of the patient's ailment that I have referred to as desirable. The facts should be systematically and accurately accumulated before the attempt is made to summarize the data or to arrange them under the different anatomicophysiological systems to which they are related.

In the application of laboratory tests it is necessary to decide upon a minimum routine required in a general diagnostic survey, because the number of such tests that it is possible to make is legion. The blood, the sputum, if there be any, the contents of the stomach, the urine, and the feces ought to be examined in almost all cases, and it may often be desirable to make further special laboratory investigations (*e. g.*, certain metabolic studies). At present, owing to the rapid rise of the scientific laboratories and the deserved respect that they enjoy, there is a tendency to make as a routine many laboratory tests

that are wholly superfluous in practice. This is to be deprecated. Just here I would caution you, too, against expecting more help in clinical diagnosis than is really available from laboratory findings; it is a mistake often made by practitioners. Now and then the findings obtained by laboratory examiners are pathognomonic, but this is true only occasionally. In the majority of cases the results of such tests can be truly valued only in association with the results obtained by means of other methods of investigation. The same remark holds good in regard to the fourth way of collecting diagnostic data to which we may now turn, namely, the roentgenological method of examination.

The application of Roentgen rays to diagnosis has greatly enriched our clinical methodology. When x -ray examinations first came into clinical use they were employed chiefly by surgeons. Today internists make even greater use of them than do their surgical colleagues. Routine examinations intended to meet the needs of a general diagnostic study of any obscure case include: (1) roentgenograms of the paranasal sinuses; (2) roentgenograms of dead teeth and of unerupted teeth; (3) roentgenoscopic examinations of the thorax, aorta, heart, lungs, pleuræ, and mediastinum; and (4) roentgenoscopic examination of the gastro-intestinal tract after the ingestion of barium. Special x -ray examinations, if required, can be made afterward, according to indications derived from the anamnesis and from the general physical examination.

The last part of the general physical and psychical examination is the utilization of methods that have been devised for the examination of special domains. Specialists have greatly improved the means of clinical investigation of certain parts of the body. They have provided us with a variety of special instruments, some of which require a considerable experience for efficient use. The medical student should familiarize himself with as many of these special methods and tools as possible and should acquire skill in the application of at least some of them, particularly if he expects to become a general practitioner. There is no mystery about these special methods. Any one of average intelligence can learn to apply them. Nevertheless, there are so many of them that it has been found desirable and useful to have certain men specialize in certain fields, so that unusual skill and experience in the examination of special domains may be available. Thus the general practitioner or the general internist may, in obscure cases,

desire to elicit the co-operation of an ophthalmologist, a laryngologist, an otologist, a gynecologist, a urologist, an orthopedist, a neurologist, a psychiatrist, or a dentist in the making of his general diagnostic study. Generally speaking, such examinations by specialists, if necessary at all, may be required in a given case in only one or two anatomical or functional domains; but in certain obscure cases, *e. g.*, when chronic infection necessitates the search for hidden foci, or when the examiner lacks training in certain special methods, it may be necessary to call upon a number of experts for aid. No hard-and-fast rule can be laid down as to how extensive such a co-operative search should be. The main thing is that he who directs the general study shall be sensitive to the problems that confront him and know how to apply skill in attacking and solving them. In one case the taking of too much pains may be foolish; in another the taking of too little pains may be disastrous. What we call "common sense" is especially necessary here.

When the diagnostician is in possession of the data supplied by the anamnesis, the general physical and psychological examination, the laboratory tests, the *x*-ray examinations, and the indicated examinations in special domains, he is ready for the *third step* in the diagnostic process, namely, the *summarization and arrangement of the facts and the allowing of suggestions of solution of the diagnostic problem to occur to the mind*. At this stage it will be found useful, first, to summarize the positive findings (abnormal phenomena) in the order of their collection; second, to rearrange the more important findings, both positive and negative, according to systems, before allowing oneself to dwell upon their significance as regards the diagnosis to be made later on.

The first summary really consists in: (1) passing judgment upon the normality or abnormality of the phenomena recorded, and (2) jotting down the several abnormalities detected in the briefest possible form for preliminary survey. It is mainly of value as a control of the data that have been collected. Thus gathered in a small space, the eye can view these data as a whole, and the mind is enabled to grasp more easily the nature and extent of the diagnostic problem presented by the case. Moreover, the examiner can see at a glance whether, in the study so far carried out, any important method of examination indicated by the anamnesis or by the general physical examination has been omitted.

For rearranging the more important findings (both positive and negative) according to bodily systems the following form, printed on a single sheet, may be employed:

FORM FOR THE REARRANGEMENT OF THE DATA ACCORDING TO SYSTEMS

Name----- Age----- Body temperature-----
 Chief complaint -----
 Habits -----
 Infections -----
 Operations: Traumatata -----
 Respiratory apparatus -----
 Circulatory apparatus -----
 Blood and hematopoietic system -----
 Digestive apparatus -----
 Urine and urogenital apparatus -----
 Locomotor apparatus -----
 Nervous system and sense organs -----
 Metabolism and endocrine glands -----
 Remarks: -----

Of the data that are to be entered upon this sheet only important points both normal and abnormal should be included, and these should be recorded in the briefest possible form, symbols being made use of for the purpose of abbreviation. Under the heading *Circulatory apparatus*, for example, will be placed (1) such symptoms as palpitation and precordial pain, if they be present; (2) physical signs referring to the heart and pulse, and (3) records of blood-pressure, teleroentgenographic measurements, and electrocardiographic abnormalities. Under the heading *Metabolism and endocrine glands* will be entered deviations from normal weight in pounds or kilos; struma; eye signs of hyperthyroidism; hypertrichosis or hypotrichosis; sellar abnormalities; glycosuria, acetonuria, hyperglycemia, azotemia, uricemia, basal metabolism, etc. Under such an arrangement there may be some overlapping, since a symptom like dyspnea, for example, can be placed under the circulatory system, the respiratory system, and the metabolic system unless the preliminary survey has made it quite plain to which division it belongs in the given case. Important negative points should, let me emphasize, be included in this systematic summary as well as positive findings. This rearrangement of symptoms and signs under the headings of the different systems implies a series of particular judgments on the part of the examiner,

for his assignment of a given symptom or sign to a definite system must be based upon his knowledge or prior conviction as to the meaning of such a symptom. Thus a whole series of partial diagnostic judgments must necessarily precede the making of the larger, more comprehensive and final diagnostic conclusions.

When you have summarized your facts and rearranged them under systems you have completed only two of the three parts of the third step in the diagnostic survey. The third part of the third step is by far the most important. It consists in allowing suggestions of solution of the diagnostic problem to occur to the mind as it broods over the facts that have been accumulated, summarized, and rearranged. Thus far, in your study of the patient, observation and the making of a series of minor experiments have been your main task; the drawing of inferences has played but a small and subsidiary rôle, but you then reach the stage of inquiry, where permitting the entrance of suggestions into the mind, forming hypotheses, and drawing inferences should occupy your attention exclusively. For the time being observation and experimentation should stop and thinking and imagining should begin. You should let your mind play among the facts collected, and allow the things observed to carry you over to things that cannot be observed, but must be thought and imagined. From the content of your present experience, which you compare with your past experience and with that of others recorded in medical writings, are to issue suggestions that you, tentatively, entertain concerning things that your present experience does not hold. The situation will call up in your minds things that are beyond what your senses can contribute. You will leap from fact to fancy. But your leaping, to be profitable, should be most carefully directed. If you have cultivated both courage and caution as habits of mind, if you have attentively watched experienced clinicians work, if you have laid up a large store of medical knowledge, and if you have taken due care in the selection and arrangement of facts in the case, from the consideration of which the suggestions of solution of your problem are to arise, you may feel sure that you have done all that is possible, both directly and indirectly, to control your forward movement. This regulation of the conditions under which the function of suggestion is allowed to take place is in itself very important, though, as I shall point out, it is transcended in importance by the regulation

of conditions under which you should yield credence to conjectures of solution that occur to you.

When you consider a group of signs and symptoms arranged under a certain system, say the circulatory system, suggestions of meaning will at once begin to come to you if you have good minds that have been medically well trained. A thickened radial or an arcus senilis will suggest the existence of an atherosclerotic process; a thrill palpable over the apex of the heart will suggest mitral stenosis due to an earlier thrombo-endocarditis; a delirium cordis will make you think of atrial fibrillation; a tachycardia, without other signs of disease of the heart, will suggest hyperthyroidism; or a pronounced bradycardia will lead you to consider a disturbance of conduction in the atrio-ventricular bundle. In thinking over the various symptoms and signs recorded under each system heading you should cudgel your memory and imagination for varieties of possible meaning. It is desirable to harbor a sufficient number of possible explanatory suggestions and to record them as rivals to be pitted against each other in a contest for supremacy.

Everyone must work out his own method for exciting plausible ideas of solution of the diagnostic problem from the data collected. For myself, as an aid in the arousal of diagnostic suggestions, I have found it useful to think, first, of the possible pathological-physiological meaning; second, of the possible pathological-anatomical basis, and, third, of the possible etiologic and pathogenetic relationships of a given datum or group of data.

The occurrence of diagnostic suggestions varies greatly with the individual mind. To some minds valuable suggestions of meaning come easily and promptly; to others they come slowly and with difficulty. The number and range of ideas of explanation and causation that occur also vary enormously with different persons. Whereas the minds of some students seem barren, almost incapable of giving birth to an idea when exposed to the fertilizing influence of a group of facts, the minds of others under the same stimulus produce an offspring that is too prolific and too varied. What is wanted is neither superfluity nor paucity of suggestions, but rather a number and range of ideas that will suffice for the purpose in view, for the requirements of the case under study. Nor is this all. The quality of the suggestions aroused is even more important than the speed with which they come or the abundance and variety of the supply. Celerity is good, but it

will not in itself atone for either redundancy or superficiality. The ideal response of the mind—quick, balanced, deep—supplies substantial ideas of solution worthy of being tested systematically for validity.

In recording diagnostic suggestions that occur to the mind it will usually be found that not only one but two or even several of the bodily systems may be involved. In older patients, especially, this is common. The entire series of suggestions must, therefore, be surveyed in order that their relative importance for the understanding of the patient's case as a whole may be estimated and a final unified conclusion, with appropriate ordination of all the data collected, may be approached. You will try to arrange the suggestions and to combine them satisfactorily with reference to one another and with reference to the data upon which their validity depends. Throughout the whole investigation of the case you will keep in mind that a human being in difficulty has applied to you for help, and that the purpose of your inquiry is to determine what is wrong with him, in order that you may direct his action, when the totality of the circumstances is known and appreciated. This realization of the object of your diagnostic study will enforce orderliness of procedure and will impart steadiness and continuity to your thinking as it moves toward its goal.

Having recorded the various diagnostic suggestions that occur to you, the *fourth step* of the systematic inquiry is reached. This step involves the *elaboration by reasoning of the implications of each of the diagnostic suggestions* that you have recorded. You will say to yourself, "If this idea of mine is correct, the patient should present such and such symptoms and signs." No matter how plausible the suggestions that issue when the facts have been arranged and brooded over, you should defer final judgment until the suggested ideas have been traced to their full consequences and until their validity has been carefully tested. You must know all the bearings of a tentative suggestion before you can compare them with the facts that have been accumulated. Very often the deductive process by which the tentative general notion is elaborated will call to your mind particular data not included in your original collection, and will lead you to a supplementary extension of the facts by further observation and experiment. Methods not yet applied may have to be used in the search for new materials to support or to invalidate the provisional ideas that you

harbor. The several ideas thus elaborated may be considered as so many intellectual keys with which you may successively try to fit the lock. If none of them fit, you will either try some modification of one of them or look for still other keys for trial.

The *fifth and last step* of the diagnostic inquiry is the *arrival at diagnostic conclusions or beliefs by establishing identity between the facts accumulated regarding the patient and the deduced implications of one or more of your tentative diagnostic suggestions*. To verify a diagnostic inference after having found out what it implies you must recognize identity of the facts with its implications. Correspondence with what has been or can be observed is the only legitimate proof of a diagnostic hypothesis. You test an idea that you have tentatively entertained and rationally elaborated by ascertaining: first, whether its consequences can be identified with the conditions actually observable in the patient; and, second, whether the distinguishing criteria of the rival tentative ideas of diagnosis can be proved to be absent. In this mode of testing you may be obliged, as I said a moment ago, both to extend your observation of the patient and to make certain additional experiments that will permit of special observations strengthening or weakening your suppositional inference. In other words, after you have thought, you must again observe, in order to corroborate, or to refute, your tentative diagnostic conjectures. For example, in a patient obviously suffering from some form of infection, exhibiting a palpable spleen, fever, and leukopenia, the ideas "typhoid fever," "paratyphoid fever," and "malaria" may have occurred to you. On closer observation of the patient you may discover some previously overlooked rose spots; or you may find on the upper lip a slight herpes, previously passed over as insignificant; or on looking carefully through a stained smear of the blood you may find a single crescent-shaped æstivo-autumnal malarial parasite; or on making a culture from the blood in bile-bouillon, you may be able to grow a motile bacillus, and, on testing it, find that it is either the *Bacillus typhosus* or the *Bacillus paratyphosus*; or, after the application of many tests, you may still remain in doubt as to the cause of the infection in question, until, a week later, you find it possible to demonstrate in the blood the presence of specific agglutinins previously not demonstrable. Diagnostic suggestions, elaborated by reasoning, have, therefore, to be tried and tested until some one of them can be corroborated and verified. Then, and only then, should you permit

yourselves to accept an inference as valid, to conclude that it is correct, to believe in it.*

Let us now quickly apply the plan of diagnostic study just outlined to the case before us this morning. It is that of a private patient who has kindly consented to come down to the clinic, as his condition is one of unusual interest.

First, before the patient is brought in, let me give you an epitome of the *anamnesis* that has been recorded. He is a married man, fifty-four years old, who was admitted to the hospital just a month ago, complaining of "loss of strength and increasing emaciation." He also said that he was nervous, did he not?

RESIDENT PHYSICIAN: Yes, he stated that he felt "very nervous."

DR. BARKER: His family history contains some reference to pulmonary tuberculosis. Thus one of his sisters died of that disease at the age of thirty, but the patient was not with her during her illness and, therefore, was not exposed to infection. Three years ago one of his sons, twenty-two years of age, died of the same disease. The patient lived in the house with this son for about three months after the disease developed.

The patient himself has, on the whole, enjoyed good health. He was born, it is true, with a lateral strabismus of the left eye, had the commoner infectious diseases of childhood, and has been subject to occasional attacks of tonsillitis. Aside from constipation and an occasional attack of indigestion with eructations he states that there have been no disturbances of his digestive apparatus. During the ten years preceding 1915 he suffered from influenza nearly every year, the attacks being accompanied by fever and being severe enough to keep him in bed for several days at the time. These illnesses, together with the death of two near relatives from tuberculosis, are suggestive of a tuberculous infection in the patient, and I would like you to bear these facts in mind. At this early stage we must, however, keep our judgments in suspense and not allow ourselves to be influenced too much as regards the diagnosis toward which we shall gradually advance. But it does no harm to allow suggestions to bob up in our

* The student desiring a fuller description of the method of the general diagnostic survey may consult: (1) The rationale of clinical diagnosis, in Oxford Medicine (Christian and MacKenzie), New York, 1919, i, 619-685; (2) The general diagnostic study by the internist, New York Med. Jour., 1918, cviii, 489; 538; 577; and (3) Group diagnosis and group therapy, Wisconsin Med. Jour., Milwaukee, 1920, xix, 329.

minds even at this point, provided we make sure to reserve judgment. If a man cannot suspend judgment in the earlier stages of his diagnostic inquiries, he will be sure to make disastrous mistakes and will fail to make adequate studies.

The patient's personal hygiene has been faulty despite the fact that he has been a hard-working and successful business man. For fifteen years he smoked twenty cigars a day, though he gave up smoking altogether about seven months ago. For the same fifteen years he was in the habit, too, of drinking fifteen or twenty glasses of whisky every day, but he gave up drinking altogether six months ago, soon after he left off smoking. He admits three attacks of specific (neisserian) urethritis, the last one occurring ten years ago. He asserts that he has never had syphilis, though there has been abundant exposure to venereal infection.

This history of the patient's habits gives you some idea of the kind of man with whom we are dealing. He belongs to a strenuous, practical type that makes great demands upon life in all its forms and denies itself no variety of enjoyment. He has been interested in the achievement of concrete results rather than in the discovery of new facts or in the communication of ideas. Science and literature are very often of little interest to such a temperament. The man has sought relaxation in alcohol, tobacco, and sexual indulgence rather than through the cultivation of any scientific, literary, or artistic hobby. Such men often break down early.

According to the patient's own account, his present illness began eleven months ago with an attack of herpes, beginning with severe pain over the left eye. The pain radiated down the face and terminated in a feeling of "sledge-hammer blows on the chin." The next day "blisters" appeared over the entire left side of the tongue and the doctor told him that they were also present on the left side of the larynx. There was one vesicle on the conjunctiva of the left eye. Such a herpes, distributed mainly in the domain of the left N. trigeminus, is suggestive, as we now know, of some acute toxic infectious lesion of the gasserian ganglion of the same side. Though the patient regards this attack as the onset of his present illness, it is difficult to harmonize this view with subsequent developments.

He states that he was ill in bed for six weeks and then went to California to recuperate. While there he suffered from an attack of conjunctivitis, accompanied by a watery discharge from the nose and

violent sneezing spells. This attack occurred about seven months ago and the symptoms lasted for two or three weeks. As the season did not correspond to that of hay-fever, the attack is suggestive of a coryza vasomotoria.

A couple of months later, when he was at French Lick Springs, Indiana, he began to suffer from pains in the knees and in the left shoulder. He asserts that his hands and feet were always cold and that he had sensations of "pins and needles" in them. There was neither redness nor swelling of the joints at the time. He says that he suffered from a series of similar attacks not so severe, however, many years ago. The question that arises here, of course, is: Were these symptoms due to a low grade of arthritis or to a mild multiple neuritis? In considering this point the mind goes back, of course, to the history of fifteen or twenty whiskies a day, for, as you know, such a history would be entirely compatible with the occurrence of an alcoholic polyneuritis.

About four months ago the patient returned to his home in Canada, and soon afterward began to lose weight rapidly. At this time he suffered from pain in the interscapular region, relievable by hot applications. He had some cough, though not much more than he had had for some time. His former cough he had attributed to excessive smoking. But he now began to bring up a considerable amount of mucoid sputum. There was little or no shortness of breath. The development of cough with mucoid sputum takes the mind back at once, of course, to the history of recurring attacks of influenza and to the occurrence of cases of tuberculosis in the patient's family. The patient continued to lose weight. He now found that he was having a slight rise of body temperature every afternoon. He lost his appetite, had some nausea, and occasional vomiting. The cough now became paroxysmal. He was shortly obliged to go to bed, and soon after this his expectoration for several days was blood streaked. Note here the presence of low fever, the loss of appetite, the nausea, and the increase of cough, becoming paroxysmal, accompanied by blood-streaked sputum. What does this combination suggest to you?

STUDENT: It suggests the possibility of pulmonary tuberculosis.

DR. BARKER: Yes, very strongly. But, again, let us hold the suggestion strongly in leash until we accumulate further data.

For about two weeks after the patient was confined to bed he had night-sweats, and he states that at that time the ends of his fingers

were continually red. In the latter part of July (about three months ago) he coughed up a mass of some sort, about the size of the end of his thumb. For the past two months he has had neither nausea nor vomiting, but his appetite has been poor, he has eaten but little, and during this time he has lost about 30 pounds in weight. He now feels very weak. So much for the anamnesis. The patient may now be brought in.

We turn next to the *objective findings of the general examination*. Physical examination, made on admission to this hospital, revealed a lateral squint of the left eye, some herpetic scars on the left side of the face, some suspect teeth, slight nasal obstruction, slight enlargement of the retrocervical, supraclavicular, and axillary glands, slight pallor of the mucous membranes, hippocratic fingers, double arcus senilis, and palpable, but not calcified, radial arteries.

The points of chief interest in the physical examination are in the chest, and these we may check up in your presence. In form the thorax is broad and flat, and the lower margins are everted. On inspection, the left half of the thorax is less prominent than the right and expansion is markedly diminished on the left side, where distinct lagging is also observable during inspiration. Evidently less air enters the left lung than the right. Over the left apex, as far down as the second rib, the percussion note is shorter and higher pitched than on the right. Below the second rib the percussion note is slightly impaired. On percussion over the right lung the note is a little hyperresonant, except at the base behind. Vocal fremitus is slightly diminished over the whole left front and back and in the left axilla. On auscultation the breath sounds over the left apex are somewhat louder than normal, but over the whole left lung the breath sounds are distant. Over the right apex the breath sounds are loud. No râles can be distinguished in either lung, despite the fact that the patient has cough and sputum. This combination of diminished expansion, impaired percussion note over the front of the left lung, distant breathing, and the absence of râles throughout the left lung excites interest. We must keep in mind, too, the slight dulness over the right base behind.

There are no abnormal pulsations visible over the thorax. No abnormal shocks or thrills are palpable. There is no tracheal tug. The heart is not enlarged and there are no heart murmurs. The blood

pressure is low, 110 systolic and 78 diastolic. There is no marked retrosternal dullness. Broadbent's sign is not present.

The abdomen, on inspection, looks symmetrical. On palpation no abnormal masses can be felt and there is no abdominal tenderness.

The testicles are rather small. The prostate is somewhat enlarged and its consistence is not uniform.

The muscles of the legs look somewhat atrophic and some fibrillation has been observed. The reflexes are all present, both superficial and deep. The thenar and hypothenar eminences of the hands are not atrophic, nor do the muscles there show any fibrillation.

The patient's hands present a good example, however, of "hippocratic fingers." The ends of the fingers, you observe, are clubbed and the finger-nails are in-curved. There is also some cyanosis of the finger-tips. The clubbing and the cyanosis are so well marked that you can see them for yourselves, even at a distance.

When you see hippocratic fingers always keep in mind the fact that they are most frequently associated with chronic intrathoracic disease. One meets with them in emphysema with chronic bronchitis, in congenital disease of the heart, and in various other conditions. Along with the finger-tips the distal extremities of the long bones are sometimes involved, so that we can perceive changes in the wrists as well as in the hands. As a rule, the *x*-ray shows in such cases a thickening of the bone beneath the periosteum. The shafts of the radius and ulna, especially, often show subperiosteal deposits.

Marie, who first described this condition, called it "hypertrophic pulmonary osteo-arthropathy," but it is really an osteoperiostitis, probably of toxic origin (Sternberg). My colleague, Dr. Thayer, first called our attention here in this hospital many years ago to the full syndrome. You will find a paper on the subject by him in the Johns Hopkins Hospital Bulletin, and I advise you to read it in connection with this case.

Next, let us consider the *laboratory findings*. The urine, when tested, was found to contain albumin and numerous hyaline and granular casts. The specific gravity was 1028. A phthalein test showed 40 per cent. excreted in the first hour and 15 per cent. in the second, making a total of 55 per cent. (in spite of the existence of albuminuria and cylindruria).

An examination of the blood showed: R. B. C., 4,600,000; W. B. C., 13,080; Hb., 80 per cent.

The differential count of the white corpuscles showed: Polymorphonuclear neutrophils, 79.5 per cent.; eosinophils, 0.5 per cent.; basophils, 1.25 per cent.; small mononuclear cells, 8.25 per cent.; large mononuclears and transitional forms, 11.25 per cent.

Should you consider this a normal blood picture?

STUDENT: The differential count is not normal. There is an increase in the polymorphonuclears and a decrease in the small mononuclears. These changes are both relative and absolute.

DR. BARKER: Yes; such a polymorphonuclear leukocytosis is suggestive of the existence of a slight infection with some pyogenic organism.

And how would you say the record differs from the normal on the side of the red cells?

STUDENT: There is a slight decrease in the number of red cells and a reduction in the percentage of hemoglobin.

DR. BARKER: Yes, and another, later, examination showed a further decrease of the red cells, as well as a further increase of the white cell count. On this second examination there were only 4,000,000 red blood-cells, and the hemoglobin percentage had fallen to 68. The white cell count was 16,000. What is indicated by these counts?

STUDENT: A secondary anemia.

DR. BARKER: Yes, you are right; there is a secondary anemia, with a low color index, and it is becoming more marked.

Examination of the sputum showed the amount expectorated to be from 1 to 2 ounces a day. It was mucoid in character. Has any blood been observed in the sputum since the patient entered the hospital?

STUDENT: A little, occasionally.

DR. BARKER: How about tests for the presence of the tubercle bacillus in the sputum?

STUDENT: It has not been found.

DR. BARKER: With the patient's personal and family history, none of us would have been surprised, I think, if you had found tubercle bacilli in the sputum. Indeed, their absence thus far is, perhaps, a surprise. What was found on examination of the stomach contents after an Ewald test breakfast?

STUDENT: No free HCl was present. The total acid was 38 acidity per cent. There was an HCl deficit of 12 acidity per cent. A little bile was present.

DR. BARKER: Do you think the stomach of this patient secretes any HCl at all?

STUDENT: Yes, it must secrete some. Most of the combined acid must be HCl.

DR. BARKER: With what is the HCl combined?

STUDENT: I am afraid I don't know.

DR. BARKER: Does anyone know?

SEVERAL STUDENTS: With proteins.

DR. BARKER: Quite right. Now, if the stomach contents of this man contain 38 per cent. combined acid, but no free HCl, and if there is an HCl deficit of 12 acidity per cent., one begins to wonder why. In carcinoma ventriculi and also in chronic gastritis there may be a complete absence of free HCl. Achlorhydria gastrica and achylia gastrica may occur in association with many different conditions. Is there any reason to suppose that this patient may have had chronic gastritis?

STUDENT: I should think that the former free use of alcohol might cause chronic gastritis.

DR. BARKER: You are quite right; I think it probable that the chronic potatorium may be responsible.

Next, let us consider the reports of the *x*-ray examinations. Those of the gastro-intestinal tract show "a normal stomach, though the small intestines are displaced to the right. There is some stasis in the ileum, suggesting right-sided adhesions." An *x*-ray report of this description, demonstrating the presence of right ileal stasis and a right lower quadrant lesion (appendix or cecum), is very common in adults. It does not in itself, however, constitute sufficient reason for operation. Indeed, if any surgeon were to operate upon all of his patients that presented such a picture, his time would be largely occupied with them. As a matter of fact, surgical measures should not be employed in cases of this kind unless operation is indicated for some other reason.

The *x*-ray report on the teeth is negative as regards abscesses, though there is some pyorrhea alveolaris.

x-Rays of the paranasal sinuses show "clouding of both antra, especially of the left, probably due to old infection."

x-Ray plate of the lumbar spine shows "lipping of the edges of the vertebral bodies (sign of infectious arthritis?)."

The *x*-ray plates of the lungs show "a thickened pleura over the

entire left upper lobe with small areas of consolidation at the right base. There is no evidence of any mass in the mediastinum. The plates suggest the end-result of an acute pulmonary infection rather than a new growth."

Let me warn you not to expect more from the *x-ray* reports than they are capable of yielding. It is not the duty of the roentgenologist to make our clinical diagnoses for us. What we desire from him is an objective report of the deviations from the normal that he can observe. His findings when considered with all the other data are often very



Fig. 1.—Roentgenogram of the lung in a case of carcinoma of bronchi (see text).

helpful for diagnosis; by themselves they may be very misleading. They would be in this case, as you shall see.

We have now to consider the reports of *examinations made in certain special domains*. In the medical wards here the staff examine the various special domains themselves. If anything abnormal is found or suggested, we have the very great advantage of specialistic control. The staffs of the other services kindly co-operate in furnishing reports on their findings in the special domains when requested. In the present instance we have been aided by reports from the nose

and throat department and from the departments of neurology, urology, and orthopedics.

The hospital *laryngologist* reported "enlargement of the middle turbinate on the left; slight deviation of the nasal septum; history of suggestive sinus trouble, but nothing active found."

The *neurologist* reported that he found "no evidence of a definite neuritis" and that "the pain in the interscapular region was probably due to a slight arthritic condition in the spine." He suggested that "the trophic disturbance of the fingers might be regarded as secondary to the pulmonary condition. The reflexes are normal. There is no true degenerative muscular atrophy, though the muscles of the legs are quite small. There are no signs of multiple neuritis."

The *urologist* reported "a mild chronic prostatitis, with benign hypertrophy. At this man's age there is usually some chronic enlargement of the prostate, in fact, only a small proportion of men are free from it when they reach this time of life. The condition is not sufficiently marked here to indicate instrumental or surgical measures."

The *orthopedist* reported "nothing wrong except some slight stiffness of the spine, probably the result of arthritis."

(At this juncture the patient was permitted to return to his room, the discussion being continued in his absence.)

We have by now accumulated a whole series of data regarding the patient, and the *third stage* of the diagnostic procedure may next be entered upon. It includes *summarizing and arranging the data collected and then brooding over them in order that suggestions of solution of the diagnostic problem may occur to the mind.*

You will have noted that as we went along I jotted down, in abbreviated form on the blackboard here, the main positive points in the order of their collection, under the captions: (1) anamnesis, (2) general physical examination, (3) laboratory tests, (4) *x-ray* reports, and (5) examinations in special domains. This brief summary has its own place in the orderly procedure of diagnosis as we pass along the way from ignorance to knowledge. It enables us to see at a glance how far the study has progressed and how complete it has been as regards the search for clues. Diagnosis consists, on the whole, of a search, first, for clues, and, second, for the meaning of clues after they are found.

The rearrangement of these clues, according to anatomical-physiological systems, is the next task, for after reassembling the

data that we have collected under the different systems of the body, namely, the *respiratory*, the *circulatory*, the *blood-making*, the *digestive*, the *urogenital*, the *locomotor*, the *nervous*, the *metabolic and endocrine systems*, we shall be prepared to consider the data bearing upon each system in turn. In order to place these various findings under system headings you are compelled to make a whole series of small partial diagnostic judgments, but the judgments are so simple and so easily made that you scarcely realize that you are drawing inferences at all. I can assure you, however, that the drawing of these preliminary simple inferences that permit of the reclassification of the data accumulated under the several bodily systems goes far toward facilitating that part of the diagnostic procedure in which we brood over the facts in order that suggestions of solution of our diagnostic problem may emerge.

REARRANGEMENT OF THE DATA ACCORDING TO SYSTEMS

Name: S. R. G., married white man, age fifty-four, railroad contractor.

Complaints: Weakness; loss of weight; nervousness; cough; duration of illness about one year.

Family History: One sister and one son died of pulmonary tuberculosis.

Previous Infections: Commoner childhood diseases; recurring influenza annually for seven or eight years until three years ago; occasional tonsillitis; gonorrhea.

Operations—Traumata: None.

Habits and Temperament: Practical type rather than scientific or literary. Hard worker. Successful contractor. Potatorium (many whiskies daily) for fifteen years. Tabagism (20 cigars) for fifteen years. Abstinence from both alcohol and tobacco for past nine months.

Respiratory Apparatus: Cough for years; history of recurrent influenza; mucoid sputum recently, occasionally streaked with blood; pain in left back; night-sweats recently; diminished expansion and lagging of left chest; vocal fremitus lessened over left chest; dulness over left upper lobe, especially in front; slight dulness at both bases; absence of râles; roentgenograms show shadow over entire left upper lobe (thickened pleura?) and small shadows (consolidated areas?) at right base.

Enlarged left middle turbinate; deviated nasal septum; cloudy antrum (old infection); larynx negative. History of recurring tonsillitis. Sputum mucoid; has been blood streaked; contains pus-cells and epithelial cells; no tubercle bacilli demonstrable. Small "mass" coughed up a few weeks ago. Family history of pulmonary tuberculosis.

Circulatory Apparatus: Pulse 76; occasional tachycardia; radial arteries palpable, not calcified; well-marked bilateral arcus senilis; heart and aorta negative. No dyspnea. No edema. Blood-pressure: 110 systolic, 70 diastolic. Acrocyanosis (finger tips).

Blood and Hemopoietic Apparatus: R. B. C., 4,680,000 to 4,000,000; Hb. percentage, 80 to 68; W. B. C., 13,080 to 16,200. Differential count showed polymorphonuclear increase (79.5 to 81 per cent.) with relative decrease in small mono-

nuclears (8 to 9.5 per cent.); no eosinophilia. Platelets increased. Lymph-glands in both axillæ slightly enlarged. Spleen negative. Wassermann test negative.

Digestive Apparatus: History of pyorrhea alveolaris; gaseous eructations; some nausea and constipation. Physical examination negative. Stomach contents contain no free HCl; total acidity, 38 acidity per cent.; HCl deficit, 12 acidity per cent.; no occult blood; no Oppler-Boas bacilli. Feces negative. x-Rays show ileal stasis and suggest R. L. Q. adhesions. x-Rays of teeth negative.

Urogenital Apparatus: History of gonococcal urethritis (three attacks); testicles small; prostate enlarged and of variable consistency (inflammation and hypertrophy); no obstruction; no evidence of malignancy. Urine normal except for a trace of albumin and a few casts and white corpuscles. Phthalein output 55 per cent. in two hours.

Locomotor Apparatus: History of pains in knees, left shoulder, and spine; recent development of hippocratic fingers; musculature of legs of small volume with slight fibrillation (?); x-ray shows lipping of vertebral bodies in lumbar spine.

Nervous System: Complaint of "nervousness" and "weakness." History of herpes of left face and tongue at onset of present illness about one year ago. Some pains in knees and left shoulder, and "pins and needles" sensation in hands and feet five months ago (alcoholic neuritis (?), arthritis (?)). Physical examination of nervous system negative except for lateral strabismus of left eye (congenital) and vasomotor trophic changes in fingers (hippocratic fingers with acrocyanosis). Night-sweats. No mental anomalies detected. Potatorium. Tabagism. Extramarital sexual intercourse. Successful contractor.

Metabolism and Endocrine Systems: Undernutrition (30 pounds); average weight, 164 pounds; present weight, 120 pounds; lost 25 pounds during past two months. Slight fever daily during past three months. No glycosuria. No tophi. No endocrine anomalies.

It is now possible to consider as a group by itself the symptoms and signs that pertain to each of the several bodily systems. By quickly glancing over the data as thus rearranged you can form ideas (1) of the number of systems involved and (2) of the predominant involvement of certain of these systems. In this patient you observe that there is not a single system that presents no abnormality, and that the system predominantly affected would seem to be that of the respiratory apparatus. The diagnostic problems here are by no means simple, but they have been defined more clearly and localized more accurately by the fact accumulation. You may now let your imagination play among these several systemic groups of facts and see what explanatory suggestions occur to you. As you brood over these groups of data, memories of your earlier clinical observations, of your studies in the physiological and pathological departments, and of your reading will doubtless be aroused. Each group of facts will suggest ideas of functional disturbance (pathological physiology), of underlying

structural basis (pathological anatomy and histology), and of causation (etiology).

(To Student): Which part of the respiratory apparatus do you think is most markedly involved?

STUDENT: The lungs, and especially the left lung. The nose and throat are not normal, but the changes in them are of but relatively little importance for the patient.

DR. BARKER: Yes. There is obviously something very wrong with the function and structure of the lungs, and especially of the left lung. The patient has, therefore, a *pneumopathy*, and it is our task to determine its nature. The persistent cough, the mucoid blood-streaked sputum, the diminished volume of the left chest, the lagging and diminished expansion of the left chest on inspiration, the dulness on percussion over the left upper front of the chest with impairment of the note at both bases, the absence of râles on auscultation, the shadows in the lung areas in the roentgenograms, and the results of the microscopic examination of the sputum (presence of pus-cells and epithelial cells; absence of tubercle bacilli) are the clues. What do these clues mean? Please tell us some of the ideas that occur to you.

STUDENT: Less air than normal enters the left lung. The dulness in the left upper front points to increased density of some of the underlying tissues, either a thickened pleura or denser tissue in the left upper lobe due either to consolidation or to atelectasis. There must be some denser areas, too, in the right lower lobe behind, judging by the impairment of the percussion note and by the shadows in the roentgenogram.

DR. BARKER: Yes, those seem to me to be justifiable inferences. How do you account for the sputum that is expectorated?

STUDENT: There must be increased secretion of mucus by the bronchial mucous membrane. The pus-cells point to some inflammatory process. The blood streaks indicate minute hemorrhages. A bronchitis or a bronchopneumonic process could account for these characters.

DR. BARKER: If there is a bronchitis or a bronchopneumonia, why do you not hear râles over the chest?

STUDENT: It is a surprise to me that we do not hear râles. Perhaps they are present at times and absent at other times.

DR. BARKER: Yes. Or there might, perhaps, be a localized erosive

process in one bronchus. Why does so much less air enter the left lung?

STUDENT: It is rather hard to explain. There are probably some pleural adhesions, but not enough to account for the marked lagging and diminished expansion. There is no marked consolidation unless it be in the left upper front.

DR. BARKER: It is evident that something prevents proper expansion of the left lung as a whole. How does air enter the left lung?

STUDENT: When the muscles of inspiration contract, air rushes through the trachea and bronchi.

DR. BARKER: Is there any evidence that the muscular action on the left side of the thorax is defective?

STUDENT: No; the respiratory muscles appear to contract equally well on both sides.

DR. BARKER: What could prevent air going into the whole left lung then?

STUDENT: I suppose there could be some obstruction to the left main bronchus.

DR. BARKER: Yes. Anything compressing the left bronchus from without, say an aneurysm, a neoplasm, or an inflammatory mass; or anything narrowing the lumen within, say a foreign body, a cicatrix, or an intrabronchial growth, could account for it. That dulness in the left upper front might have something to do with it. Has any sign of aneurysm been made out?

STUDENT: There is no abnormal pulsation visible, nor is there any shock to be felt. There is no tracheal tug. The x-ray revealed no signs of aneurysm.

DR. BARKER: What is the technical name for the condition in which the flow of air through a bronchus is interfered with?

STUDENT: Bronchostenosis.

DR. BARKER: Are you of the opinion that a bronchostenosis exists here on the left side?

STUDENT: It seems to me very probable, though I do not understand why. The patient had recurring attacks of influenza and has a tuberculous family history. I suppose he could have had an ulcer in the bronchus and afterward a scar that contracted and narrowed the lumen.

DR. BARKER: That is certainly a suggestion that should be given due consideration. What could be other causes of a bronchostenosis?

STUDENT: A growth either inside or outside the bronchus, or a foreign body lodged in the bronchus. There is no history of the latter.

DR. BARKER: Persons occasionally have foreign bodies in the bronchi with no knowledge of how they got there. Sometimes they are demonstrable in roentgenograms. Sometimes they can be clearly seen on inspection through a bronchoscope.

STUDENT: Why shouldn't we make a bronchoscopic examination of this patient?

DR. BARKER: It can be done if necessary, though it requires special skill and is rather hard for the patient to bear. Perhaps we shall be able to arrive at a satisfactory diagnosis without bronchoscopy.

You spoke of a growth as a possible cause of bronchostenosis. What kind of a growth were you thinking of?

STUDENT: I meant any kind of a developing mass due to inflammation or to tumor. An inflammatory mass might be due to tuberculosis, syphilis, or some form of mycosis. A tumor mass might be inside or outside the bronchus; it might be a polyp, a cancer, a sarcoma, or other form of tumor.

DR. BARKER: There are changes in the right lower lobe, too. Do you regard them as connected with the process in the left lung?

STUDENT: They might be, or they might have a separate origin.

DR. BARKER: With this man's history of many attacks of recurring grip (whatever that was), it is easily conceivable that there are old lesions in the lungs that may be entirely unconnected with the main process under study.

Well, you have made a number of suggestions of possible explanation of the bronchostenosis and of the areas of consolidation in the left lung and at the right base.

As I recall them they include:

- (1) A foreign body in the bronchus with complicating inflammatory changes.
- (2) An inflammatory pneumopathy with either cicatricial contraction of the bronchus or compression without due to simple inflammation, to tuberculosis, to syphilis, or to pulmonary mycosis of some form.
- (3) A neoplastic pneumopathy, the neoplasm arising either in the bronchus or in the lung outside it (cancer, sarcoma, polyp, etc.).
- (4) Pressure on the left bronchus from a mediastinal mass (aneurysm, enlarged glands, neoplasm).

From the introductory remarks made at the beginning of the clinical lecture, what would you say was the best way to proceed to determine which, if any, of these possible diagnostic suggestions is the correct one?

STUDENT: We should see whether the facts of the case are consistent, or inconsistent, with the implications of the suggestions.

DR. BARKER: Yes. Recalling the fourth stage of the general diagnostic procedure, you should now ask yourself, If a foreign body is responsible for the bronchostenosis, what facts should be determinable? If syphilis is the cause, what symptoms and signs should be elicitable? If a neoplasm is the cause, what would its presence imply? And so on, through each of the several suggestions that have occurred to you. In other words, you should now elaborate by a process of deductive reasoning the full consequences of each diagnostic conjecture, in order that you may compare these consequences with the actual facts of the case, those already collected, or others that can still be gathered. To do this at all thoroughly, at the present stage of your medical studies, would require considerable leisure and application. Perhaps during the next few days, with the aid of text-books, monographs, and special articles in the medical journals to which I shall refer you, you will seize the opportunity to reason out carefully just what are the bearings and implications of each of the tentative ideas of diagnosis that you have mentioned. For such a process of deductive reasoning is desirable in order that the fifth and last stage of the diagnostic inquiry, that in which you test the validity of your suggestions by comparison of their implications with the facts available, corroborating or refuting them according as identity can or cannot be established, may be satisfactorily entered upon. I cannot emphasize too strongly the steps or stages involved in a systematic, diagnostic inquiry, even though the short time at our disposal this morning compels us unduly to abbreviate them. If we pass very rapidly from this point onward, you will understand that we are omitting during this hour much that is desirable and that would be helpful for a full consideration of the diagnosis.

The suggestion of obstruction of the left bronchus by a foreign body we may temporarily dismiss as improbable on account of (1) the negative history, (2) the slow development of the symptoms, and (3) the negative roentgenograms.

The suggestion of bronchostenosis due to inflammation may not

so easily be disposed of. Luetic inflammation is improbable owing to the negative Wassermann test. Tuberculous inflammation is a more plausible hypothesis, for (1) there is a family history of tuberculosis, (2) there is a personal history of recurring attacks of so-called grip, over many years, (3) there are distinctly abnormal physical signs in the lungs, (4) there has been a productive cough for some time, the sputum consisting chiefly of mucus, but containing also a little blood (slight hemoptysis), as well as pus-cells and epithelial cells, (4) the patient has had, and still has, a little fever, with tachycardia and weakness, (5) there have been night-sweats, and (6) recently the patient has lost rapidly in weight. But there are several points that militate strongly against the diagnosis of pulmonary tuberculosis. Thus, (1) the physical signs in the lungs do not favor it, for there are no râles, despite the extensive dulness, and a tuberculous involvement as extensive as one that would correspond to the dulness demonstrable in the left upper lobe would almost certainly be associated with definite signs in the right upper lobe also; furthermore, (2) the roentgenograms of the lungs do not reveal shadows suggestive of tuberculous lesions; and, finally, (3) despite the presence of mucopurulent sputum, no tubercle bacilli can be demonstrated in the sputum.

The suggestion of bronchostenosis depending upon a space-occupying mass in the mediastinum is not corroborated, for the physical signs and the x -ray examinations rule out aneurysm, enlarged glands, and any large retromanubrial neoplasm.

This leaves us still the suggestion of an intrabronchial neoplasm, or of an extrabronchial intrapulmonary neoplasm, compressing the left bronchus and causing stenosis. There are certain facts in the physical examination that strongly support this suggestion. Thus, (1) the signs of a bronchostenosis, combined with (2) dulness in the left upper front, (3) the absence of râles, and (4) a mucoid sputum containing pus and blood, favor the idea of neoplasm.

One of my colleagues, Dr. Louis Hamman, with whose special skill in pulmonary diagnosis you are all familiar, went over the patient carefully recently, and from the history and physical signs alone thought that the diagnosis of neoplasm was very probable, though he could not be certain without further data whether the neoplasm was primary or metastatic.

Bronchoscopy would, of course, help to differentiate an intrabronchial from an extrabronchial growth. We shall not have to resort

to it, however, for we have convincing evidence from another source that makes bronchoscopy unnecessary. This additional evidence I have thus far withheld from you, for it is evidence that is not always available in similar cases, and I desired to have you consider the case first without it.

Some three months ago the patient coughed up, he now tells us, a solid mass about the size of the end of his thumb, but the mass was not histologically examined. During his stay in the hospital here the patient expectorated another similar mass. This has been fixed, hardened, sectioned, stained, and microscopically examined in the pathological laboratory. The pathologist reports that "the tissue is neoplastic, consisting chiefly of stratified epithelium, characteristic of one form of primary carcinoma of the bronchus."

Through this fortuitous circumstance we are able, therefore, to arrive at an unequivocal diagnosis of the nature of the main lesion in the lung of our patient. That he has complicating lesions (inflammatory and, possibly, metastatic neoplastic) there can be no doubt. Some of the intrathoracic changes may be residues of his earlier non-tuberculous pulmonary infections.

We could, if we had the time, go through each of the several systems and discuss the other local diagnoses. But the hour is nearly up and we must hasten on. The results of our total diagnostic survey in the private ward may be summarized as follows:

1. Primary squamous-celled carcinoma of the left bronchus with bronchostenosis, atelectasis, and complicating pneumonia.
2. Undernutrition (30 pounds).
3. Secondary anemia with polymorphonuclear leukocytosis.
4. Chronic gastritis, with achlorhydria gastrica.
5. Pyorrhea alveolaris.
6. Hypertrophic osteopulmonary arthropathy.
7. Slight atherosclerosis (with thickened radials, arcus senilis, albuminuria, and cylindruria).
8. Chronic potatorium and chronic tabagism.
9. Chronic catarrh of the nose and paranasal sinuses.
10. Congenital strabismus.

The prognosis, owing to the existence of carcinoma of the bronchus, is, of course, grave. The other abnormalities obviously sink into relative insignificance when contrasted with the neoplasm.

During the coming week I hope that you will find time to read upon the subject of cancer of the bronchus and of the lungs. You might well begin by consulting your text-books of medicine and pathology. After that you will be interested in examining the larger special treatises on diseases of the respiratory apparatus, such as that of F. T. Lord, that of Norris and Landis, that of Powell, or that of A. Fränkel. Finally you should consult some of the special monographs and journal articles dealing specifically with this subject of bronchial carcinoma.

Primary carcinoma of the lungs or of the bronchi is a rare condition, though not so rare as it was formerly supposed to be. Edlavitch, writing in 1914, commented on the fact that it would *a priori* seem rather to be expected that an organ so rich in epithelial elements as the lung should not infrequently be the seat of epitheliomatous or carcinomatous change. Weller, in a careful paper on primary carcinoma of the larger bronchi, published in 1913, states that he found it present in 0.36 per cent. of all autopsies investigated by him, statistics that agree with those of Lavrinovitch, published four years later. Since the appearance of Weller's article the literature upon this subject has become increasingly important, partly by reason of the advance in intrathoracic surgery and partly on account of the introduction of radio-active substances into the treatment of malignant disease in general. Excellent papers have appeared in the medical periodicals of different countries, including South America and Japan.

In the case now before us the diagnostic findings point to a primary squamous-celled carcinoma of the left bronchus, with invasion of the lung. The two chief forms of bronchial carcinoma are: (1) the adenomatous cylindrical-celled type, (2) the squamous-celled type. Much can be said in favor of the theory that the malignant change in the latter type is associated with a metaplasia of the surface epithelium of the bronchus to the squamous-celled type. The signs over the left lung of our patient indicate bronchial stenosis and atelectasis, conditions that would account for the fact that the physical findings show greater dulness than might be expected from an examination of the *x*-ray plates. I cannot help thinking that the condition is complicated, however, by some subacute or chronic inflammation of the lungs due to some form of bacterial infection.

Examination of the patient's blood, you will recall, revealed a

secondary anemia and a polymorphonuclear leukocytosis. Packard, in a paper on primary malignant growths of the lung, published in 1917, states that leukocytosis was present in each of the 7 cases studied by him, the number of white blood-cells varying from 10,000 to 20,000 per cmm.

The diagnosis having been determined, we come, of course, to the matter of *treatment*. Early recognition and complete extirpation offer the only hope of permanent cure in cases of bronchial cancer. Intrathoracic surgery has advanced so rapidly within the last ten and especially the last five years that it is now possible to accomplish what, up to recently, would have been considered unjustifiable to attempt. The operative removal of one lobe of a lung or even of an entire lung has now become compatible with recovery. Willy Meyer stated in 1914 that, up to that date, 16 cases of pneumonectomy had been performed for bronchiectasis. Resection of the lung is technically a difficult procedure, but if the operative difficulties are skilfully overcome the prospects of success are good. Recent experimental investigations by Bernard and Mantoux have shown that the respiratory function can be carried on when the lung capacity is reduced to one-sixth of its normal volume. It seems reasonable to conclude, therefore, that no case of primary carcinoma of the bronchus or lung should be permitted to go on to its natural fatal issue when it is possible to save the patient by operative interference. In order that the operation may succeed in its purpose the diagnosis must be made very early, before extensive invasion or metastases have occurred, and this is only occasionally possible. The fact that the possibility of cure in certain instances exists, however, makes it very important that you should learn how to recognize carcinoma of the respiratory tract in its early stages. As Adler remarks, "The physician may meet it any day in his practice, among the young as well as among the old." If you will bear in mind that cough, accompanied by hemoptysis or by sputum resembling raspberry jelly, together with signs of pulmonary stenosis, but *without evidence of tuberculosis*, is strongly suggestive of carcinoma, you may be able to establish the existence of malignant disease soon enough to give your patient the chance of recovery now offered him by the recent advances in surgery.

The only other form of treatment that offers any prospect of either temporary or permanent relief in such cases is the use of *x-rays*,

radium, thorium, or mesothorium. These have all been tried in the treatment of malignant disease in general, but, so far as such disease in the lungs or bronchi is concerned, the general opinion seems to be that it is too soon to pass judgment as to their efficacy. I am myself very incredulous of the benefit to be thus derived.

For the patient you have seen this morning it is obviously too late to apply radiotherapeutic measures or to suggest operative interference. Nothing can be done for this man except to prevent severe pain and to make him as comfortable as possible up to the end. For the relief of pain, should it be severe, Schlesinger's solution (scopolamin. hydrobrom., 0.0025; morphin mur., 0.2; dionin, 0.4; aq. destill. ad 10) is valuable in these cases of neoplasm. Small doses (5 to 7 minims subcutaneously) night and morning will keep the patient comfortable, and it is often not necessary to increase the amount (unlike our experience with the use of plain morphin). It is certainly our duty to make the end of human beings unfortunate enough to develop incurable cancer as euthanasic as possible.

[*Subsequent History of the Case.*—The patient grew steadily weaker and the emaciation increased rapidly. The sputum continued to contain many fragments of necrotic neoplasm and a little blood. Further microscopic examinations of the sputum did not reveal any tubercle bacilli. Death occurred within four weeks after the clinic was held. The family declined to grant permission for a postmortem examination.]

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INFECTIOUS DISEASES

II. ACUTE RHEUMATIC FEVER AND SOME OF ITS COMPLICATIONS

CASE I. A BOY OF TWELVE, WITH POLYARTHRITIS, THROMBO-ENDOCARDITIS CAUSING MITRAL STENOSIS AND MITRAL INSUFFICIENCY, MANY SUBCUTANEOUS FIBROID NODULES, AND SLIGHT CHOREATIC DISTURBANCE OF MOTILITY.

CASE II. A BOY OF THIRTEEN, WITH RECURRING TONSILLITIS, RECURRING POLYARTHRITIS, RECURRING CHOREA, AND MITRAL ENDOCARDITIS.

DR. BARKER: We have before us today 2 patients who are suffering from the same disease, a very common disease, and at the same time one of the most important with which the practitioner of medicine comes in contact. Dr. Thomas McCrae, on analyzing the clinical material at the Johns Hopkins Hospital, found that for the fifteen years ending in 1904 there was an average of 24 admissions per year for this disease. Over half of these patients entered the hospital between January and April. You cannot be too familiar with the disease. The 2 cases that we shall deal with today are interesting because they both illustrate not only the disease itself, but some of its most noteworthy complications.

The first patient, Joseph O'G., twelve years of age, entered the hospital on April 19th, complaining of "rheumatism."

His *family history* is negative except that his mother's health failed shortly after her marriage, and she is said to have died of syphilis shortly after the birth of our patient, who weighed only 1½ pounds when born. He himself gained rapidly after birth.

Turning to his *personal history*, we find that in his early childhood he had pertussis, mumps, measles, and chickenpox. He gives a history of having suffered from several severe sore throats, but it seems doubtful whether he ever had an outspoken tonsillitis. In early childhood he had also several attacks of bilateral earache, but there is, otherwise, no definite history of otitis media or of mastoiditis,

nor has there ever been any discharge from the ears. He has frequent frontal headaches and often has nosebleed. He is also subject to attacks of dizziness without apparent cause. Of late he has been troubled with dyspnea and showed signs of it on admission. After any indiscretion in diet he suffers from nausea, vomiting, and abdominal pain, with occasional diarrhea. His highest weight was 80 pounds and his present weight is 67 pounds, so that he is now 13 pounds below his maximal weight.

The *present illness* began four months ago with a "cold in the head," without discomfort in the throat. After a day or two the patient began, he says, to have severe pain in all his joints, including his spine. He became delirious and does not remember the details of his illness, except that he had severe "pains all over." This is an interesting sequence: cold in the head, followed by joint pains, fever, and delirium. The patient was ill for three or four weeks and then began to recover, getting strong enough to go back to school, though he still had occasional "pain in his right leg and hip." He did not feel well, however, and suffered from constant headache, with shooting pains in his legs. Four weeks ago he had a chill and went to bed with pain in his elbows, followed by pain in his hips and knees. He was restless and very weak. You will notice that this is the history of recurrent attacks of infection accompanied with joint pains. This second attack lasted two weeks, during which time he was in bed with pain and stiffness in all his joints and in his spine. He was brought to the hospital because he did not improve.

On admission to the ward there was slight stiffness of the joints, with dyspnea on exertion, weakness, and anorexia. There was no heat, redness, or swelling of the joints, however, at that time.

Physical examination showed a poorly nourished boy, having a blotchy erythema of the neck, chest, and legs. The mucous membranes were pale and the tongue was slightly coated. The teeth were in good condition. The tonsils were deeply situated, ragged, and adherent, but not at the time injected. Slightly enlarged lymph-glands could be felt at the angles of the jaws. The lungs were clear on percussion and auscultation. Examination of the heart showed a heaving precordial area and a diastolic thrill was palpable over the apex. There was no Broadbent sign. The heart moved about 2 cm. on change of position. The relative cardiac dulness extended 8 cm.

to the left and $3\frac{1}{2}$ cm. to the right. The second sound was followed by a rumble, which disappeared before the first sound was heard. A loud systolic murmur was audible at the apex and was transmitted to the axilla and to the back. The second sound was not accompanied by a murmur, but was followed by the rumble already mentioned. The pulmonary second sound was accentuated. The pulse was regular in force and rhythm. The blood-pressure measurements were 85 systolic and 55 diastolic. There were thus evidently signs of a double mitral lesion, that is, of mitral stenosis and of mitral insufficiency, present. Examination of the extremities showed them to be normal except for tenderness on pressure over the elbows and the shoulders and for some nodules to which I shall soon refer. The reflexes were normal, but there was a slight disturbance of motility, which I shall dwell on later.

The hemoglobin on admission was 64 per cent.; the count of the red blood corpuscles 5,472,000; of the white blood corpuscles 11,400; in the differential count the polymorphonuclear percentage was 60.

An interesting point in this case is the presence of small nodules beneath the skin in several localities. Those first to be observed were discovered in the flexor tendons of the wrists; they appeared about a week after the patient was admitted. These nodules are small, firm, tender, about the size of a split pea, and are not in the skin or in the subcutaneous tissue just beneath the skin, but are attached to the tendons. The day after they were first observed some more made their appearance, and on April 22d, six days later, a large number developed on the left side of the head.

On April 24th the patient's temperature rose to 104° F., and he had a chill, accompanied by aching of the joints. Since then he has had three or four similar attacks, each of them presenting the characteristics of chills and fever, with stiffness and soreness of the joints accompanied by an increase in the number of nodules in different parts of the body.

Most of the nodules now present are scattered over the vertex of the skull and in the posterior triangle of the neck. Some are also to be found on both elbows, on the flexor surfaces of the wrists, and on the backs of the hands; a few can be felt over the tip of the acromion process on both sides, as well as on the tendons of the medial hamstring muscles. One or two can also be seen and felt on the dorsum of each foot.

(To the Student): There has plainly been an infection in this patient. What would you take that infection to be?

STUDENT: Acute rheumatic fever.

DR. BARKER: Yes. Acute rheumatic fever involving the joints and also the endocardium; in other words, a rheumatic polyarthritis and endocarditis injuring the mitral valve, and causing mitral insufficiency and stenosis of the mitral orifice. In this form of infection, endocarditis, once established, has a greater tendency to become a chronic process than has the associated arthritis. What do you think is the cause of this condition?

STUDENT: Some infective micro-organism, but I do not know what it is.

DR. BARKER: Yes, the facts (1) that the disease comes on with a chill, followed by fever and profuse sweating; (2) that it is prevalent at certain seasons of the year, at certain periods of life and in epidemics with irregular periodicity; (3) that it gives rise to a leukocytosis and anemia; (4) that it causes acute inflammations of synovial and serous membranes; (5) that it tends to relapse; and, finally, (6) that it responds to a definite form of treatment, namely, salicylic acid therapy, all favor the theory of an infection as its cause, and I cannot help but believe that we are dealing with a specific infectious agent. The organism causing it, however, is not yet known with certainty.

The infectious theory of rheumatism was first emphasized by Mantle in 1887. He was convinced, he said, that rheumatism was produced through the agency of a bacterium, which, he thought, entered the system in most cases through the lymphatic structures of the tonsils. The morbid anatomy of the disease was chiefly confined to the lymphatic system, the serous membranes being affected in preference to other structures. Mantle examined serum taken from the joints of rheumatic patients, and found, as he believed, two kinds of bacteria, namely, a micrococcus and a small bacillus.

Since Mantle's paper a good many theories have been advanced as to the nature of the infectious agent concerned in acute articular rheumatism. Sahli believed the disease to be an attenuated septicemia due to either the streptococcus or the staphylococcus. The French school of observers regarded it as due to a bacillary infection, and some of the French investigators have reported finding a bacillus in the joints or in the blood. But the theory that has had the greatest vogue in recent years is that held by the English physicians,

Poynton and Paine (and also by Walker, Beattie, and others), who believe the disease to be caused by a bacterium called by them the *Diplococcus rheumaticus*. This micro-organism, they found, grew best in the local lesions accompanying the disease. It is often present, they assert, in the blood, but does not thrive there, a fact that, Poynton considers, is not strange. It would be much stranger, he says, if one had only to take a minute quantity of blood from a finger or a vein in order to show the infective agent, or if the micro-organism dropped from a synovial fluid "like pepper from a pepper-pot." "If that were the case," Poynton remarks, "rheumatic fever would indeed be a terrible malady." Experimental investigation into the nature of this organism was carried on independently by Shaw (Jour. Path. and Bacteriol., 1903), who asserted that he produced, by injecting it, the lesions of acute rheumatism in rabbits and in monkeys.

Poynton's view of the etiology of acute rheumatic fever was supported to a certain extent by Rosenow, who asserted that he found in acute rheumatism a coccus that is closely related to the *Streptococcus viridans*. He believed that this organism can be transformed into a typical hemolytic streptococcus, on the one hand, and into a pneumococcus on the other. When Dr. Rosenow was doing this work in Chicago I asked Dr. Bloomfield, of our staff, to go there for the express purpose of working in his laboratory and under his direction for a short time in order to acquire his technic. Since Dr. Bloomfield's return this technic has been applied here to the study of infection in acute rheumatism, and a good many cultures have been made—with what result, may I ask, Dr. Bloomfield?

DR. BLOOMFIELD: We have grown organisms from the blood in some cases, but recently we have had a number of cases in which we got entirely negative cultures. I could hardly say that Dr. Rosenow's results have been confirmed in their entirety here.

DR. BARKER: It is an interesting fact that one does, not infrequently, get a positive culture of some sort of bacterium from the blood in cases of acute rheumatic polyarthritis, but the cultures are not always of the same micro-organism, and many cultures are negative. Dr. Rufus I. Cole, while working in this hospital, repeatedly produced endocarditis and arthritis experimentally in rabbits with strains of streptococci from various sources, but this does not prove that acute rheumatic fever is due to streptococci. Recently Swift and Kinsella have published the results of a series of bacteriologic

studies on acute rheumatic fever, showing, they assert, that the etiological relationship between streptococci and rheumatic fever has not been definitely proved. They are of the opinion that if a streptococcus is really the etiologic agent in acute rheumatism the various members of the viridans group are responsible, a fact that they assert is established by their cultural and immunological studies. They emphasize that no one member of the group can properly be called the *Streptococcus rheumaticus*. It is quite possible, as Dr. Osler has suggested, that the streptococci so often found in acute rheumatic fever "may simply indicate the presence of secondary invaders, such as occur in scarlet fever and smallpox."

I myself have felt that this disease—I mean true acute rheumatic fever, as distinguished from other forms of acute infectious arthritis—must be due to some one specific virus. The disease is so characteristic in its manifestations—(1) in its relations to tonsillitis, to endocarditis, and to chorea; (2) in its response to the salicylates; and (3) in the manner in which the joints clear up without residual lesions—that I cannot but feel that we are dealing with a specific infectious disease due to a single virus, as yet not seen or isolated. This view is supported by the tendency to epidemic prevalence (Newsholme). The virus in question gives rise to a "viremia" with metastatic infection of the joints, and sometimes to other local inflammatory processes (thrombo-endocarditis simplex, myocarditis, pericarditis, pleuritis, subcutaneous fibroid nodules, and cerebritis with chorea). It is better, I think, not to commit ourselves too definitely concerning the etiology of this remarkable disease until more positive knowledge concerning it has been acquired.

This particular patient has a very interesting complication of his acute rheumatic fever in addition to the endocarditis, namely, multiple subcutaneous fibroid nodules, but before I go on to speak of the nodules I want to say a word regarding the occurrence, dangers, and management of cases of endocarditis of this kind.

Acute simple thrombo-endocarditis is the commonest complication of acute rheumatic fever, especially in the young, and it is by far the most frequent cause of chronic valvular cardiopathy. The mitral valves are most often involved, though not infrequently the cusps of the aortic valves are also diseased. It is rather rare, however, to have the aortic valves involved without simultaneous involvement of the mitral. In many cases there is a pancarditis, the

disease causing inflammation not only of the endocardium but also of the myocardium and the pericardium at the same time. In some of the worst cases of rheumatic fever in children, where the endocardium, the pericardium, and the myocardium are all affected, acute dilatation of the heart occurs and the apex-beat moves right out into the axilla. When this happens there may be *exitus* during the attack from the cardiac complication. Poynton cites 59 fatal cases occurring during a first attack in patients under twelve years of age. Even when the patient recovers the most serious consequences are to be apprehended if the heart has been involved. A mild endocarditis, such as we see in this boy, may not be so serious if due care be taken, but in severe cases, such as I have just described, we may see a youth between ten and twenty mutilated and crippled for life. In a considerable number of the cases where valvular heart disease makes itself evident toward middle life it is due, originally, to infection of the endocardium by the virus of acute rheumatic fever from which the patient suffered in childhood or youth. In many cases, too, the myocardial invasion by the rheumatic virus in childhood is portentous. Though the patient seems to recover, when he reaches thirty, forty, or fifty years of age, the late results may become manifest, impairing health and activity and often shortening life. Of course, there are many other causes of endocarditis and of myocarditis, but it is not too much to say that, in the majority of instances, infection by the rheumatic virus during early life is the responsible agent. Hence it is obvious that, as Poynton says, "If we could learn how to prevent the infection, or, if that proves impossible, the cardiac complications resulting from it, we should confer a boon on mankind." In a large proportion of all cases the heart is more or less disabled in the first seizure; hence, when this disease occurs in a child, it is one of the most serious misfortunes that can befall it. We must see to it that we prevent the occurrence of acute rheumatic fever and of rheumatic endocarditis as often as we can.

It is not necessary that the initial attack of rheumatism should be a severe one in order to lay the foundation of chronic valvular heart disease. The slighter forms of infection, such as we see today in these two boys, are not to be lightly treated, since the results of even the mildest endocarditis may eventually incapacitate the patient in later life. In caring for a case of acute rheumatism we must never lose sight of the fact that an attack of the disease so slight as to

escape any but the closest observation may, nevertheless, be the cause of serious heart disease later on. So-called "growing pains" and mild unexplained pyrexias in childhood should be looked upon with suspicion, for they are often mild attacks of "rheumatism" due to the same mysterious virus that causes acute rheumatic fever.

Mitral insufficiency without myocardial lesion is not necessarily a serious handicap, but mitral stenosis, if at all severe, is an especially lamentable complication, since the stenosis is liable gradually to increase, the opening between the mitral valves constantly tending to diminish in size. And, as Dr. Thomas Lewis has observed, "mitral stenosis and auricular fibrillation are bosom companions." Many of the cases of atrial fibrillation that we observe in older people are associated with mitral stenosis. For these reasons it is all important, in the treatment of rheumatic fever, to prevent, if we can, cardiac complications. Every effort should be made to secure a speedy cure of acute articular rheumatism in order that the infection may die out before the heart is attacked by it.

One essential in the treatment of acute articular rheumatism, whether it be mild or severe, as well as the best means of preventing endocarditis, is rest. Rest is, in fact, imperative, and when I say *rest*, I mean *rest in bed* for a prolonged period. When there has been a pancarditis with acute dilatation of the heart the child should be kept in bed for months or even for a year. Some physicians advise even two years, though anyone who has tried to keep a small boy in bed for any length of time will be able to form some idea of the difficulties involved in such a scheme of treatment. In not a few cases the situation is complicated by the difficulty of convincing the parents or guardians of a child that prolonged rest, which occasions them more or less trouble or inconvenience, is of vital importance. As Lowenburg remarked during a discussion on rheumatic fever before the New York Academy of Medicine, "Rest in bed is the most important part of treatment, but it is sometimes necessary to treat the parents as well as the child."

Even when all possible care has been exercised in a case of rheumatic endocarditis the heart is apt to be left in a more or less crippled condition. In the mildest cases the patient ought not to be allowed to get up, as he frequently is permitted, if not encouraged to do, a few days after the fever subsides. He should stay warm and at rest in bed for weeks, and, in my opinion, for at least two months. An-

other important factor in treatment is the removal of any focal infection, such as infected tonsils, adenoid growths, infected teeth, that may serve as a portal of entry for the rheumatic virus.

I desire now to say a few words in regard to the nodules that present an interesting complication of the disease in this particular case. They are so plain that I think you can see them, even from a distance, as a row of small, firm, tender nodules, resembling a row of beads, and extending all along the tendon of the *M. flexor sublimis digitorum*. They are not connected with the skin, nor are they in the subcutaneous tissue. It is easier, perhaps, to feel than to see them, but if the skin be drawn a little tightly and the light thrown obliquely, it is possible to bring them exquisitely into view. Here, again, you see them grouped on the lateral side of the left elbow. (To patient): Are these lumps sore? He says that they are a little sore when I press upon them. Over the right elbow there is a remarkable group of the nodules. Evidently they occur in the fascia, on tendons, or else in the periosteum. As a rule, they are not present in the skin or in the subcutaneous tissue itself. In this case there are a number of them on the head. I cannot feel them beneath the scalp on the right side, but on the left they are plainly to be felt under the skin over the frontal bone, though they are most abundant over the posterior part of the parietal bone. They seem to be about the size of split peas and they feel as hard as buckshot. Here is quite a large one connected with the bone over the tip of the acromion process. How about his ankles? Are there any nodules about the malleoli?

STUDENT: There were some there, but they were small.

DR. BARKER: One interesting thing about these nodules is that they may appear and reach full development within a very short period. You may sometimes observe successive crops of them within a few days of each other. Another interesting point is that they may disappear as quickly as they came, though they are often present for weeks or months. Dr. T. B. Futcher, of this clinic, has made an especial study of these peculiar "rheumatic nodules." Formerly they were spoken of as subcutaneous fibroid nodules, but they do not consist of fully developed fibrous tissue; they are little masses that resemble, histologically, the structure of granulation tissue. They contain fibroblasts and peculiar small round cells; the blood-vessels about them are dilated; sometimes areas of necrosis occur in

them. In this particular case their histology has not yet been investigated (see below).

As to the frequency with which these rheumatic nodules are found, let me read you what Dr. Osler said upon the subject in 1894:

"I am of the belief that rheumatic fever is not nearly so frequent in Philadelphia and Baltimore as in London. Here, at any rate, some of the most striking rheumatic manifestations are conspicuous by their absence; for instance, a case of subcutaneous fibroid nodules is a great rarity. In my five years' service at the Infirmary for Diseases of the Nervous System not a single instance was seen. Since 1881, when I saw cases at the Great Ormond Street Hospital, I have been in the habit of looking for them in a case of rheumatism as systematically as I examine into the condition of the heart. I have seen a larger number of instances in adults than in children. The matter of their rarity was a subject of comment among the members of the Pediatric Society at the Boston meeting in 1892. They may exist independently of acute arthritis or even of any rheumatic manifestations. I have had in my wards for three years a girl with chronic valve disease—mitral and tricuspid—who has never had, so far as can be ascertained, any signs of rheumatism. During the past eighteen months she has developed many subcutaneous fibroid nodules about the elbows and hands and along the tendons in various places. As I write (June 30, 1894) there has been admitted to the wards the first case which I have seen in this country with the combination of chorea, arthritis, subcutaneous fibroid nodules, and mitral endocarditis. The only case which, so far as I know, has been reported in the United States with this combination is the remarkable case by C. H. Brown (*Jour. Nerv. and Ment. Dis.*, 1893)." In an addendum to these remarks Dr. Osler added that, so far as he knew, the first case reported of subcutaneous nodules in acute rheumatism was one in his own clinic at the University Hospital, Philadelphia, recorded by Dr. J. K. Mitchell (*Univ. Med. Mag.*, vol. 1).

It is obvious that if Dr. Osler could write in this manner about these nodules, they were not of common occurrence in London and were still more uncommon in Philadelphia and Baltimore. Since he called attention to them in 1894 we have had a good many cases in this hospital; nevertheless, they are undoubtedly rare, and I advise you to avail yourselves of the opportunity to feel them as you pass

out of the amphitheater today. They are a little tender, so you should be careful to palpate them gently.

The second patient today, Arthur W. P., thirteen years old, presents conditions that are equally interesting. He, too, is of school age and has been in a military school since September, 1916. His father has had pulmonary tuberculosis for the last four years. Otherwise his family history is negative. The patient himself has never had good health, having always been frail and without much endurance. In infancy he had measles and otitis media. When he was four years old he had an attack of tonsillitis, followed by another a year later, after which his tonsils were removed, together with some adenoid growths. When he was seven years old he had pertussis, followed a year later by chickenpox and mumps. At nine years of age he had an attack of chorea, accompanied by weakness in both legs; it was succeeded by aphonia lasting for several weeks. He recovered from this illness completely in eight weeks from the onset of the chorea, but two months later he had a second attack of it. Since then he has had no other illnesses, except that eighteen months ago he broke his left leg. He has never had diphtheria, malaria, typhoid fever, pneumonia, or pleurisy. In January, 1917 he had an attack of rheumatism (so called), but without redness or swelling of the painful joints.

The patient's present illness began six weeks ago with frontal and orbital headache and difficulty in writing, owing to twitching and jerking of the fingers. A week later he noticed that his right foot dragged when he walked. He complained of this, but he was under military discipline in a school where he was believed to be shamming. A doctor was not consulted until two weeks ago. I would have you notice this fact, because it is an important point and merits observation also in schools other than those under military organization. The irritability, restlessness, and so-called "naughtiness" exhibited by children suffering from chorea are apt to be regarded as delinquencies, deserving, it may be, of corporal punishment. It is important that teachers, especially in the primary and grammar schools, should have sufficient knowledge of the nature of chorea not to punish a child for its manifestations. As to this boy, when the doctor finally saw him, he was sent to bed and kept there on a meat-free diet and under a course of Fowler's solution up to the time he entered this hospital on April 26th.

On admission to the ward the patient complained of inability to control the movements of his right arm and leg. Physical examination at that time showed that the important points in his physical state were the condition of his heart and extremities.

There was a manifest inability to control the movements of his right arm and leg. In this connection it is rather an interesting point that during this clinic this second patient has shown more control over his muscles than the first, although chorea has been decidedly more marked in his case than in that of the other. The first patient, in whom the symptoms are ordinarily much less evident, has been making choreatic movements all the time I have been talking. The second patient lies relatively quiet in bed with his right hand under his head as a means of controlling the twitching and jerking of his right arm. Despite his efforts at control, the involuntary muscular contractions, as you must have noticed, have been visible from time to time. Examination of the patient's heart, made on admission, showed no bulging or any heave over the precordium. The point of maximum impulse was well marked in the fifth intercostal space, 9 cm. from the midsternal line. There was no evidence of Broadbent's sign and the heart moved with changes in position. The first sound was indistinct at the apex and there was a long systolic murmur, beginning with systole and transmitted to the axilla and the back, as well as a long, low-pitched rumble throughout early diastole, which was best heard toward the apex and disappeared before systolic contraction. The pulmonary second sound was very loud; the aortic sound was normal in quality. There was no murmur at the base. He has, then, mitral stenosis and mitral insufficiency, with slight enlargement of the heart, doubtless the result of a thrombo-endocarditis of "rheumatic" origin.

An examination of the nervous system in this patient on admission showed that he suffered from a definite choreatic disturbance of motility, and this disturbance we shall in a few moments try to analyze rather carefully. There was no disturbance of sensation, either of common sensibility or of the special senses. The superficial reflexes are normal. The deep reflexes are somewhat diminished, especially in the lower extremities, but they are approximately equal on the two sides. He has good control of the sphincters.

Here, then, we have a boy who exhibits the tetrad of phenomena common in acute rheumatic fever, namely, tonsillitis, polyarthritis,

endocarditis, and chorea. A fifth phenomenon, occasionally present, the existence of rheumatic nodules, observable in the other case, is absent in this patient.

Let us now turn to an analysis of the disturbance of motility that this patient exhibits. You will have noticed the spontaneous occurrence of quick, irregular contractions of muscles in different parts of this boy's body (fingers, hands, arms, legs) as he has been lying here in bed. They were purposeless movements, though some of them resembled, to a certain extent, movements or portions of movements that are often voluntarily made. (To the patient): Hold your right hand up, please; and hold it as still as you can. When the choreatic movements are at all difficult to bring out you can nearly always succeed in eliciting them by asking the patient to hold his hand steadily above his head. In this case, as you see, there is inability to maintain the right arm in a fixed position. The left arm is held fairly steadily, but on observing his right hand you notice that there is deviation, rotation, flexion of the fingers, etc.

(To patient): Grip my hand, please. Grip as hard as you can.

Sometimes the choreatic movements are easily observable when the patient tries to grip the examiner's hand. He makes a number of extraneous movements without giving a firm solid grip, because there is an inability to maintain the innervation necessary for the continuance of firm contraction.

This same inability may be detected by placing the patient's hand in dorsal flexion and asking him to hold it in that position, or by asking him to hold his tongue out.

(To patient): Touch my finger, please. Now touch this one.

He did that fairly well, but sometimes, in cases of chorea, the psychic processes are retarded to such an extent that an involuntary movement takes place before the "willed" movement occurs, the latter appearing later, as though by chance.

Spontaneous involuntary movements are characteristic of this condition. Some movements occur when the patient is trying to be at rest, and are, as we say, "unmotivated." Just now this boy is very quiet, but he has during his stay in the ward, nevertheless, exhibited outspoken choreiform movements; indeed, in his right arm and leg the movements have been almost incessant except during sleep, when, as is the rule in chorea, the muscles are quiet.

In this boy, as you have seen, there is a weakness of certain

muscles, in fact, all the muscles on the right side are weak on comparison with those on the left. In some cases of chorea the muscles of the neck may be much weakened. When the muscular weakness is pronounced the terms "paralytic chorea," "limp chorea," and "chorea mollis" are used to designate the type. The weak muscles are not grouped as in the paresis that accompanies partial lesions of the pyramidal tracts, and the Babinski test is negative. In this country Camp (in 1910) has made an interesting report on "paralytic chorea."

In the report on this boy the student, Mr. McCartney, told us that the knee-jerks were enfeebled. Since Eshner's studies in 1901 and Gordon's in the same year we have all been interested in the behavior of the deep reflexes in chorea. We shall, therefore, test them now. (To the patient): Sit up, please, and let your legs hang over the edge of the bed. You see that, when I test the knee-jerks, the reaction is sluggish; when I quickly move the legs passively in order to test the tonicity of the musculature I find the tonicity to be less than normal and such muscular hypotonicity is another disturbance often observable in chorea, where it has been given the special name "choreatic atony."

Sometimes disturbances of associated movements are easily demonstrable in chorea. The disturbance may either inhibit associations that normally occur or, as is more often the case, be characterized by the occurrence of abnormal associations (pathological synkinesias) due, perhaps, to an overflow of the "willed" innervations into other than the normally associated systems of neurones.

Another disease in which there is disturbance of associated movement is double congenital athetosis, which is characterized by continuous, involuntary, slow, rhythmical movements. I wonder how many of you have seen a girl who walks up and down Charles St., of this city, with her sister, and who is a remarkable example of pathological increase of associated movements. She makes most extraordinary contortions of the extremities, neck, face, and jaws, so extraordinary that, if you have once seen her, you can never forget her. She suffers from double congenital athetosis.

Chorea and athetosis, though both characterized by disturbances of associated movements, are two conditions that, otherwise, are entirely separate and distinct. In chorea the movements begin suddenly, are quick and jerky in character, and when they are over

the part involved in them remains at rest. In athetosis, on the contrary, the movements are slow and worm-like and are continuous while the patient is awake. The muscles affected by chorea are relaxed and the movements show no sign of rhythmic character, whereas in athetosis the muscles are always hypertonic and the movements are rhythmical. In the patient now before us you observe just a little pathological increase of associated movements, but the characters of the disturbance of mobility in this boy are those of chorea; there is nothing to suggest an athetotic condition.

Summing up our findings on analyzing the motor symptoms this boy presents we may say that he exhibits:

(1) Quick, irregular, involuntary contractions especially of the right side of his body (hemichorea); (2) weakness of the muscles, more marked on the right side than on the left; (3) enfeeblement of the knee-jerks and hypotonicity of the musculature; (4) inability to maintain the innervations necessary for the maintenance of firm contractions (hand grip), and (5) a slight pathological increase in synkinesia (or associated movements). You will be interested, if you can find the time, to compare these disturbances that you have actually observed in this boy with the choreatic disturbances that have been described in medical literature, especially in the article by Bonhoeffer (1897), in the monograph by Foerster (1904), and in the thesis of J. Cambies (1915).

Now why should patients who suffer from acute rheumatic fever so often present this choreatic disturbance of motility? All the evidence goes to show that rheumatic fever is not merely a disease of the joints, but is a blood-borne general infection, the virus being distributed throughout the whole body, though focal manifestations, due to localizations in the joints, in the endocardium, or in the brain are prominent features, owing to the fact that they give rise to disturbances that depend upon the locality affected and the extent of the local disease. Now the brain may be affected in different ways in chorea. Thus clinicians have long recognized what is known as "cerebral rheumatism," characterized by hyperpyrexia, delirium, convulsions, and coma; and, in addition, a "rheumatic meningitis" has been described, though it is rare and needs further study. But by far the commonest cerebral complication of acute rheumatic fever is "chorea." Some have thought that chorea is due to multiple minute emboli having origin in the vegetations of a complicating

endocarditis, but chorea may occur in rheumatism when there is no evidence of a coexistent endocarditis. Others believe that the chorea is due to a complicating disseminated encephalitis, the choreatic disturbance of motility appearing only when the encephalitic foci are located in certain areas. This view has much in its favor, though it must be admitted that supporting evidence from the pathological-histological side still leaves much to be desired. Encephalitis has often been but is not always demonstrable in patients dead of rheumatic fever and chorea. At present we do not know for sure what part or parts of the brain must be involved in order that chorea shall be manifested, and investigation in this direction should claim our attention in the near future. It would not be surprising if the locality involved should prove to be the red nucleus or the basal ganglia, for certain cerebral conditions involving the red nucleus and the basal ganglia, as, for example, brain tumors or vascular lesions in these localities, are sometimes associated with choreatic disturbances of motility.

Meanwhile much may still be gained by careful clinical analyses of large series of cases of chorea. Let me advise you in this connection to read especially the monograph by Dr. Osler on "Chorea and Choreiform Affections" (1894) and the important articles by H. M. Thomas (1901) and by W. S. Thayer (1906).

Now before we close we must consider what can be done to hasten the cure of chorea. Cases of rheumatic fever in which chorea is present must, of course, receive somewhat different treatment from those in which it is absent. These 2 patients are both suffering from chorea, but they are affected by it in different degrees. In the first patient it is comparatively mild, whereas, in the second, it is present in quite a severe form. In bad cases of chorea the involuntary movements may be very violent and there is no sight more pitiable, perhaps, than a severe case of this description. I remember that once when I was going through the wards of a large hospital with the chief physician we came to just such a case. The physician took me to the bedside to show me the movements, which had been marked, and on turning down the bedclothes he was horrified to find the child lying in a pool of blood. The movements had been so violent that they had resulted in abrasions severe enough to cause considerable loss of blood. An experience of this kind emphasized the fact that whenever the choreatic movements are at all violent it

is extremely important to take precautions to prevent the patient striking himself against the framework of his bed. The mattress must be soft or a water-bed may be employed if one be available. Measures must be taken to prevent the child's falling out of bed, but these must not be such as to inflict unnecessary restraint. Any sort of apparatus designed for that purpose, such as a restraining sheet, for example, is to be avoided. In hospitals and in the homes of well-to-do patients there should be padded sides to the patient's bed. Among poorer patients, where such an arrangement may not be practicable, the child must have a bed upon the floor. In cases characterized by great excitement the patient should be kept in a continuous warm bath. These are just the cases in which mild hydrotherapy may be very beneficial.

Always bear in mind that the two essentials in the treatment of chorea are: first, *rest*, both physical and mental; and, second, *isolation*. But you must also remember that in order to obtain the full benefit of these measures the rest must be as complete as is possible in the circumstances. If the case is a severe one the patient must be taken away from his family and put to bed in the recumbent position in a room where, except for the nurse, he will be quite alone; and everything tending to cause excitement should be eliminated. In severe cases two special nurses, one for the night and one for the day, should, if possible, be provided.

As regards medicines, arsenic is usually given in chorea, but I do not know whether it really shortens the course of the disease or not. It probably does something toward maintaining nutrition, for it slows the rate of metabolism. Abt and Levinson, in an analysis of 226 cases observed by them and reported to the American Medical Association, came to the conclusion that arsenic is of little use. Abt states that when he treated a child in one bed without arsenic while a colleague was at the same time treating another child in the next bed with it, the results were the same. If arsenic be administered, one must take care not to give so much as to cause neuritis. If sedatives are needed, sodium bromid and chloral, 5 grains of each, given, perhaps, by the rectum are probably as good as anything we have at command.

Quite recently the treatment of chorea by means of inoculation with autoserum into the subarachnoid space has been tried with some promise of success. In 1916 T. L. Goodman reported to the New

York Academy of Medicine a very severe case of chorea treated by him in this manner successfully. The child had had maximum doses of the salicylates, arsenic, the bromids, chloral, and codein—all without relief. When it was decided to try the serum treatment, 45 to 50 c.c. of blood were withdrawn from the patient and centrifugized, after which the serum was pipeted off and transferred to beakers, in which it was kept for at least two hours at room temperature. Then spinal fluid (20 c.c.) was withdrawn by lumbar puncture and the serum introduced with extreme slowness, ten to fifteen minutes being consumed in injecting 15 c.c. In this case there was no reaction; response to treatment was prompt, and the child recovered rapidly. The patient was treated in 1913, and Goodman, when reporting the case in 1916, stated that he had used the autoserum treatment on various occasions since with success and had never seen it followed by any harmful results. In some cases after an injection there is a slight reaction manifesting itself in headache and a trifling rise of temperature.

Aside from other treatment it is very important to keep up and, if possible, improve the general nutrition of the patient. The association of chorea with rheumatism makes it essential to prevent chill and exposure to dampness, which also increases, it is believed, the liability to endocarditis. A century ago Chambers, when lecturing on rheumatism, was accustomed to tell his students: "Wrap your patients in blankets and let them alone."

During convalescence the child should be carefully guarded, and measures that improve the general nutrition should be maintained. Relapses are all too common, but a careful régime will go far toward preventing them. Mental and physical strain are to be avoided. A quiet life in the country is desirable for a time, even if this necessitates a rather prolonged absence from school.

[*Subsequent History of Case I (Joseph O'G.)*.—On May 5th, a week after the clinic, a nodule was excised from the patient's right elbow for the purpose of microscopic examination. The report, made by Dr. Joseph C. Bloodgood, was as follows:

"The sections show chronic inflammatory tissue. There are lymphoid cells, spindle-shaped cells, and fibroblasts, with numerous capillaries. In certain zones the tissue is edematous. This is the usual picture of chronic inflammatory nodules seen in infectious diseases, chiefly of the rheumatic type. Comparison of the section with

some granulation tissue excised from a breast wound, previous to grafting, showed almost the same histological appearance, except that it was not quite so vascular."

By the end of ten days the nodules had practically disappeared. At this time there was tachycardia, the pulse being 120. The course continued to be characterized by ups and downs until the middle of July, two months after the admission of the patient. He was then put upon a course of the infusion of digitalis, after which there was steady improvement. On September 6th he was in good condition, his weight being 77 pounds; a presystolic and a systolic murmur could still be heard at the apex of the heart. He was then discharged from the hospital with instructions to report at the out-patient department from time to time.

Subsequent History of Case II (Arthur P.).—This boy's general condition improved steadily, though his cardiac condition remained unchanged. He was discharged as "improved" on May 24th. When he entered the hospital the chorea was so marked that he was unable to write; but three days before he left he wrote a letter without any difficulty.]

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DISEASES OF THE RESPIRATORY APPARATUS

III. POSTOPERATIVE PNEUMONIA

ACUTE POSTOPERATIVE PNEUMONIA OF UPPER LOBE OF RIGHT LUNG, WITH REMITTENT AND INTERMITTENT FEVER OF SEPTIC TYPE, TACHYCARDIA, LEUKOCYTOSIS, SECONDARY ANEMIA, SIGNS OF CONSOLIDATION IN THE RIGHT UPPER LOBE, STREPTOCOCCI IN THE SPUTUM, AND NEGATIVE BLOOD-CULTURES. DISCUSSION OF THE NATURE AND MODE OF THE INFECTION

DR. BARKER: This young colored girl of seventeen was operated upon twenty-six days ago, since when she has developed, first remittent and then intermittent fever, and signs of consolidation in the right upper lobe. We are to spend the hour this morning upon a clinical analysis of this case.

Mr. Price, will you please give us the history of this patient?

STUDENT: This colored girl, Nannie F., aged seventeen years, a hotel maid by occupation, was admitted to the gynecological service (Professor Thomas S. Cullen) on December 30, 1920, complaining of "pain in the lower abdomen and back."

She stated that her symptoms dated back some three months (to October, 1920), when she first noticed aching pains in the back, sides, and lower abdomen. Though these pains were never very severe, they interfered with her sleep. At the onset in October there seems to have been some fever and the patient stayed in bed for the first week. After this she was up and about, doing her work in the hotel for eight hours each day. She admitted that there had been some burning pain on micturition during the illness, but denied any discharge from the vagina or urethra and any knowledge of venereal infection. She is unmarried, though she has a child two years of age that is living and well.

As to her previous history, she stated that she had had measles, mumps, and pertussis in childhood and also frequent attacks of chills and fever when she lived in a malarial district in Virginia. She has suffered from recurrent headache, and has worn glasses

during the past four years for some refraction error. Otherwise she has been a healthy working girl. She looks rather mature for her years and seems intelligent and alert.

On admission to the gynecological service Dr. Brady elicited, on physical examination, slight but definite tenderness in both hypogastric regions, more marked on the right than on the left, as well as marked tenderness over McBurney's point. In addition, he reported laceration of the cervix, tenderness and induration in both fornices, and an adherent right ovary. He made the diagnosis of "chronic pelvic inflammatory disease, chronic appendicitis, and lacerated cervix," and operated upon the patient on December 31, 1920. As the appendix was injected and adherent to the rectum and to a right tubo-ovarian mass, appendectomy was done and bilateral shaggy, tubo-ovarian masses were excised together with the supravaginal portion of the uterus.

The patient did well for the first few days after operation. On January 5, 1921 the drains were removed from the pelvis. There seemed to be no evidence of infection and her general condition was very good.

On January 6th (seventh day after operation) the temperature rose a little (see chart), and for the next several days a remittent temperature curve was recorded. On physical examination râles could be heard in both lungs, but no dulness could be made out. On January 12th the white cell count had reached 13,740; by the 15th the white count was 19,520. At this time an *x*-ray plate of the lungs was made (No. 86912), which revealed signs of consolidation in the right upper lobe. Despite the high fever (temperature 105.8° F.), the patient felt comfortable and did not look very ill. Examination of the lungs on January 15th revealed dulness, crepitant râles, and tubular breathing in the right interscapular space at the level of the scapular spine. There was no cough, no pain, and no expectoration. Smears of the blood for malarial parasites were negative and a blood-culture made on January 13th remained sterile. A catheterized specimen of urine taken at this time was negative. The spleen was not palpable. Examination of the pelvis showed no local abnormality.

Two days later (January 17, 1921), the râles persisting and the spleen having become palpable, Dr. V. Mason, the resident physician of the medical service, was asked to see the patient in consultation. The septic temperature curve, the local focus in the lungs, and the palpable

spleen indicating a severe infection, the patient was, at the request of the gynecological service, transferred to the medical ward.

On admission to the medical service a full note was dictated by the house-officer, Dr. Felty, the main findings being as follows: Patient comfortable; does not look ill; shows marked pallor; is mentally alert. No cough, dyspnea, cyanosis, or pain. Slight general glandular enlargement. Slight thickening of thyroid isthmus. Head negative except for coated tongue, dental caries, and pyorrhea; tonsils small.

Chest: Vocal fremitus increased over the right upper lobe, both in front and behind, though the percussion note is fairly resonant in front and in the axilla. In the back, slight impairment of the percussion note over the body of the scapula and tubular breathing there. Tubular breathing audible also in the right interscapular region, where a few moist râles could be heard. Over the same area bronchophony and whispered voice sounds greatly intensified. High up in the right axilla, breathing bronchovesicular in character, and many crepitant râles audible. A few fine and medium-sized râles audible over both lower lobes, these being more numerous on the right than on the left side. Lungs otherwise negative. Heart negative except for a soft systolic blow at the apex and moderate accentuation of the pulmonic second sound. Abdomen negative except for a palpable spleen felt just below the left costal margin. Extremities negative. Nervous system negative. Dr. Felty gave as his impression "consolidation in the right upper lobe; the septic temperature suggests the possibility of pulmonary abscess."

Dr. Felty's findings in the lungs were, in the main, confirmed by Dr. Guthrie on January 22d, and again by Dr. Mason on January 24th. All who have examined the patient in the ward have been struck by the fact that the patient is comfortable and looks well, despite her very high fever and the pronounced changes in the upper lobe of the right lung. There has been considerable discussion among members of the medical staff as to the precise nature of the case, and particularly with regard to the relations of the process in the right upper lobe to the septic temperature chart, some thinking that a local septic process in the abdomen or a general sepsis followed the operation and that the lung involvement was secondary to this sepsis originating in the pelvis, others thinking that the pulmonary process was primary and accounts by itself for the septic temperature chart.

DR. BARKER: What did examinations of the blood reveal?

STUDENT: The patient has a rather marked secondary anemia with polymorphonuclear leukocytosis. The Wassermann reaction is negative. The red cell count is 3,872,000; the hemoglobin, 65 per cent.; the white count has varied between 8500 and 19,500; at present it is 18,100. In the differential count about 70 per cent. of the white cells are polymorphonuclear neutrophils. The eosinophils are reduced in numbers. In one smear no eosinophils at all were seen. Two blood-cultures have been made and neither has thus far shown any growth. A search for malarial parasites has revealed none.

DR. BARKER: This infection, whatever it is, is associated with a polymorphonuclear leukocytosis and not with a leukopenia. If this patient were suffering from malaria or typhoid fever she would almost certainly show a leukopenia rather than a leukocytosis. If she had an uncomplicated tuberculosis in the right upper lobe she would not have so marked a leukocytosis as this; of course, a pulmonary tuberculosis with a pyogenic complication might be associated with leukocytosis. This polymorphonuclear leukocytosis in connection with this septic temperature chart points to an infection with some variety of pyogenic organism (Fig. 2).

(To student): What are some of the common pyogenic organisms?

STUDENT: Streptococcus, staphylococcus, pneumococcus, gonococcus, and meningococcus.

DR. BARKER: Yes, attempts have been made to draw conclusions regarding the nature of the pyogenic organism by considering the form of the temperature chart. The matter has been fully discussed in Lenhartz' monograph, but if you will go over the cases of pyogenic infection of known etiology in this hospital I think you will be very chary of drawing too definite conclusions regarding the kind of organism present merely from the appearance of the temperature chart. I fear that you would more often be wrong than right if you made a guess as to the etiology from the temperature chart alone.

Let us examine the patient's chest for ourselves and see what can be found this morning. You observe that the chest is well formed and that the two sides are approximately symmetrical. The respiration rate is not markedly accelerated. The rate now is 24 per minute. It is easy to see, however, that the expansion of the right chest is less marked than that of the left, and that there is a definite lag in the right upper chest on inspiration. On palpation, vocal fremitus is distinctly increased over the right upper lobe both in the front and in

the back, but elsewhere the vocal fremitus is normal. On percussion, there is no dullness in either front, but there is definite dullness in the right interscapular space and over the body of the right scapula; the area of this dullness corresponds approximately to the right upper lobe behind, though you will note that the percussion note over the apex of the right upper lobe above the clavicle and over the front of the right chest is not dull. The area of dullness corresponds then to the posterior part of the right upper lobe. Over this dull area the breath sounds are increased, and in the right interscapular space,

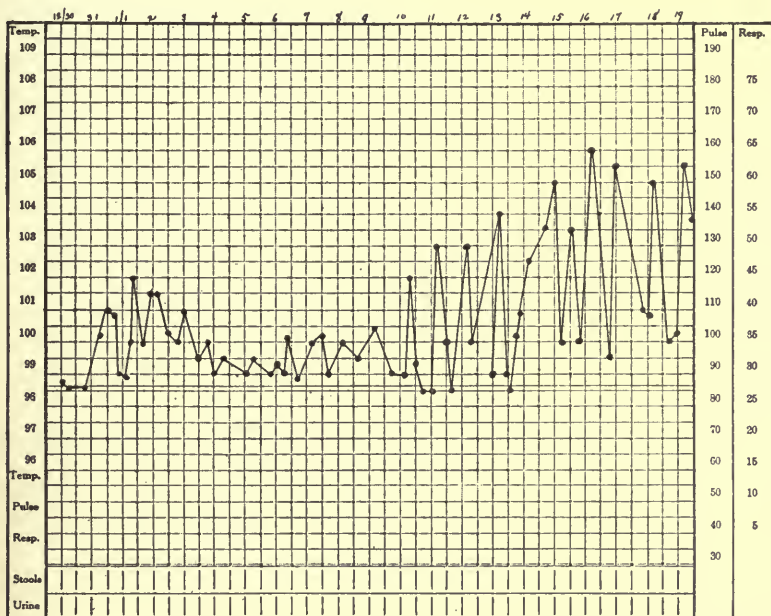


Fig. 2.—Temperature chart of patient suffering from postoperative pneumonia of the right upper lobe.

opposite the spine of the scapula, there is an area about the size of a silver dollar over which there is outspoken bronchophony and there the whispered voice sounds are especially loud. There is a slight "bleat" to the voice sounds in this area also. I can hear no adventitious sounds at present over the right lower lobe or over the right middle lobe. The sounds over the left lung are normal.

The heart is quite negative except for a slight systolic blow at the apex and a slightly accentuated second sound in the second left intercostal space.

The spleen is just palpable at the left costal margin and seems rather firm. Whether this slight enlargement of the spleen is the result of the pre-existent malaria or is due to the present infection is not certain, though with this height of fever it may easily be due to the present infection. Aside from the slight oral sepsis, already mentioned, there are no local signs of infection to be made out anywhere. The abdomen is soft and not distended. There is no sign of local inflammation in the neighborhood of the operative field, nor can I make out anywhere signs of phlebitis in any of the veins accessible to palpation. There are no skin lesions to be seen except a slight acne of the face. There is no evidence of petechiæ in the skin or visible mucous membranes. The pallor of the lips corresponds to the blood findings.

(To student): Was the urine examined?

STUDENT: Yes, but the urine is entirely negative. There is not even a trace of albumin. No casts have been seen, nor have any white or red corpuscles been found in catheterized specimens.

DR. BARKER: Has the blood-pressure been low or high?

STUDENT: The blood-pressure is rather low, 110 systolic and 70 diastolic. The pulse-rate has varied while the patient has been in the ward between 80 and 120.

DR. BARKER: Please tell us of the sputum.

STUDENT: It has been difficult to obtain any sputum, and in the few specimens examined no tubercle bacilli have been found, though smears show cocci in chains and some bacilli. Sputum cultures have been made and will be reported on later.

DR. BARKER: Has the lung been punctured in the consolidated area?

STUDENT: No, this has not yet been done. It has been discussed.

DR. BARKER: This could be done, I think, with practically no risk to the patient, and perhaps material could thus be obtained for microscopic and bacteriological examination that would reveal the nature of the organism present in the exudate in the consolidated area.

Let us look at the roentgenograms of the chest. Here is one made on January 15th and another made yesterday, January 24th (Fig. 3). In the former you see a rather dense shadow corresponding to the area of the right upper lobe with the exception of its apex, the shadow being most dense at the lower part of the lobe. In the

second roentgenogram, made yesterday, the shadow is much less dense and looks more mottled. Evidently, the consolidated area is undergoing partial resolution.

[The patient at this juncture was sent back to the ward.]

Let us now summarize our findings. We have to deal with a young colored girl whose occupation is that of a maid in a hotel, and who, though unmarried, became a mother at fifteen years of age. She has been healthy in earlier life except for some of the ordinary



Fig. 3.—Abnormal shadow in roentgenogram due to consolidation of the upper lobe of the right lung in a patient suffering from postoperative pneumonia.

childhood diseases and for recurring attacks of malaria. Last autumn she began to have pain in the lower abdomen and back which kept her from sleeping. About this time she noticed some burning on micturition. She was found, on the gynecological service here, to have a lacerated cervix, signs of pelvic inflammatory disease, and tenderness in the region of the vermiform appendix. Appendectomy and panhysterectomy were done about four weeks ago. She seemed to be undergoing an uneventful recovery from the operation, though she continued to have a little fever during the days immediately

following it. Eight days after the operation there was a sudden elevation of temperature, though the fever was at first not high; and ever since (that is, for the past eighteen days) she has had fever, first remittent and then intermittent, the temperature going as high as 106° F. during this hyperthermic period. She has had chilly sensations, but no outspoken rigors. There has been some sweating, but otherwise she seems comfortable and does not look ill. Physical examinations revealed signs of a diffuse bronchitis in both lungs when the temperature first became elevated, but a little later the diffuse signs in the lungs disappeared and signs of consolidation, involving the right upper lobe (except its apex and the anterior portion of the lobe), could be made out and have been corroborated by x-ray examinations. Despite these local signs there has been no cough, no dyspnea, no cyanosis, and very little sputum. Physical examinations otherwise have been remarkably negative, except for a slightly enlarged spleen, a soft, systolic murmur at the apex with accentuation of the pulmonic second sound, slight general lymph-gland enlargement, and a little oral sepsis. The blood shows a secondary anemia and a moderate leukocytosis of polymorphonuclear type. The urine is entirely negative and blood-cultures made on two occasions have remained sterile.

We may now turn to a consideration of the nature of the process in the patient who has been before us. Let us see what conclusions we dare draw regarding this infection, its location, and its nature. Is it in any way related to the gynecological operation that preceded it, or is it an infection that has developed entirely independently of the operation? Does the disturbance that can be made out in the right lung account for the whole of the infectious process, or is there a lung infection associated with some local infection elsewhere, or with a general septic infection? Can we get any clues as to the nature of the infective agent or agents concerned? These are some of the special diagnostic problems that confront us.

We shall perhaps do well to consider first the etiology of the subacute pelvic inflammatory disease that led to her gynecological operation. What micro-organism has, in your opinion, been the cause of the patient's salpingitis and perisalpingitis?

STUDENT: The gonococcus.

DR. BARKER: Yes, that is decidedly the most probable. For, in the first place, the gonococcus is by far the commonest cause of pelvic

inflammatory disease of this type, and, in the second place, the history of this young colored girl would strongly corroborate this view. Her sexual relations have been illicit; her occupation has strongly predisposed to such relations, and, at the onset of her trouble last autumn, there was burning micturition. It must be kept in mind, however, that gonococcal infections within the pelvis are sometimes complicated by suprainposed streptococcal or other infections, particularly as the appendix had become adherent to the rectum and to the right tubo-ovarian mass, and a subacute appendicitis existed at the time of operation. The possibility of a general sepsis secondary to the pelvic sepsis must be kept in mind, also the possibility of metastatic infection from a primary pelvic focus. Do you think that this patient has a general gonococcal sepsis?

STUDENT: This is, of course, a possibility; but there is no evidence of gonococcal endocarditis or of gonococcal arthritis, and the two blood-cultures thus far made have been negative.

DR. BARKER: Yes, this evidence, as far as it goes, is against the existence of a bacteriemia due to invasion of the blood with either the gonococcus or the streptococcus. But you must remember that, even when a general sepsis exists, blood-cultures may be either positive or negative. Sometimes two or three cultures will be negative and then one will secure a positive culture. This is especially true in gonococcal sepsis, for the gonococcus is not an easy organism to grow, as you know. The absence of endocarditic signs and of arthritic signs is, however, rather strong evidence against gonococcal sepsis. Moreover, it would be very unusual to see a metastatic pneumonic process due to the gonococcus. I do not recall having seen one in our experience here, nor do I remember any case of the sort in the bibliography.

Since the existence of a bacteriemia has not yet been proved, let us turn for a moment to a consideration of the process in the right upper lobe. There has evidently been a consolidation there, and it appears to have developed about eight days after the operation. What is the commonest cause of pneumonia occurring after operation?

STUDENT: I think the most common cause of pneumonia after abdominal and pelvic operations is pulmonary embolism.

DR. BARKER: Pulmonary embolism is certainly one of the commonest causes of so-called postoperative pneumonia. A pulmonary

embolism may cause an infarction, and, if the embolus be a septic embolus, an embolic pneumonia may follow.

Pulmonary embolism after operation is much more common than is generally supposed. The onset, however, is usually characteristic (sudden pain in the chest, hemoptysis). But sometimes these characteristic marks are absent. I cannot emphasize too strongly the fact that *venous thrombosis is especially common after operations in the abdomen and pelvis*. Doubtless such thrombi often form without any subsequent occurrence of embolism. Dr. Louis Hamman, in his article in *Oxford Medicine*, lays stress on the fact that venous thrombosis is the commonest cause of a little unexplained fever persisting through convalescence from operation. You should remember, too, that extensive pulmonary embolism and infarction may occur without the patient having bloody sputum or, indeed, any sputum at all. Septic embolism after an abdominal or pelvic operation is a not uncommon cause of pulmonary abscess, and though such pulmonary emboli most often lodge in the lower lobes of the lung, they may lodge in the upper lobes and be the cause of an embolic pneumonia or of an embolic abscess in an upper lobe.

If this patient has had a pulmonary infarction due to septic emboli derived from the site of the pelvic operation, it is a little surprising that there should have been no signs of embolism elsewhere (spleen, kidneys, brain, skin). Moreover, if we can judge by the history, the pulmonary process began rather as a diffuse bronchitis, and only later did the signs of consolidation of the right upper lobe develop. On surgical wards the pressure of the surgical work sometimes interferes with close observation of medical conditions, and it is possible that the localized signs in the right upper lobe might have been made out earlier under closer supervision. I do not know. In the surgical wards here, however, medical as well as surgical conditions are very closely observed. Certainly, embolic pneumonia of the right upper lobe secondary to the pelvic operation and pelvic infection is a possibility in this case that should be kept in mind.

How, otherwise, might this process in the lungs, and especially in the right upper lobe, be accounted for?

STUDENT: The patient may have developed an acute bronchitis in the ward subsequent to operation, and this could have been followed by a bronchopneumonia of pseudolobar type, involving the most of the right upper lobe.

DR. BARKER: Yes, that is a possibility. This process in the right upper lobe may have been of bronchogenous origin, in which event it might be due to the pneumococcus, the streptococcus, the influenza bacillus, or some other common lung-invading micro-organism. Cocci in chains have been seen in smears of the sputum. The diffuse bronchitis reported at onset and the subsequent appearance of signs in the right upper lobe favor the view, though, here again, the absence of cough, dyspnea, cyanosis and the paucity of sputum are peculiar.

There is another possibility that perhaps should be considered.

STUDENT: It might have been an ether pneumonia.

DR. BARKER: Yes. The so-called "ether pneumonias," that is, pneumonias that follow operations in which ether has been administered as an anesthetic, are usually "aspiration pneumonias." During the narcosis or during the feeble state after the operation the patients aspirate food particles or other substances from the mouth or throat; these lodge in the bronchi and the bacteria carried in with them set up a bronchitic and a bronchopneumonic process. It is rare, however, for such aspiration pneumonias to affect an upper lobe rather than the lower lobes. Though occasionally an upper lobe may be predominantly affected, in an ether pneumonia it is far more common to find involvement of both lower lobes. Such an aspiration pneumonia sometimes terminates in a lung abscess, sometimes in gangrene. Is there any sign of lung abscess or lung gangrene here?

STUDENT: The outspoken bronchophony and dulness in the right interscapular space are somewhat suggestive. But there have been no signs in the sputum pointing to abscess or gangrene, and no odor to the breath suggestive of either. In abscess there is a sweet, "sickish" odor; in gangrene, an almost nauseating putrid odor.

DR. BARKER: We have pushed our analysis perhaps as far as we dare with the data as yet at our disposal. I do not think we can positively decide whether this pneumonic process is of hematogenous or of aërogenous origin. Should we obtain further light upon the case I shall be glad to make a report to you at a later clinic. In the meantime I hope that you will seize the opportunity to consult at least a part of the bibliography on this subject, references to which are written on the blackboard.

[*Further History of Case.*—The culture made from the sputum on January 21, 1921 yielded a mixed flora, including hemolytic streptococci and diphtheroid bacilli. Blood-cultures remained sterile. The

patient was discharged on February 9th, about two weeks after the clinic. On physical examination before discharge the lungs were found to be practically clear (Fig. 4). There were a few crackles beneath the scapula on the right and in the interscapular region. No tubular breathing. Another roentgenogram of the lung showed



Fig. 4.—Roentgenogram of chest of patient suffering from postoperative pneumonia; plate made about three weeks later than the preceding one. The marked lessening of the shadow over the right upper lobe shows that the pneumonic exudate has been largely absorbed.

shadows suggestive of tuberculosis of the right upper lobe. The patient said she felt perfectly well.]

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IV. SPACE-OCCUPYING MASSES IN THE MEDIASTINUM

CASE I. LYMPHOSARCOMA OF MEDIASTINUM INVADING RIGHT LUNG AND SUPERIOR VENA CAVA AND METASTASIZING INTO LYMPHGLANDS, BONES, AND SUPRARENALS. NO BENEFIT FROM RADIUM TREATMENT. DEATH. AUTOPSY.

CASE II. AORTIC ANEURYSM COMPRESSING THE RIGHT BRONCHUS AND THE SUPERIOR VENA CAVA IN A SYPHILITIC AND ALCOHOLIC LABORER

WE have 2 patients for study this morning, both feeling very ill and both of them illustrating intrathoracic abnormalities. The cases manifest such interesting points of resemblance, and no less interesting points of difference, that it would be hard to find 2 more instructive patients in the domain to which they belong. We are fortunate in having the opportunity to observe both at the same clinic.

The first patient is William O'K., a policeman, fifty-seven years old. He was admitted to the hospital two weeks ago complaining of "pain in the chest and spitting of blood."

Though his family history is unimportant, there are some points in his personal history that are interesting. Thus, he tells us that he had measles, mumps, chickenpox, and scarlet fever in childhood,

and that fifteen years ago, that is, when he was forty-two, he had typhoid fever. His general health has otherwise always been excellent, except that many years ago he suffered occasionally from sore throat. Fifteen years ago he had a discharge from his right ear, which left his hearing slightly impaired, and he has had some ringing in that ear ever since. For some years past he has had occasional toothache, but when this happened he would have the offending tooth promptly extracted. The gastro-intestinal history is negative except for occasional slight "twitching" in the epigastric region after eating and the existence of constipation for the last year or two. In regard to his genito-urinary history, the patient has had nycturia (two or three voidings a night) for the last twenty years. He denies ever having had gonorrhoea, but says that he had a local venereal sore about twenty years ago. He was married for thirty years; his wife died of pneumonia about eight years ago. She never had a miscarriage. He has 4 children, living and well. He lost one child from "stomach trouble" at eighteen years of age and another from cerebrospinal meningitis at twenty-one.

The patient's habits as regards eating and sleeping are regular. His work as a policeman exposes him to all kinds of weather. He has always smoked a great deal of strong tobacco. Up to fifteen years ago he chewed 5 cents' worth of plug tobacco every day. He takes an occasional glass of beer.

The present illness began four months ago, when early one morning the patient was drenched in a heavy rain and remained on duty all day in his wet clothes. Two days later he developed a slight cough, which became steadily worse, and was accompanied by shortness of breath that gradually increased until, at the end of three weeks, he could not walk half a block. I would have you note the rather insidious nature of this onset despite the rapid increase of disability. A month after this illness began he had a severe coughing spell, which, after lasting between two and three hours, terminated by his spitting up a large amount of black, clotted blood. Since this occurrence he has had constant paroxysms of coughing, often ending in hemoptysis. He says he thinks he spits up as much as a pint of blood a day, but the blood comes only when he coughs. These attacks of coughing are especially prone to come on after meals, and on one occasion a coughing spell immediately after eating was followed by vomiting, the vomited matter being streaked with bright red blood. About three

weeks ago he had a prolonged attack of coughing, during which blood ran from his mouth and nose. This may, of course, have been due to epistaxis brought on by straining and the associated congestion of the circulation in the head.

About the time the first hemoptysis occurred the patient says that he was "seized with severe pain in the spine"; from his description it seems to have been between the scapulæ, radiating to the xiphoid process, and also extending to the right side of the chest, the right shoulder and arm, and thence passing up the neck to the right side of the head. Some pain of this character has continued until the present time. Five weeks ago the patient began to have, in addition, severe shooting pains in the left leg, running from the hip to the foot. These pains come on mostly at night and are relieved, he says, only by cupping over the spine. (To patient): In just what part of your leg is the pain?

PATIENT: In the back of my leg and the outer side of it.

DR. BARKER: A posterolateral pain of the left lower extremity. A few weeks ago the patient was at St. Agnes' Hospital for between two and three weeks, but, he thinks, without any benefit. While he was there several *x*-ray examinations were made. Since then he has become very weak and has lost his appetite. He applied recently to our out-patient department for treatment and was advised to enter the hospital.

Physical examination, made on admission, showed a fairly obese man, lying in bed, supported by pillows and suffering from frequent paroxysms of cough, accompanied by severe respiratory distress. His temperature was 98.6° F.; his pulse-rate 104; his respirations were 32 to the minute, and his blood-pressure 146 systolic and 96 diastolic. He breathed with difficulty, the respirations being accompanied by stridor. His face was livid and his ears were blue. (To patient): Let me see your tongue, please. You can all see that there is a certain amount of cyanosis in his tongue. The conjunctivæ are a little suffused. Inspiration is now somewhat difficult. Here you observe some dilatation of the veins of the neck. From time to time, since entering the amphitheater, the patient has had paroxysms of coughing. The cough, you notice, is rather hoarse and not well phonated. Has he had any edema of the face?

STUDENT: He has had a little subcutaneous edema of the head and face at times.

DR. BARKER: His upper teeth are all gone save one, and that one shows signs of pyorrhea about it. The gums near the lower teeth show marked pyorrhea. There are sordes on the lips.

Examination of the chest shows it to be quite asymmetrical, the right side moving less during respiration than the left. The left side expands very well; the right side does not. I would have you note the enormously distended venules all over the anterior thorax, especially at the level of the attachment of the diaphragm and over the precordium. There is still slight edema of the face, also over the wall of the chest, and over the upper parts of the arms. The whole wall of the thorax is a little tender. (To patient): Is the place where I am now pressing painful?

PATIENT: Yes; that is the place where it hurts most.

DR. BARKER: Notice the marked shortness of breath. Notice also the thickening of the patient's neck and of the soft parts of the thorax. When edema like this is associated with dilatation of the veins from the neck to the diaphragm it forms a very characteristic picture; this swelling is known as the "collar of Stokes." We have had some very well-marked examples of this sign in this hospital, some of them more typical, perhaps, than the present instance; still, you can see it well enough here. (To student): What does this sign indicate?

STUDENT: I think it must mean that the superior vena cava is in some way obstructed.

DR. BARKER: Yes, the "collar of Stokes" always indicates obstruction of the superior vena cava, though it is not always present when the superior vena cava is obstructed. There are two types of venous circulation in mediastinal disease. In one of them the obstruction develops slowly and there is opportunity for the establishment of a good collateral circulation, with veins of large caliber extending over the whole chest, back and front, and upper abdomen communicating with the inferior vena cava. In the other the obstruction develops quickly, as it has done in this case, and the superficial veins are only moderately dilated. In some instances the dilated veins can hardly be seen at all, the disturbance of the circulation showing itself in a general cyanosis of the upper half of the body, with pitting upon pressure and consequent obliteration of the normal contours of the neck and the thorax, extending downward as far as the level of the diaphragm. It is this second type of obstruction that gives rise

to the "collar of Stokes." Very little is said about it in the textbooks, but it is an interesting phenomenon, and I hope you will not forget it.

In the right lower triangle of the neck above the clavicle I can feel some swollen glands extending from the anterior border of the trapezius to the lateral border of the sternocleidomastoid muscle. There are two groups of these glands: one just lateral to the border of the sternocleidomastoid muscle and another, larger mass just anterior and medial to the border of the trapezius. These glands are firm and elastic, and they are definitely matted together. Has one been excised for microscopic examination?

STUDENT: Yes; one of them has been excised and the tissue has been examined under the microscope.

DR. BARKER: We shall return to the findings in it, then, a little later.

Examination of the chest shows that the percussion note is a little hyperresonant on both sides, except over the right apex, where it is impaired down to the border of the first rib. There is, perhaps, a little dulness over the upper part of the chest on both sides in front, but no flatness, even upon the right side. The breath sounds are vesicular over the whole left chest. Over the entire right chest, front and back, the breath sounds are absent except high in the axilla, where impure breath sounds can be heard. Vocal fremitus is present over the whole left side, but absent on the right; the same is true of the voice sounds. The explanation of the sounds and of the vocal fremitus will be easier when we come to examine the *x*-ray plates of the chest.

The thyroid gland is not enlarged and nothing abnormal can be made out in the episternal notch.

The borders of the heart cannot be easily located by percussion because of the edema of the chest wall and the emphysematous condition of the chest. It is surprising, however, that the area of cardiac dulness should be as large as it is when the chest is emphysematous. This fact, together with the feeble heart sounds, suggests fluid in or thickening of the pericardium. There is definite retromanubrial and paramanubrial dulness. The apex-beat can be neither seen nor felt. The sounds at the apex of the heart are distant, but they seem to be clear. At the base the sounds are even more feebly audible than at the apex. No murmurs can be distinguished anywhere over the heart.

The abdomen is held very rigidly during examination; many abdominal examinations have been made in the ward, and at none of them could signs of enlargement of the liver, the spleen, or other organ in the abdominal cavity be made out. I would have you make a note of this as an important point, for it shows that the liver, the spleen, the pancreas, and the suprarenal regions show no gross physical change. Metastases to these localities are quite common with some mediastinal tumors.



Fig. 5.—Lymphosarcoma of mediastinal space.

The spine is held quite rigid during examination. There is definite tenderness over the spinous processes in the midthoracic region at the present time, and there is a large, fleshy growth over the spine, attached by a small, thin pedicle at the level of the eighth dorsal vertebra. This is evidently an old fibroma. How about the deep reflexes?

STUDENT: The reflexes are all present; the knee-jerks are over-active.

DR. BARKER: How about the Wassermann test?

STUDENT: It was negative.

DR. BARKER: Now let us look at the *x*-ray plates (Fig. 5). The borders of the heart cannot be very distinctly made out. But observe that the heart is farther to the left than it should be. The knuckle of the aorta is a little prominent. Notice that the outline of the first curve of the cardiovascular stripe, as well as that of the second curve, on the right is obscured by something. You can see a shadow extending from the right clavicle to the heart. The heart itself, you observe, is in an upright position, owing to the fact that the base is dislocated to the left. The shadow obscuring the two curves is most intense in the mediastinum and extends lateralward into the lung area. At this point there is some mottling of the lung area. Then you see a clearer area, possibly due to the presence of a partial pneumothorax. There is evidently a mass situated in the mediastinum, extending more to the right than to the left; it evidently involves the right lung and the right pleura, and the plate suggests the existence of a partial pneumothorax and of partial collapse of the right lung.

When was the piece of gland removed from the right neck for examination?

STUDENT: The day before yesterday.

DR. BARKER: A stained section is here now under the microscope. Let us examine it at once in order to ascertain whether it shows the inflammatory changes suggestive of tuberculosis, syphilis, or Hodgkin's disease, or whether we have to deal with a metastasis from a neoplasm, say a carcinoma or a sarcoma. (To student): What does the specimen under the microscope look like to you?

STUDENT: It looks to me like lymphosarcoma.

DR. BARKER: Yes. It is, we believe, a true lymphosarcoma. Dr. L. T. Webster's report on the microscopic study of the gland excised from the right supraclavicular fossa is as follows:

"The section shows the framework of a lymph-gland. The capsule is not definite; hemorrhage and large round cells have distended and infiltrated the connective tissue. A few trabeculae stand out clearly, but the structure of the gland is entirely obliterated. No germinating nodules and very little lymph-tissue is seen. The gland is filled with large round cells with pale staining, generally spherical nuclei and little or no protoplasm. These cells, closely packed, do not seem to have other stroma than that of the lymph-gland. They are invading the capsule and the surrounding fat. *Diagnosis:* Lymphosarcoma. Metastasis from mediastinum."

Please tell us what the examination of the patient's blood showed.

STUDENT: The report is as follows: Red blood-cells, 4,270,000; white blood-cells, 11,000; Hb., 63 per cent.

The differential count was: Polymorphonuclear neutrophils, 72.6 per cent.; large mononuclears, 6 per cent.; lymphocytes, 20 per cent.; transitionals, 2.4 per cent.

DR. BARKER: How about the urine?

STUDENT: The examination of the urine yielded practically negative results.

[At this juncture the patient was permitted to return to the ward.]

DR. BARKER: Now the question is, What can we do to help this patient? He has a large mediastinal lymphosarcoma with metastases. (To student): What do you think might be done therapeutically?

STUDENT: Two possibilities are open to us: one, radical treatment by extirpation, and the other, treatment by the use of radium.

DR. BARKER: Which of them would you advise?

STUDENT: I should think that radium offered the better prospects of relief in this case.

DR. BARKER: I think you are right. Any attempt at surgery in this case would, in my opinion, be futile. And even with radium, it is a question whether much can be gained.

Now let us epitomize the more important points in the case: This man of fifty-seven began to be ill about four months ago, noticing first a cough and then shortness of breath, both symptoms growing rapidly worse, so that within three weeks of onset he was incapacitated. The paroxysms of coughing soon became associated with severe hemoptysis. Pain in the midthoracic region of the back soon appeared, with radiations. Later, severe pain began in the left lower extremity. There was rapid loss of appetite and strength. On examining him, we found tachycardia, tachypnea, stridorous dyspnea, cyanosis with dilated veins, and edema over the upper half of the body ("collar of Stokes"), abnormal dulness over the mediastinum and extending to the right thorax, with absence of breath sounds and vocal fremitus over most of the right lung, enlarged glands above the right clavicle, distant heart sounds, and a surprisingly large area of cardiac dulness considering the emphysematous type of thorax. The Wassermann test was negative. x -Ray examinations of the chest have revealed an abnormal shadow in the mediastinum extending toward the right lung and pleura with a clear area that suggests a slight pneumothorax.

The histological examination of an excised lymph-gland shows the presence of a metastatic lymphosarcomatous growth.

We can, I think, safely make the diagnosis of primary lymphosarcoma of the mediastinum with direct extension into the right lung and right pleura, compressing or invading the superior vena cava so as to cause obstruction, and metastasizing into the lymph-glands of the right neck and possibly into the spine. The explanation of the large area of precordial dulness and the distant heart sounds is not quite clear; there may be an effusion in the pericardial cavity or the pericardium may be infiltrated by the neoplasm.

Now, as to therapy, in such a case as this I think that it is worth while to try the effects of radium. We have known marked improvement to follow its use in a number of mediastinal growths. Even if cure be not effected, some relief may be obtained. Dr. Lichty, of Pittsburgh, has told me of a case in which Hodgkin's disease had invaded the whole mediastinum, the glands of the neck and of the abdomen, as well as the liver. The patient was apparently *in extremis*, but after the application of radium the glands diminished in size, the breathing was much easier, and the patient is now able to be up and about.

I know of another patient, a woman in Washington, who had a large mass in the mediastinum, extending from the neck to the diaphragm, and accompanied by dyspnea, substernal pain, and cyanosis. Under radium treatment the whole mediastinal mass, as far as the x -ray could show, disappeared.

Still another interesting case of this kind that has come under my observation is one that I saw with Dr. Henry C. Buswell, of Buffalo. In this instance the x -ray examination showed a mass that looked like that of a thoracic aneurysm, but the clinical signs of aneurysm were not present and the Wassermann test was negative. Excellent roentgenologists, however, thought that an aneurysm was certainly there. Dr. Buswell thought, despite the x -ray findings, that the mass was more probably a neoplasm. The question was settled, ultimately, by applying radium treatment, under which the supposed aneurysm disappeared completely. The patient now seems to be quite well, and it was certainly fortunate that Dr. Buswell had the courage of his conviction. It would be interesting to observe the effect of radium treatment in this case. Dr. Bloomfield, do you think Dr. Burnam could undertake to apply radium.

DR. BLOOMFIELD: Yes; he will do so if it is desired.

DR. BARKER: I am glad of it. I think it offers the prospect, at least, of some relief. Within the last year Dr. Burnam has published a report of 8 cases of mediastinal growths treated with radium, 6 of which, he asserts, were greatly benefited by it. In one case there was no response. The eighth case, at the end of nearly three years, was apparently perfectly well; the patient was a farmer, and, at the time the report was written, he was able to do full work. A roentgenogram, taken when the radium treatment was begun, had shown a deep-seated mediastinal tumor, probably sarcomatous in character, causing various pressure symptoms, especially difficulty in deglutition. Another roentgenogram, taken two years later, showed no signs whatever of the growth. In the article referred to, Dr. Burnam says that as far as he has been able to ascertain there has never been a surgical cure of a malignant mediastinal tumor.

Subsequent History of the Case.—During the patient's further stay in the hospital he was extremely uncomfortable. He was treated twice with radium by Dr. Burnam at Dr. Kelly's sanatorium. On the first occasion 3 mgm. of radium were applied, at 5 inches, for three hours over the chest, and for three hours over the back. On the second occasion, a week later, 3282 mgm. of radium were applied to the neck for one hour, to the anterior chest for three hours, and to the posterior chest for three hours. After the first treatment there seemed to be considerable temporary relief, especially in regard to breathing. The improvement lasted only for a day or two, however, and otherwise the radium treatment of this case was a failure. The pain in the patient's left leg became so severe and the cough so troublesome that large doses of morphin were required to alleviate these symptoms. The patient grew steadily worse; his heart began to fail, and he died about six weeks after admission.

Summary of Autopsy Report.—"Primary lymphosarcoma of the mediastinum, invading the right lung and the superior and inferior venæ cavæ, with metastases to the suprarenal glands and to the bone-marrow. Secondarily, there was hemothorax and hemopericardium. Fibrous pleural adhesions at the right apex were also present. The application of radium to the thorax had caused early degeneration of the tumor cells."

Our second patient, John S., is a farm laborer, forty-four years old. He was admitted to the hospital yesterday, complaining of

“fulness of the chest and shortness of breath.” His family history is irrelevant and his past history is negative, except that he has had two Neisser infections, the second of them twelve years ago. Twenty years ago he had a local sore. Until about six months ago, when he was obliged to stop on account of illness, he worked hard upon a farm. He eats regularly and sleeps well. He has never smoked to excess, but until a year ago, when his illness obliged him to stop, he was in the habit of drinking as many as 40 glasses of beer every week, as well as $\frac{1}{2}$ pint of whisky.

The patient's present illness began between three and four years ago, with cough. After about six months he developed a pain in his right side, in the second intercostal space, just to the right of the sternum. This pain radiated to the right shoulder, and was increased by violent exertion, which usually occasioned dyspnea as well. I would have you note these three symptoms, namely, cough, pain in the chest, and dyspnea. The symptoms became steadily worse, and about two years ago, that is, eighteen months after the beginning of his illness, he noticed that he was becoming very short of breath. He also at that time observed a change in his voice. At present the pain in the chest has disappeared, but the dyspnea and the cough are greatly increased and he has occasional attacks of hemoptysis.

Physical examination, made on admission, showed a small, slightly built man, of the cretinoid type, sitting up in bed and apparently suffering considerable respiratory distress, especially during expiration. His temperature was 100° F.; his pulse, 90; and his respirations, 24. His face and neck were suffused and cyanotic. If you look at him now you perceive the cyanosis and also that the orthopnea is still well marked. He is obliged to sit up in bed, supported by pillows, in order to breathe with any comfort. The veins in his neck, as you see, are overfull and he is quite blue. There is some purulent gingivitis. A slight degree of exophthalmos and a slight von Graefe sign are present. The pupils react normally to light and on accommodation. The left pupil is, however, slightly larger than the right. Over the anterior chest and the abdomen the superficial veins are dilated, and a few larger vessels can be traced, running from the chest to the abdomen. I would have you observe that when I press upon these large veins the resulting fulness is above the pressure rather than below it, showing that the flow of blood is from above downward, indicating a collateral circulation between the tributaries of the

superior vena cava and those of the inferior vena cava. There is evidently some interference with the passage of the blood through the superior vena cava to the right atrium.

The large veins are greatly distended, forming a beautiful example of a collateral circulation. The small veins do not seem to be much enlarged. Whatever the obstruction may be, it has evidently developed slowly enough to permit the establishment of an adequate collateral circulation, without the formation of a "collar of Stokes," such as we saw in the preceding patient. We are fortunate in having the opportunity to observe 2 cases of obstruction of the superior cava manifesting such interesting points of resemblance and difference as regards the collateral circulation. In the first patient we saw the effects of the rapid development of an obstruction, where there was not time for the development of an adequate collateral circulation, a condition of things resulting, as we saw, in the formation of "Stokes' collar." In this second case, now before us, the obstruction has developed so gradually that the collateral circulation could keep pace with it, and "Stokes' collar," accordingly, has not appeared. In the first instance the onset of the obstruction was relatively rapid; in the second it has been relatively slow.

Now let us examine the respiratory system in this patient. (To patient): Cough, please. You notice at once that there is a certain "brassy" quality to the cough, but it falls short of that of typical "brassy cough." (To patient): Which is harder for you—to breathe in or to breathe out?

PATIENT: To breathe out.

DR. BARKER: Evidently there is both inspiratory and expiratory dyspnea, with stridor. When you have stridor of this type it usually means that there is obstruction to the entrance of air into the lungs through the larynx, the trachea, or the bronchi. An examination of the larynx has shown that there is no actual paralysis of the laryngeal muscles and no obstruction in the larynx. We shall have to try to make out, in our further study of the case, whether there are any signs pointing to stenosis of the trachea or of one or both of the larger bronchi.

The patient's chest can be seen to bulge markedly to the right of the sternum, and, on careful palpation, I can make out definite expansile pulsation over it. A bulge of this kind might go entirely overlooked if the patient were not undressed. I have known pro-

trusion of the chest wall and marked expansile pulsation accompanied by diastolic shock to pass undetected simply because the examining physician did not make the patient undress. It may sound incredible to you, young men and women, trained under modern hospital conditions, that a reliable physician should think of treating a patient without examining him from top to toe. But you must remember that a medical man with a large general practice, whether in town or country, who has to see as many, perhaps, as 30 to 40 patients a day, cannot always command the time required to make all his patients undress completely. It is but little wonder, considering the circumstances in which many busy physicians are compelled to work, that they often temporize a little, treating a patient who complains, say, of a slight cough, unaccompanied by fever, by palliative measures without making a complete physical examination. Of course, if there is no serious trouble, the patient will often soon recover. But such temporizing has its dangers both for the patient and the reputation of the physician. I hope that your experience here, during school days, will convince you of the importance (1) of insisting upon your patients undressing and (2) of your making of complete physical examinations, even in cases in which the complaints suggest the existence of only minor ailments. That way only does safety lie.

Over the base of the heart there is on palpation a diastolic shock with a marked systolic heave; both can be felt to the right of the upper sternum over an area a handbreadth in size. On percussion I can make out an area of dulness that extends 6 cm. to the right of the sternum, at the level of the second intercostal space. On outlining the area of cardiac dulness I find it enlarged, and the apex-beat of the heart is in the fifth intercostal space, $11\frac{1}{2}$ cm. to the left of the middle line. A to-and-fro murmur is audible at the base of the heart, and the diastolic murmur is propagated downward along the left sternal margin. The pulses are equal and synchronous at the two wrists. The pulse is a little quick, but there is no outspoken pulsus celer, and I do not see, on testing for it, any capillary pulse in the finger-nails. The blood-pressure in the right arm is 138/80 and in the left arm 144/90. No tracheal tug can be felt. Over the left lung the percussion note is clear. Over the upper part of the right lung, both front and back, the percussion note is somewhat impaired. On auscultation, numerous squeaking râles can be heard on both

sides, and these are especially marked over the area of dulness on the right. The breath sounds are roughened and the vocal fremitus is increased over the right upper lobe both front and back; breath sounds and vocal fremitus are both slightly decreased in the lower right axilla.

The abdominal wall is rather rigid. On admission the edge of the liver could not be made out, but I can feel it now, four fingerbreadths below the costal margin. The spleen is not palpable. No abnormal masses other than the palpable liver are to be made out in the abdomen. The reflexes—biceps, triceps, periosteal radial, knee- and ankle-jerks—are all somewhat exaggerated. Babinski's sign is negative on both sides. The abdominal and cremasteric reflexes are present and active. Bear in mind that when the reflexes are all overactive, along with anisocoria, in a man who has had a sore on his penis years before, you should not neglect to test for speech disturbances and for inability to calculate. (To patient): Please pronounce for me the following words: *Truly rural*. Now say *Episcopal*. Next, *riding artillery brigade*. Now try *British Constitution*.

You see there is no syllable stumbling. (To patient): How much is 7 times 9? How much is 9 times 7? Subtract 7 from 100; 7 from 93; 7 from 86; 7 from 79. You observe that he makes these simple calculations promptly and accurately. These two simple tests go far toward ruling out a dementia paralytica, especially as there is no Argyll-Robertson pupil.

(To student): How about the urine?

STUDENT: Examination of it was practically negative.

DR. BARKER: And how about the blood?

STUDENT: The blood count showed:

Red blood-cells	5,272,000
White blood-cells	6,500
Hb	85 per cent.

The differential count was:

Polymorphonuclear neutrophils	76.8	per cent.
Polymorphonuclear eosinophils	2.5	" "
Polymorphonuclear basophils	0.5	" "
Large mononuclears	6.01	" "
Lymphocytes	11.5	" "
Transitionals	3.01	" "

DR. BARKER: This shows a slight relative increase of polymorphonuclears. How about the Wassermann test?

STUDENT: It was positive in the blood.

DR. BARKER: One could have ventured to prophesy that it would be positive from the signs and symptoms in this patient. Whenever we have to do with an expansile pulsation of this kind in the upper right chest, in a patient under fifty years of age, we may feel reasonably sure that he has had lues. Of course, a pulsating neoplasm or an empyema pulsans might lead us astray.



Fig. 6.—Roentgenogram of the chest revealing an aortic aneurysm that is compressing the right bronchus. Notice the smaller volume and the greater density of the right lung area consequent upon the bronchostenosis.

Now let us look at the *x*-ray plates of the chest (Fig. 6). The first thing that we notice in them is that the third curve on the left in the cardiovascular stripe is unusually rounded and prominent, indicating what is known as a “bullock’s heart,” due to hypertrophy of the left ventricle. This is an ordinary chest-plate. I suppose a teleroentgenogram has not yet been taken?

STUDENT: No; not yet.

DR. BARKER: A teleroentgenogram would permit us to make exact measurements of the size of the heart for comparison with our percussion results.

Notice, please, in this *x*-ray plate that the aortic arch is far to the left of its normal position. The pulmonary artery and the left atrium are obscured by a shadow in the mediastinum. To the right we find a remarkable condition. There is a large shadow extending lateralward, high up. You will observe that it corresponds in position to that of the area of pulsation and dullness, where the diastolic shock and the systolic lift are to be felt.

There can be no doubt from the physical signs and the *x*-ray findings that we have to deal here with a sacculated dilatation of the ascending arch of the aorta, involving the transverse arch of the aorta as well, and, perhaps, also the descending arch. During the roentgenoscopic examination two pulsating areas could be made out, one large one in the ascending arch of the aorta and one smaller one in the descending arch.

Next I would have you notice particularly the difference in volume between the right and left lung areas in this *x*-ray plate of the chest. The area of the left lung is a good deal larger than that of the right. Observe, also, the difference in clearness on the two sides. The lung area on the left, you perceive, is very clear, probably on account of some compensatory emphysema. On the right, however, you see a slight clouding of the whole lung area from top to bottom. This indicates increased density of structure on that side of the chest. We have already seen on physical examination that the right side of the chest moves much less than the left during inspiration.

Now the question is: How should we interpret these interesting *x*-ray signs when we consider them in association with the physical signs that we have made out? I think that you will agree with me that we must believe that the aneurysm of the aorta has obstructed the right bronchus, and that bronchostenosis exists on the right side. This easily explains the increased density of the whole right lung and its smaller volume.

There are two interesting articles on the appearance of the lung in *x*-ray plates in bronchostenosis, one by Jacobsohn and one by Ziegler, both published in 1913. Perhaps you will find time to look them up in the library during the coming week.

To sum up, then, this patient's history of cough, dyspnea, and

hemoptysis, the physical signs of decreased movement of the right side of the chest and of enfeeblement of the respiratory murmur on the right side, and the findings in the *x*-ray plates yield indubitable evidence of obstruction to the right bronchus, that is, of bronchial stenosis. From the bulging in the upper right front, the expansile pulsation there, the diastolic shock over the same area, and the pulsating shadow on roentgenoscopy, there can be no doubt that the pressure on the right bronchus is caused by an aortic aneurysm. We know also, from the enlargement of the left ventricle and the loud diastolic murmur, that there is aortic insufficiency. We know, too, that the Wassermann reaction is positive in the blood. We are therefore in possession of sufficient data to picture for ourselves the condition of this patient's aorta. We can feel sure that, if we could look at it and could examine it histologically, it would show the characters of luetic aortitis.

Syphilitic aortitis was first described by Döhle in 1895, and then by Heller in 1899. More recently it has been the subject of many interesting papers, especially those by Longcope (1913) and by Winternitz (1913). You must have had yourselves manifold opportunity, during your studies in the Laboratory of Pathology here, to observe for yourselves, both with the naked eye and under the microscope, the characteristic lesions of syphilitic aortitis. You will recall how the tunica media and the tunica adventitia of the aortic wall become infiltrated in circumscribed patches, due to local invasions by the *Treponema pallidum*; how in such areas the muscle-fibers and the elastic tissue fibers are destroyed and replaced by granulation tissue, for this luetic mesaortitis is a productive inflammation; how, as the granulation tissue grows older, cicatrices are formed causing retraction and giving rise to certain peculiar puckerings of the tunica intima; how, as a result of such changes, the wall of the aorta is thinned and weakened, with resulting dilatation and, sometimes, true aneurysm formation. In the present patient, as in most, the changes have been most marked in the ascending thoracic aorta. The wall has yielded and a saccular aneurysm has formed; the latter has compressed the right bronchus and obstructed it, and has also caused pressure upon the superior vena cava partially and gradually obstructing it, so that the collateral circulation already discussed has developed.

Large space-occupying masses in the mediastinum, such as we have had the opportunity of observing today, are of great clinical

interest. The mediastinum may be regarded as a septum, running down the middle of the thorax, between the two lungs. It serves as an area for lodging various important channels of communication, including the heart; the great arteries and veins; the trachea and larger bronchi; the esophagus; and certain nerve trunks, including the vagus, the sympathetic, the phrenic, and the proximal portions of the intercostal nerves. Pressure upon any of these channels of communication produces characteristic symptoms. In our 2 cases of today we have seen the results of compression as it affects especially the circulatory and respiratory systems. When the esophagus is compressed there is difficulty in swallowing and, it may be, localized pain. Has this second patient had any dysphagia?

STUDENT: No; none has been observed in the ward.

DR. BARKER: When the nerve channels situated in the mediastinum are compressed we have corresponding diagnostic signs. If the pressure be exerted upon the sympathetic nerve there may be, first, irritation (dilated pupil, widened lid-slit, protrusio bulbi, and unilateral hyperhidrosis) and, later, loss of function (homolateral miosis and enophthalmos with ptosis sympathica). Compression of the phrenic nerve may cause hiccup, or may give rise to inequality of contraction in the two halves of the diaphragm. Pressure upon the intercostals induces severe intercostal neuralgias. Compression of the vagus and especially of its branch, the recurrent laryngeal nerve, causes paralysis of a part of the laryngeal musculature. The brassy cough, typical of aortic aneurysm, arises from pressure upon the recurrent laryngeal nerve. Other symptoms that may be caused by compression of the vagus include bradycardia or tachycardia (according to the extent of pressure exerted upon it), nausea, vomiting, hyperacidity, and disturbances of the intestinal functions.

Nitsch has shown that there are two weak spots in the mediastinum and that it may be displaced lateralward, either as a whole, or at one or other of these weak places. One of the weak spots is in the upper anterior mediastinum, in front of the trachea, in the region of the thymus fat. The other is in the posterior part of the inferior mediastinum behind the esophagus. If one pleural sac be blown up in the cadaver, these weak areas will balloon out into the opposite side of the thorax. A large pleural effusion on one side will bulge over in this manner and can sometimes be seen on examination with the x -ray. In bronchostenosis, when air cannot get into the stenosed

side, the mediastinal septum will bulge over into it. For some time it was thought that this bulging of the mediastinum accounted for the area of dulness, known as Grocco's triangle, in pleural effusion, but it has been shown that this is not the case.

Aneurysm is one of the most common of large mediastinal masses. Next to aneurysm the most frequent form of abnormal space-occupying mass is some kind of neoplasm, benign or malignant. Sarcoma, usually in the form of lymphosarcoma, is the most common of the malignant tumors; carcinoma comes next in frequency. It is an interesting fact that, though carcinoma of the mediastinum occurs more frequently in women, mediastinal growths as a whole are more frequent in men. Ross found that the sex incidence in the 60 cases observed by him was 2.15 in men to 1 in women. As far as aneurysm is concerned, the reasons for this preponderance in men is, of course, obvious. As regards neoplasms, however, they are not so apparent, though the comparative frequency of carcinoma of the mammary gland in women would make it seem reasonable that carcinoma (metastatic) of the mediastinum should occur frequently in them. Carcinoma of the male breast is, as you will recall, extremely rare. Next in frequency to carcinoma of the mediastinum comes inflammatory enlargement of the lymph-glands there. In children, when the lymph-glands are diseased, involvement of the mediastinum is quite common, especially in connection with Hodgkin's disease and with tuberculosis. Hodgkin's disease is also not uncommon in adults, and when it does occur in them, the mediastinum is frequently involved. Whenever you meet with enlargements of discrete glands in the neck, axilla or groin, especially if they be associated with ascites and enlargement of the liver or spleen, you should at once think of the possible existence of Hodgkin's disease. To make sure of one's diagnosis in enlargement of superficial lymph-glands, however, it may be necessary to excise one of the affected glands, and to examine sections of it under the microscope. In our first patient, you will remember, we were not certain of the exact nature of the disease process until we had done this. In many instances it is a certain means of diagnosis, yet, strange to say, many able physicians fail to avail themselves of it. Especially when there are signs of intrathoracic growth with enlargement of lymph-glands above the clavicle the best way of making the diagnosis secure is to excise a gland under novocain, or under brief general anesthesia, and to make a microscopic examination of sections from

it. Such an excision causes no pain and the wound soon heals. The little operation should, however, be done by a surgeon who is accustomed to the method of procedure required. There is often quite a little bleeding on account of venous obstruction. Moreover, it is desirable to remove a gland as a whole, and not to cut into a gland until it has been removed. I need not explain to you why. I once knew a case in which a country practitioner, unaccustomed to perform the simplest surgical operation, undertook to obtain a bit of gland and to send it to a laboratory for microscopic examination. He went to considerable trouble, made quite a big opening, caused profuse bleeding, and finally succeeded in sending only a fragment of fat! Of course, the whole procedure had to be gone through with again. The gland tissue should be fixed quickly in formalin or in Zenker's fluid; a frozen section of a small fragment may also be made at once for quick orientation. When this procedure is carried out as it should be there is usually no difficulty in diagnosis. In the case of Hodgkin's disease the typical histological appearances with which we are here all well acquainted since the careful studies of Dorothy Reed are easily recognizable. The tissue appearances in carcinoma, lymphosarcoma, and the leukemias also are characteristic. In our first patient we ruled out leukemia by the blood examination. We could not, however, rule out an aleukemic lymphadenosis or an aleukemic myelosis by the blood examination alone, and, in cases in which we have reason to suspect their existence, a diagnosis, to be made with certainty, must rest upon histological examination of an excised gland. Tuberculous adenitis also is characteristic in its histological appearances, though it must be remembered that it and the changes of Hodgkin's disease may be present in the same gland. In children, in whom tuberculous lymph-glands are quite common, the mediastinum is often involved. Syphilis of the mediastinal lymph-glands may also give rise to a large space-occupying mass (gumma). You should keep in mind, too, the fact that compression of the great vessels (causing "Stokes' collar" or the development of a collateral circulation) points to the presence of a mass in the anterior mediastinum, whereas compression of the esophagus (causing dysphagia) and compression of the air passages (causing dyspnea or the signs of bronchostenosis) more often point to a mass in the posterior mediastinum. Of course, we may meet occasionally with cases of intrathoracic struma, of teratoma, and of echinococcus cyst occurring in

the mediastinum, but these belong to the rarer forms of mediastinal masses. An expert roentgenologist can often supply the internist with very helpful differential diagnostic data when he is confronted with a space-occupying mass of doubtful nature in the mediastinum.

I am very glad that I have been able to show you 2 such instructive cases illustrating disease in the mediastinum, and, before I close, may I not express the hope that none of you who may meet with similar ones will ever fail to make use of the several means of differential diagnosis now at our command for the study of these conditions.

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DISEASES OF THE CIRCULATORY APPARATUS

V. THREE CASES OF LUETIC AORTITIS ILLUSTRATING DIFFERENT MANIFESTATIONS OF THIS DISEASE (DIFFUSE DILATATION OF THE AORTA; ANGINA PECTORIS; ANEURYSM OF ABDOMINAL AORTA)

CASE I. A SYPHILITIC, ALCOHOLIC LABORER OF FIFTY, WHO, AFTER A "COLD," DEVELOPED SIGNS OF CIRCULATORY FAILURE AND WAS FOUND TO HAVE MODERATE ATHEROSCLEROSIS AND ARTERIAL HYPERTENSION, ALONG WITH LUETIC AORTITIS, AORTIC INSUFFICIENCY, DIFFUSE DILATATION OF THE AORTA, AND A HYPERTROPHIED AND DILATED HEART.

CASE II. A GROCER'S CLERK, AGED FORTY-FIVE, WHO FOR ONE AND ONE-HALF MONTHS HAD SUFFERED FROM ATTACKS OF ANGINA PECTORIS, IS FOUND ON EXAMINATION TO HAVE AORTIC INSUFFICIENCY, MITRAL INSUFFICIENCY, ADHERENT PERICARDIUM, AN ENLARGED HEART, A DILATED AORTA, AND A POSITIVE WASSERMANN REACTION.

CASE III. A MAN OF THIRTY-ONE, WHO, EIGHTEEN MONTHS EARLIER, BEGAN TO HAVE PAIN IN THE BACK SUPPOSED TO BE DUE TO RHEUMATISM, AND WHO, LATER, DEVELOPED DEFINITE RADICULAR PAINS AND A PULSATING MASS IN THE LEFT HYPOCHONDRIUM. CLINICAL DIAGNOSIS: ANEURYSM OF THE ABDOMINAL AORTA ERODING THE SPINE AND COMPRESSING THE SPINAL NERVE ROOTS. OPERATION AND APPLICATION OF ALUMINUM BAND. DEATH LATER FROM SECONDARY HEMORRHAGE. AUTOPSY.

DR. BARKER: We have today 3 interesting cases before us for study. This would seem a large undertaking for one clinic, but I hope, by abridgment of the histories, to examine all 3 within the hour, for it is important that you should see them all at once in order that you may receive an impression of the different conditions in the aorta that can follow from the variable localization in it of a peculiar, pathological process that is due to the activity of one of

man's worst enemies, the protozoan parasite that we now know as the *Treponema pallidum*.

CASE I

The first patient, John S., is a laboring man, fifty years of age. He entered the Johns Hopkins Hospital on March 16th complaining of having "caught a cold," which was followed by "pain in the chest and shortness of breath."

His family history is unimportant, and as to his personal history he asserts that he has never had a serious illness, though he admits that he had a hard chancre thirty years ago when he was twenty years old. Make a special note of the fact that his luetic infection occurred thirty years since. The patient has been accustomed to heavy work all his life. He uses tobacco moderately and has always used alcohol freely, especially when he was a young man. At present he sometimes drinks to excess on Saturday nights, when he takes as many as 20 "whiskies" and a few glasses of beer as well. Hard physical labor, chronic alcoholism, and syphilitic infection are, then, the important points in the past history.

The patient's present illness began, he tells us, early in December of last year, that is, about four months ago, with a "cold," on account of which he lost a few days from work. Late in January he caught cold again and became very short of breath. It is interesting that he should describe the shortness of breath as occurring after his cold, for, in the particular disturbance of the circulatory system from which he suffers it is quite common, on recording the anamnesis, to hear that the patient had "a cold" or "grip," or some other respiratory affection, after which dyspnea and other symptoms of myocardial insufficiency are first observed.

The patient first applied to a dispensary for treatment, and his condition was somewhat relieved by medicine obtained there, but at the end of a week he had a severe attack of dyspnea accompanied by cyanosis, for which he consulted a doctor, under whose treatment, he says, he improved. Did the doctor do anything for him except prescribe medicine? The report says that he attended the patient for several weeks. Did he outline a mode of life for the patient?

STUDENT: The history is not very definite as to that.

DR. BARKER: Did the patient have to stop work?

STUDENT: Yes; he has not worked since January.

DR. BARKER: So he has been at partial rest since then, if not actually at rest in bed. I emphasize this point, for rest is more important than drugs in the treatment of myocardial insufficiency. If a choice had to be made between rest and drugs, I do not think that any doctor would hesitate for a moment which to choose. It is desirable to make use of both, but "medicine" without rest is far less beneficial than rest without "medicine."

The patient applied to the Out-patient Department of the Johns Hopkins Hospital on February 5th, complaining of shortness of breath and of fulness of the abdomen, both symptoms being more marked after eating. He was instructed to rest and cardiogenic therapy was prescribed. The medicine given him at this time induced polyuria, followed by a decrease in the size of the abdomen, as well as by relief from the discomfort after meals. There was no edema of the extremities in early February, but during the latter part of the month the patient noticed some puffiness of the face, and, about three weeks later, some swelling of the feet and ankles. On March 26th he returned to the dispensary with a racking cough, accompanied by marked shortness of breath and cyanosis, and he was then admitted to the stationary clinic. On entrance to the ward he was dyspneic and somewhat orthopneic. He had a loose, productive cough, with numerous coarse râles that could be heard at some distance.

Let us now examine him for ourselves. In appearance, you note that he is a fairly well-nourished and well-developed man, with a ruddy complexion, and moderate cyanosis of the lips. On the extensor surface of the left forearm and on the back of the right hand there is a scaly papular eruption that tends to be arranged in semicircular forms. He says that this eruption has existed to a variable extent for about three years. It resembles psoriasis, but may be of syphilitic origin. The teeth are poorly kept; several of them are carious, and there is marked pyorrhea.

The thorax is symmetrical and the expansion on inspiration is good, though it is less marked on the upper right side than on the corresponding left. Examination of the lungs and pleuræ shows that the percussion note is impaired over the right apex and also over the right base from the level of the eighth thoracic spinous process downward. The breath sounds are everywhere harsh, with prolongation of expiration. There are numerous moist râles at both bases. At the apex of the right lower lobe there is an area over which moist

râles, both coarse and fine, can be heard, with modified tubular breathing. You perceive that these sounds indicate not only the presence of fluid in the bronchi but also a condition that permits of abnormal transmission of the breath sounds to the ear. Have the signs changed since the patient has been in the hospital?

STUDENT: The lungs appear to be clearing slowly. He still has many coarse moist râles at the bases, but they are not so abundant as they were.

DR. BARKER: Examination of the heart shows a slight general precordial heave. The point of maximum impulse is in the sixth intercostal space in the left mammillary line, but it is diffuse. Relative cardiac dullness extends 15 cm. to the left and 3 cm. to the right of the median line. The normal heart sounds are replaced at the apex and at the base by a loud to-and-fro murmur. The sounds over the tricuspid area are similar to those at the apex. The pulse is a typical water-hammer pulse, and capillary pulsation is plainly visible in the finger-nails and in the mucous membranes. An occasional extrasystole is audible, apparently of ventricular origin. Our electrocardiograph is, unfortunately, out of order at the moment, so no electrocardiogram has been made. Nor have sphygmograms, as yet, been recorded.

The radial and brachial arteries are tortuous and show moderate diffuse thickening. Over the femorals a pistol-shot sound can be heard, though Duroziez's sign has not been made out. The blood-pressure in the Out-patient Department was 200 systolic, 73 diastolic. Since the patient has been in the ward it has been only 150 to 142 systolic, 45 diastolic. The records of the diastolic pressure are, of course, of little significance, owing to the existence of aortic insufficiency.

Examination of the abdomen reveals no abnormal masses, no rigidity, and no shifting dullness. The edge of the liver is palpable three fingerbreadths below the costal margin, and the liver itself is somewhat tender on pressure. No pulsation of the liver can be made out. Make a special note that the liver is enlarged and tender, for this is a point of importance in connection with other signs of myocardial insufficiency.

The reflexes are all present and the deep reflexes are slightly hyperactive. Examination of the genitalia shows the scrotum distended to about the size of a small cocoanut. It is distended and

fluctuating and transmits light. This is not, however, due to edema, but to double hydrocele. The testicles cannot be felt. There is a white scar, the size of a pea, on the prepuce.

How about the blood examination?

STUDENT: It showed:

Red blood-cells.....	4,816,000
White blood-cells.....	5,560
Hemoglobin.....	62 per cent.

DR. BARKER: There is, then, a secondary anemia, with a low color index. Tell me, please, the results of the other laboratory tests that have been made.

STUDENT: The *sputum* is abundant, yellowish, purulent in appearance, and very tenacious. Microscopic examination of the sputum shows pus-cells, numerous cocci, and typical Charcot-Leyden crystals.

The *Wassermann reaction* in the blood-serum is quadruple plus.

The *x-rays* show a large dilated heart and a marked diffuse dilatation of the arch of the aorta.

The *urine* is negative for albumin, sugar, and casts.

DR. BARKER: It is interesting that there are no casts and that there is not even a trace of albumin in the urine, for it shows that there could not have been a high grade of venous stasis at the time of the examination. Prolonged myocardial insufficiency with chronic passive congestion is always accompanied by a stasis-nephropathy, and albumin and casts are usually present in the urine. Moreover, with an arterial hypertension such as this patient exhibits, there must have been some arteriolar change, and in arteriolar nephropathy we meet with at least transitory albuminuria and cylindruria. As we follow this patient's urine from day to day we shall, I feel sure, be able to demonstrate, from time to time, the presence of some albumin and of casts.

Have you the *x-ray* pictures here? Turn the teleroentgenogram the other way, please, so that the heart will be on the left side. I would have you notice what an enormous cardiovascular stripe is to be seen here. The transverse diameter of the heart is greatly increased; there is dilatation not only to the left but also the right. In orienting yourself as to the cardiovascular stripe, remember that there are normally three curves to be made out on the left side and two upon the right. On the left, from above downward, the upper curve cor-

responds to the left edge of the shadow of the aorta, the middle curve to borders of the left atrium and the pulmonary artery, whereas the third curve corresponds to that of the left ventricle. On the right there are two curves, one above and one below. The lower curve is due to the shadow of the right atrium; the upper is due to the shadow of the superior vena cava. Normally, the lower curve on the right will not extend farther than from 4.2 to 4.6 cm. from the median line, and the lowest curve on the left not farther than from 8.5 to 9.3 cm. to the left of the median line. But here the measurements are much greater. What are they?

STUDENT: About 15 cm. to the left and over 5.5 cm. to the right.

DR. BARKER: Yes; the measurements known as M. R. and M. L. are both markedly increased. The advantage of the teleroentgenogram, that is to say, of a roentgenogram taken with the *x*-ray tube at a distance of 2 meters from the patient's back with a very short exposure (one-tenth to one-eighth second), is that it gives us measurements so accurate that they correspond almost exactly to the size of the heart. The limit of error is probably within 2 mm. for either margin of the heart. So, when a permanent record of the size of the heart and aorta is desired, it is best to have a teleroentgenogram made. M. R. corresponds to the maximal distance from the median line to the right margin of the heart and M. L. to the maximal distance from the median line to the left margin of the heart. In this case there is, as you see, a great increase in both measurements (M. R. and M. L.). There is here hypertrophy and dilatation of both sides of the heart. The configuration of the cardiac shadow is interesting too. You are struck by the fact that the shadow looks more transverse than in normal cases and that the lower curve on the left (shadow of the left ventricle) is plump and rounded, projecting like a sheep's nose. Another striking point in the cardiovascular stripe in this case is the broad band that extends downward, both to the left and the right of the sternum. It is due to marked dilatation of the aorta. The *x*-ray plate, like the percussion findings, makes it plain, then, that there is outspoken dilatation of the aorta, as well as marked enlargement of the heart. The aortic dilatation is diffuse, not circumscribed. When we discussed the physical signs you heard that, ever since admission, a loud, blowing, diastolic murmur, replacing the aortic second sound and due to aortic insufficiency, has been audible, as well as a systolic murmur that is probably due to a relative mitral

insufficiency. The diastolic murmur is now exquisitely audible up and down both sides of the sternum. The apex of the heart is situated now more medialward than on admission, but it is still much displaced to the left, being now about in the left mammillary line.

Remember that when you find aortic insufficiency in a middle-aged man, especially if the Wassermann reaction is positive, you should always take particular pains to make sure whether there is also an aneurysm or not. In every such case the patient should be studied with especial care for the presence or absence of signs of either diffuse or circumscribed dilatation of the aorta, and it goes without saying that, for the physical examination, the patient should be fully undressed. Aortic insufficiency is a valvular heart lesion that can often be recognized by inspection alone, and inspection of the thoracic wall is also a most important method when aneurysm is suspected. One should not allow the shirt to be pulled up instead of being taken off altogether, for it is important to examine above the sternum and the clavicles, and this is hard to do satisfactorily unless the patient is fully undressed. You must be careful also to have the patient in a good light, for you need to use your eyes to their uttermost when inspecting the chest wall for the presence or absence of the pulsations of an aneurysm. I think it is wise to follow a definite routine in looking for abnormal pulsations. Begin at the apex of the heart, glance at the precordium as a whole, and go up and down the sternum, with the patient between you and the light; then inspect most carefully the jugular fossa, the infraclavicular and mammary regions, and, later, the scrobiculus cordis (the depression in the epigastrium between the hypochondria). Finally, with the patient sitting up, inspect the back and especially the interscapular region. In examining for abnormal pulsations the following of a definite plan that ensures that no part of the chest or of the aorta can possibly be omitted from inspection will go far toward preventing grave errors of oversight.

Those of our staff who were fortunate enough to be here when Dr. Osler gave clinics on aneurysms will remember with what extraordinary care he inspected every chest in which there was a possibility of aneurysm, and how greatly he was interested in making a diagnosis of aneurysm, whenever possible to do so, by means of the symptoms and the physical signs, without the assistance of the *x*-ray. Examination of the chest by *x*-rays has made the diagnosis of aneurysm in most cases so easy that medical students and even physicians are,

I fear, apt to grow somewhat negligent in the employment of the older methods of physical examination. You should always bear in mind that the x -ray is only one diagnostic method among many. Not long ago I showed you, in this clinic, an instance of the fact that the examination for aneurysm by the x -rays is not infallible. You will all of you remember the case of Mary L., a young woman in whom symptoms and physical signs of aneurysm of the aorta were present, but the x -ray examination was reported negative. The patient died about ten days later and the autopsy revealed an aneurysm of the aortic arch, which had ruptured into the pericardium! In all cases of suspected aneurysm it is wise to avoid reliance on any one method of examination alone, and to employ all the methods of diagnosis that we have at our command.

Certain methods of examination for aneurysm other than those to which I have already referred are of value. Let me remind you of some of them. Remember always to feel the pulse simultaneously in both wrists, so as to ascertain whether there is delay, inequality, or any difference of any kind between the two sides—whether, in short, a “pulsus differens” exists. In this patient, as it happens, there is no difference in the pulsations at the two wrists. Notice also whether there is any difference in the size of the two pupils, for anisocoria is a very common symptom in luetic aortitis and in aortic aneurysm. In this patient one pupil—the right—is distinctly larger than the other. Ascertain, too, whether the respiratory murmur is equal on the two sides of the chest. Sometimes an aneurysm will compress one bronchus, in which event the breath sounds on the two sides will be quite different owing to the unilateral bronchostenosis. In this patient there is no marked difference in the breath sounds of the two sides. Finally, in making a rapid survey of a patient for aneurysm, you should never overlook the so-called Oliver-Carderelli sign; in other words, a tracheal tug. To examine for this incline the patient’s head slightly backward, as I am doing now; grasp his trachea between the thumb and forefinger just beneath the cricoid cartilage of the larynx, press upward, and watch for any sign of a cardiosystolic tug. There is no tracheal tug to be made out in this patient, nor is there any abnormal pulsation visible or palpable in his back. It is interesting that these particular signs are more often present in saccular aneurysm than in diffuse dilatation of the aorta.

In our patient we recognize the diffuse dilatation of the aorta by

demonstrating a wide area of retromanubrial dulness, and by inspecting the aorta itself through the fluoroscope and its shadow in the teleroentgenogram.

Now, why is this man's aorta dilated? He has no high-grade hypertension now, though there is some thickening of the radial and brachial arteries. His systolic blood-pressure is now 150, and that is only a slight elevation above the normal, but you will recall that on admission the systolic pressure was 200. He gives a history of lues contracted thirty years ago and the Wassermann reaction in his blood-serum is quadruple plus.

There are, as you know, two chief causes of diffuse dilatation of the aorta: one is lues and the other is atherosclerosis. In young men lues is the more frequent cause; in older men atherosclerosis (which, you must remember, is not, necessarily, nor indeed usually, dependent upon lues) is the commoner cause. A third cause of diffuse dilatation of the aorta is aortic insufficiency of rheumatic origin, but this dilatation is dynamic rather than organic (as in aortic sclerosis and in luetic aortitis).

In this patient both of these two chief causes are present. For, on the one hand, the patient gives a history of lues and his Wassermann reaction is still positive and, on the other hand, he has led a life of hard labor and has used alcohol to excess, and these are habits of life that are conducive to atherosclerosis; moreover, he has definitely demonstrable thickening of his peripheral arteries and he has had, earlier, a distinctly high blood-pressure, suggestive of arteriolar sclerosis and of arteriolar nephropathy, though at present the blood-pressure is only slightly above normal and the urine is negative.

When both of the diseases that are the chief causes of diffuse dilatation of the aorta are present in one and the same patient, it is difficult, indeed, often impossible, to decide which of the two has contributed the more to the widening of the vessel. Certain criteria have been established, however, by which the facts may be tried in order to help us to form a correct judgment respecting them. Thus, we know that in dilatation of the aorta due to lues the dilatation usually begins at the root of the aorta and in the ascending portion of the aortic arch, this dilatation being the result of a luetic mesaortitis, which most often and most seriously involves that portion of the aorta that is just above the aortic semilunar valves. The condition is very often associated with aortic insufficiency, due

either to involvement of the valves of the aorta in the luetic inflammation, or to a dilatation of the ring where the valve is located as a result of a luetic myocarditis. This diffuse dilatation of the aorta due to syphilis is most often demonstrable, as is sacculated aneurysm due to syphilis, between the ages of thirty-five and forty-five. On the other hand, the diffuse dilatation of the aorta that is due to atherosclerosis is commoner after middle life and is relatively rare in the young. The atherosclerotic changes develop slowly (the intima being involved first) and the elasticity of the vessel is gradually lost. The atherosclerotic change does not show that elective preference for the aorta ascendens that characterizes the localization of luetic aortitis. Still, involvement of the root of the aorta and of the valves of the aorta in an atherosclerotic process is common enough, despite the non existence of a predilection for these parts. Since the Wassermann reaction is positive and the luetic infection is thirty years old in the patient before us, I am inclined to think that we are dealing with a diffuse dilatation of the aorta and with an aortic insufficiency that are mainly of luetic origin.

It is surprising to find how long a luetic aortitis may be in existence before causing discomfort to the patient or endangering his life. A. R. Elliott, in a recent article, remarks that, though syphilitic aortitis, before it has involved the valves, is often latent for a long period of time, its progress, after it has produced aortic valve incompetency, is rapid, often bringing life to an end within two or three years. Levy quotes Stadler as saying that about twenty years usually elapses between the date of infection and death, though he has seen the disease run its course in five years, and Brooks reports seeing it do so in two. You will find comments of importance as regards prognosis in Longcope's excellent article on luetic aortitis.

The time of life at which an aortic insufficiency appears is significant of its etiology. Aortic insufficiency in older men may, of course, be due to atherosclerosis alone, and in younger persons, who have not had lues, the most common cause of aortic insufficiency is, as I have already said, endocarditis due to rheumatic infection. But in the rheumatic cases it is very rare to have an endocarditic aortic insufficiency without simultaneous involvement of the mitral valves. In other words, if you divide life into three periods, aortic insufficiency in early life (up to the age of thirty) is generally due to rheumatic endocarditis; in middle life (from thirty to fifty) it is most often due

to lues, or to atherosclerosis, or to both; whereas the cases of aortic insufficiency that develop in later life (after fifty) are in most instances due to atherosclerosis alone. This is a good working division.

We must not spend any more time upon this "man of fifty years," but I would have you bear in mind that he has been a hard worker, using alcohol to excess, and that in his case there is history of lues of thirty years' duration, a quadruple plus Wassermann reaction being still present; that he came into the hospital after having contracted a "bad cold," complaining of cough, expectoration, shortness of breath, blue lips, and swelling of the abdomen and of the extremities, and that the examination revealed a bronchitis, oral sepsis, secondary anemia, thickened arteries, arterial hypertension, a much enlarged and dilated heart, aortic insufficiency with relative mitral insufficiency, and a marked diffuse dilatation of the aorta. The infection with the *Treponema pallidum*, the hard work, and the chronic alcoholism have, together, done irreparable damage to his circulatory system; and under a superimposed respiratory infection there has been circulatory failure. We shall try (1) to overcome the respiratory infection, (2) to give rest and support to the heart, (3) kill off as many as we can of the syphilitic spirochetes that are still active in his body, and (4) to plan a general dietetic-hygienic regimen suited to a man in his station of life thus seriously handicapped.

CASE II

Our second patient, John B., forty-five years old, a clerk, on entering the hospital complained of "pain in the left side, running down the left arm." His work has been of a heavy character in a grocery store. Up to about seven years ago he was in the habit of drinking moderately; he smokes about one package of cigarettes a day. He has been married two years and his wife has no child and has had no miscarriages. He states that he has not had rheumatism or tonsillitis, though he suffered from the ordinary diseases of childhood.

The patient's present illness began, he tells us, seven and a half months ago, with indefinite pains in the left chest, and since then it has shown an interesting development. The pains occurred only occasionally at first, causing no great suffering or anxiety until about a month after they began, when he had a severe, stabbing pain in the lumbar region, which increased in frequency and intensity until

it forced him to stop work, about three months from the onset of his illness. While at home, making little or no exertion, he suffered less, until January of this year, when the pains in his chest became more severe and changed their character somewhat. They now began to come in attacks, and the pains, starting in the region of the right nipple, extended across the left side and down the left arm, often localizing in the flexor surface of the left forearm and sometimes being accompanied by tingling in the fingers. These attacks, sudden in onset, lasted several minutes. The pain was so severe during an attack that he was forced to stop whatever he was doing, and to sit or to lie down. He found that he could get some further relief by lying face downward, with a pillow under his chest, or by lying over the side of a couch, in such a position as to exert pressure upon the chest. Pellets of nitroglycerin dissolved on the tongue or ampules of amyl nitrite broken and inhaled, he was glad to discover, relieved him almost immediately. He thinks that the attacks were brought on most often by exertion or by becoming chilled. The pain was accompanied by a feeling of constriction in the chest, but he does not remember ever feeling particularly anxious or fearful while it lasted. During the latter part of January these attacks began to increase in frequency and in severity, until, when he entered the hospital, about March 21st, ten days ago, they averaged in number two per day.

On *physical examination*, this man is seen to be fairly well nourished still, though there are evident signs of recent loss of weight. There is marked visible pulsation of the arteries of the neck and of the brachials and radials. The patient has some carious teeth, as well as a good many crowns, and the gums show some pyorrhea. The epitrochlear glands are palpable, but not markedly enlarged. There is no general lymph-glandular enlargement. The thorax is thin and symmetrical, and the expansion on inspiration is approximately equal on the two sides. The percussion note is somewhat impaired on both sides in front, down as far as the second rib. The breath sounds are harsh, with prolonged expiration and occasional coarse, squeaking râles at both apices. The lungs descend freely on inspiration on both sides.

Examination of the heart shows a marked heave of the precordium as a whole, but there is systolic retraction of the interspaces in the precordial area. The patient had a severe attack of precordial pain

during one of our examinations. There is, as you see, an extensive Broadbent's sign here in the left back; observe how the thoracic wall is drawn in (at each systole of the heart) just below and lateral from the angle of the scapula. The retraction is especially well seen when the patient holds his breath. No diastolic shock can be felt at the base of the heart, nor can one feel a thrill at the base or apex. The point of maximum impulse is in the sixth intercostal space, 15 cm. to the left of the median line. We have here another instance of very marked enlargement of the heart. The relative cardiac dulness extends 5 cm. to the right and $16\frac{1}{2}$ cm. to the left of the median line. There is marked retromanubrial and paramanubrial dulness extending 4 cm. to the right and 6 cm. to the left of the median line. Over the apical area there is a dull booming first sound, followed by a short, high-pitched systolic murmur, well transmitted to the axilla, and audible also in the back. The aortic second sound is almost replaced and followed by a loud diastolic murmur, which increases in intensity down the left side of the sternum. Over the tricuspid area there is a to-and-from murmur; the systolic murmur here is somewhat different in character from that heard elsewhere. In the second left intercostal space one can hear a diastolic murmur, apparently transmitted from the aortic area.

The pulse is regular in force and in rhythm; in character it is a typical water-hammer pulse. The arterial tension is equal on the two sides. I can see marked capillary pulsation in the nail-bed as I press gently upon a finger-nail. What is the blood-pressure?

STUDENT: On admission the systolic pressure was 150 mm.

DR. BARKER: There is diffuse thickening of the walls of the radial arteries and the brachial arteries are visible and tortuous. All the superficial arteries, as you see, are strongly pulsating. A pistol-shot sound is audible over the femoral artery, indeed, over all the large arteries. The arterial sounds are characteristic of this condition and are worthy of attention. Normally, when one listens over the femoral artery, he hears either no sound or a low (arteriodiastolic) tone; but in aortic insufficiency this arteriodiastolic tone may be very loud, so loud that it has been designated "the pistol-shot sound." Often one hears two tones that quickly follow one another (Traube's "double tone") and, if you press down upon the artery, these tones disappear and you hear, first, a normal pressure murmur, and, later, on stronger pressure, a second murmur ("double murmur" of Duro-

zicz). In this patient I hear the pistol-shot sound, though it is not so loud as one might expect it to be. Durozicz's double murmur can be brought out easily by pressure upon the artery with the stethoscope.

(To student): What is the report on the Wassermann test of this patient's blood-serum?

STUDENT: It is quadruple plus.

DR. BARKER: Now let us examine the roentgenograms of this patient's chest and compare them with those of the other patient. You see we have here, too, a much enlarged heart and you will be particularly impressed with the large size of the left ventricle. On the left the lowest of the three curves is very characteristic of dilatation of the left ventricle in aortic insufficiency. The second curve is not especially exaggerated, but in the third curve on the left the marked distention of the left ventricle is obvious. There is also considerable enlargement of the heart to the right, and there is marked diffuse dilatation of the aorta, though there is no sign of circumscribed dilatation. In fact, the cardiovascular stripe shows the typical changes of aortic insufficiency and diffuse aortic dilatation with enlargement of the left ventricle. In this case, as well as in the preceding one, the dilatation of the aorta is diffuse rather than sacculated.

The abdomen of this patient is negative except for the marked dynamic pulsation of the abdominal aorta, always present in aortic insufficiency.

The extremities, aside from the arterial system, are negative. The deep reflexes are equal and active.

He has a secondary anemia (Hb. 65 per cent.; R. B. C. 4,500,000) and his urine contains a trace of albumin and a few casts.

The symptoms and signs in this patient point to extensive disease of the heart, of the aorta, and of the coronary arteries. The whole heart is enlarged and the left ventricle especially is hypertrophied and dilated. There is outspoken aortic insufficiency and slight mitral insufficiency and there is an adherent pericardium. There is marked diffuse dilatation of the aorta and, probably, partial stenosis of one or of both coronary arteries, causing angina pectoris. The man is forty-five years old and his Wassermann reaction is positive. Could the luetic infection account for all these findings? I think it highly improbable. It seems to me more likely that this man had in childhood or later a rheumatic endocarditis and pericarditis that caused

valvular lesions and an adherent pericardium. He has, of course, had lues in addition, and it is very probable that he has had a luetic mesaortitis causing diffuse dilatation of the aorta and narrowing of the orifices of the coronary arteries. Whether the aortic insufficiency here is luetic or rheumatic in origin, who can say? The mitral lesion and the adherent pericardium could scarcely be due to the lues.

An interesting feature of this case is the existence of stenocardiac attacks (angina pectoris). This man has had several severe paroxysms. There can be no doubt, I think, that we are dealing with true angina pectoris, despite the fact that the blood-pressure is a little above normal.

In my experience most patients with severe angina pectoris have a low blood-pressure—arterial hypotension rather than arterial hypertension. On the other hand, I have seen severe anginal attacks occur in patients with a blood-pressure of over 200.

I remember one patient, who came here from York, Pa., last year with a blood-pressure over 200, complaining of severe pain, beginning in one tooth, extending down into the chest, and thence to the left arm. The Wassermann reaction in his blood-serum was positive. He was treated, first, with iodids and mercury, and then with salvarsan, but half an hour after he had had a salvarsan injection *exitus* occurred. Now whether or not his death was due to the administration of salvarsan I am not prepared to say. It may have been coincidence only, as he was suffering frequently from severe anginal attacks.

I have seen many cases of angina pectoris associated with lues treated by salvarsan, with apparent benefit, and I would not hesitate to give salvarsan in cases in which a luetic mesaortitis has caused the coronary narrowing, provided its use was preceded by a preliminary course of mercury and the iodids. Longcope, who has studied luetic aortitis most carefully, is convinced that many such patients are greatly benefited by salvarsan, in fact, he has found the relief of pain and of paroxysmal dyspnea to be the most striking results of salvarsan therapy. It must be acknowledged, of course, that there is always some danger in the administration of salvarsan, but, in my opinion, the risk from the persistence of the lues is, in most cases, greater than the risk of administering salvarsan.

In all cases of angina pectoris we have to consider whether the malady is due to lesions of the aorta, or to lesions of the coronary

arteries, or to lesions of the myocardium. The point is one that has given rise to much discussion. Clifford Allbutt thinks that the aorta rather than the coronary arteries is responsible for the pain of angina pectoris. Certain it is that angina pectoris is a frequent accompaniment of certain diseases of the aorta, such as luetic aortitis, aortic aneurysm, atherosclerosis aortæ, and aortic valvular stenosis or insufficiency. But angina pectoris may also occur in diseases of the coronary arteries, in the myocardopathies, and in arteriolar sclerosis with arterial hypertension. James Mackenzie is of the opinion that the pain in angina pectoris, no matter which of these diverse conditions is concerned, is caused by an impairment of the function of contractility of the heart muscle, the heart muscle itself producing "pain when it is confronted with work greater than what it can readily overcome." The fact that "the pain rarely arises at the first exposure of the heart to the effort that induces the pain" he explains by assuming that "the heart muscle induces pain on the principle of summation of stimuli."

It is generally admitted that an actual occlusion of one of the coronary arteries may be accompanied by an attack of angina pectoris and that such an attack is often fatal. One important sign, by which it can sometimes be ascertained that a branch of a coronary artery has actually been occluded, is audible pericardial friction detected by listening over the heart just after an attack of stenocardiac pain. In cases of this nature, characterized by pain and actual occlusion of a branch of a coronary artery, there is anemic necrosis of the heart muscle (*myomalacia cordis*), in consequence of which pericardial friction develops over the surface of the necrotic area. In my experience that sign in angina pectoris is, generally speaking, of bad omen, though instances do occur in which patients recover even after the occlusion of a branch of a coronary artery. Indeed, we have often positive evidence to that effect in autopsies, where we see hearts with scars in the myocardium, obviously due to former attacks of this nature.

In angina pectoris due to lues the prognosis is much better than in other forms. Some writers seem to think that the majority of cases of angina pectoris are due to lues, but that view does not at all agree with my own observations. Though luetic aortitis is a common cause of angina pectoris, I am sure that lues has nothing at all to do with the majority of cases. Angina pectoris occurring in the thirties

is, I believe, most often due to lues. Dilatations of the aorta and aortic aneurysms, developing at that period of life, are also most often due to lues. But later in life, and especially after fifty, atherosclerosis of the aorta and of the coronary arteries is the most frequent cause of angina pectoris. It is probable, I think, that lues (luetetic aortitis and coronaritis) has played an important part in the etiology of the angina pectoris in this second patient studied today.

CASE III

Our third patient presents a condition that is, perhaps, the most interesting—certainly it is the rarest—of the pathological states that we have chosen for study this morning. There was little or no doubt that lues played a part in the etiology of the diseased states of the 2 patients already examined. Thus the first patient admitted venereal infection thirty years previously and the Wassermann reaction in his blood-serum was positive; the second patient denied all possibility of venereal infection, but the Wassermann reaction, in his case also, was reported as positive, quadruple plus. In this third patient, however, the Wassermann reaction is negative and the patient denies luetetic infection. Nevertheless, I am inclined to believe that he has had lues and that, as a result of it, he has developed a lesion that is of rare and of unusual interest.

The *anamnesis* of this patient, also a clerk, Frank C. C., who comes from a small town in Pennsylvania, contains several facts of importance. He entered the hospital on March 28th, that is, three days ago, complaining of "pain in the back and numbness of the left hip." His family history is unimportant. He himself has, he says, always had good health until the present illness, except that, about two years ago, he had a neisserian infection. Though he thus admits exposure to venereal infection, he denies ever having had a chancre. (To patient): How old did you say you were?

PATIENT: Thirty-one.

DR. BARKER: About eighteen months ago he began to have attacks of pain in the small of the back. At first the pain was not very severe, though occasionally it was bad enough to wake him at night. In July of last year it became considerably worse, sometimes keeping him awake for several hours at a time. This pain was always localized, he asserts, in one place, namely, a small area in the back,

which, when he points it out, is seen to be at the level of the lower end of the thoracic spine and a little to the left of it. The character of the pain is described by the patient as "beating and throbbing."

By the following November the pain had grown so much worse that he was compelled to give up work and went to a local hospital for treatment. A diagnosis of "rheumatism" was made and treatment by baking was instituted, but without affording relief. That is an erroneous diagnosis that has more than once been made, and a form of therapy that is not infrequently employed in the early stages of the affection from which I believe this man to be suffering. It is true that the diagnosis of this lesion in its early stages often cannot be made with certainty by anyone; and, even when the lesion has progressed to a stage at which recognition is possible, the correct diagnosis may easily be missed if the physician fails to examine closely, or to pay due regard to all the facts.

The pain continued to grow steadily worse, and by Christmas the patient had to go to bed, where he remained for three weeks upon a buttermilk diet, since when he has lost weight rapidly. His maximum weight was 133 pounds; a week ago he weighed only 110 pounds, most of this loss of 23 pounds having occurred since last November.

After Christmas he began to have pain also in the left groin and in the front of the left upper thigh. These painful areas have gradually become numb, to such an extent that, paradoxical as it may seem, the patient burnt himself with a hot-water bottle that he applied to relieve the pain!

During the past two months he has consulted several physicians, as well as a "bonesetter," who, he asserts, manipulated his spine and "almost killed him." Notice how interesting the history of the groping therapy in this case is becoming. More light was needed on the diagnostic side to find the meaning of the symptoms. In such circumstances the therapist will do well if he keep in mind the comment of Rosaline in *Love's Labor's Lost*: "Look, what you do, you do it still i' the dark."

On the 18th of March, on a suspicion that a tuberculous kidney might be causing the pain in the back, a cystoscopic examination was made and ureteral catheterization undertaken by a local surgeon, who reported that he "could get nothing from the left kidney." Recently, though still suffering severe pain, the patient has been able to work about half the time.

(To student): Will you please epitomize for the class the results of the several physical examinations that have been made in the ward.

STUDENT: Physical examination on admission showed a poorly nourished man, lying in bed with a pillow under the buttocks (putting the thoracolumbar spine into a position of lordosis), with a marked degree of scoliosis with convexity to the left. The mobility of the thoracic and lumbar spine was markedly restricted, owing to pain. He was in some pain at the time of the examination, and has had more or less severe pain ever since. Examinations of the head and neck were practically negative. On examining the thorax there was impairment of the percussion note at the apices, and the base of the left lung did not descend appreciably on inspiration. The movements of the right lung were quite free. The breath sounds were rather harsh over the two lungs, both in front and in the back. The heart was negative. Inspection of the abdomen revealed a definite, lifting systolic pulsation almost synchronous with the apex-beat and limited in extent to the triangular area high up in the epigastrium above the level of the tip of the eighth rib, extending down 8 to 10 cm. below the xiphoid process. On bimanual palpation, a firm, smooth, pulsating mass that descends slightly on inspiration can be felt. This mass extends from the ensiform cartilage to the left, around to the spine, its lower boundary being about two fingerbreadths below the costal margin. Definite pulsation is imparted to the lower ribs on either side, though this pulsation is more marked on the left than on the right. A definite expansile pulsation can be made out when one hand is placed over the epigastrium and the other over the left upper lumbar region. The percussion note was flat over the mass. The spleen and the left kidney were not palpable. The inguinal glands were somewhat enlarged. Examinations of the genitals and of the rectum were negative. The deep reflexes were hyperactive, but equal on the two sides.

DR. BARKER: Was there any bruit audible over the mass on admission?

STUDENT: None could be made out. There is an area of definite anesthesia to cold and heat, as well as to pain, in the left groin, and it is surrounded by an area of tactile anesthesia, outside of which there is a zone about 2 cm. wide of partial tactile anesthesia.

DR. BARKER: How about the Wassermann reaction?

STUDENT: It was negative. Examination of the urine was also negative.

DR. BARKER: Was there no blood in the urine? In pulsating tumors in the left upper abdomen one must always make sure about this point.

STUDENT: No. There has been no hematuria.

DR. BARKER: What was the report of the examination of the blood?

STUDENT:

Red blood-cells.....	3,696,000
White blood-cells.....	10,000
Hemoglobin.....	65 per cent.

The differential count of the white cells was practically normal, except that the P. M. N. percentage was 74.5 and no eosinophils were seen.

DR. BARKER: There was, then, a secondary anemia, with a slight leukocytosis.

I may tell you that a roentgenogram of the spine shows no erosion of the bones. It was taken in the anteroposterior direction. We should also have a lateral view in order to be sure.

α -Ray examinations after a contrast meal showed a fishhook stomach, displaced downward into the pelvis and over to the right toward the region of the appendix. Now let us turn our attention to the patient.

(To patient): Hold your breath a moment, please. When he holds his breath, I think you can all see the heave of the epigastrium, and the lower ribs on the left side are lifted at each heart-beat also. When I put my hand over this area of pulsation on the left I feel a strong, powerful heave, and when I exert pressure I meet with resistance; but there is no thrill, and I can feel no diastolic shock associated with it. When I put my hand upon the patient's back near the spine, and below the margin of the ribs, I can feel a similar very marked heave. (To patient): Sit up a minute, please. The pulsation is not quite so marked when he is sitting up as it is when he is lying down, but in the area to the left of the upper lumbar spine there is a strong, definitely expansile heave. When I listen over this area I can detect no bruit. (To patient): You may lie down again, if you will. Now, when I listen over the mass in front, I hear no

bruit, but a coarse gurgling sound, due to the movement of gas in the stomach. On palpating such a mass as this great care must be exercised to avoid exerting too much pressure. There is a soft, rounded lower border, compressible, and not nodular. Now the question is, What can this mass be? What do you think it is?

STUDENT: Aneurysm of the abdominal aorta.

DR. BARKER: That is a bold diagnosis to suggest at the outset. What else would you think of as a possibility in this case?

STUDENT: There may be a tumor of the kidney, lying in contact with the aorta and transmitting pulsation from it.

DR. BARKER: Yes; there might be some neoplasm in front of the aorta transmitting the pulsation. Or there might be a new growth of a very vascular character, as, for example, an angiosarcoma, originating in the bone or in one of the viscera. But you had no hesitation at all in stating your opinion as to the diagnosis, despite the fact that aneurysm of the abdominal aorta is one of the rarest diseases that comes under the observation of the medical man. Moreover, when aneurysm of the abdominal aorta is present it is often overlooked. On the other hand, a mistake is often made—perhaps more often—in the opposite direction, that is to say, conditions that are not aneurysm of the abdominal aorta are taken for it. Why have you no doubt in regard to your diagnosis?

STUDENT: On account of the marked expansile character of the pulsation, practically synchronous with the systole of the heart, limited to a relatively small area, and not felt well down in the abdomen. Also, the history of dull pain, localized in that particular area, over such a long period of time is strongly suggestive of aneurysm.

DR. BARKER: But what is aneurysm in young men usually due to? Remember this man is only thirty-one.

STUDENT: It is most often due to lues.

DR. BARKER: Yes; and that is a very important point in this case, for, as you have heard, the Wassermann reaction is negative. Of course, if the Wassermann reaction were positive it would afford very strong confirmatory evidence of the existence of an aneurysm. A recent review of the published reports in regard to the frequency with which the Wassermann test is obtained in cardiovascular disease shows that it is positive in from 25 to 50 per cent. of cases of aortic insufficiency and in from 75 to 100 per cent. of cases of true

aneurysm. Wolfsohn has recently reported his investigations regarding the Noguchi test, with which he obtained 95 per cent. positive reactions in cases of aneurysm. Nevertheless, you must remember that the Wassermann reaction may be temporarily negative in the blood of a patient with aneurysm that is undoubtedly luetic in origin. P. G. Woolley has recently reported a series of 9 cases of ruptured aortic aneurysm, in 3 of which there was no evidence during life of luetic infection, though in all of them the anatomical evidence of lues was positive at autopsy. Was there not some confusion in regard to the report on the Wassermann reaction in this third patient of ours?

STUDENT: Yes; the first test taken was reported positive, but it was afterward found that this report really referred to another case. A second Wassermann test gave a negative result.

DR. BARKER: It would be advisable to make tests on the blood of this patient at intervals over a considerable period before concluding that the Wassermann reaction here is permanently negative. But, notwithstanding the negative Wassermann reaction, there are one or two points in this case that make the diagnosis of aneurysm of the abdominal aorta almost certainly correct. Let me enumerate them.

First, the character of the pain. This began in the spine and has been persistent. It was relieved, to some extent, by rest, but not much by any other means, and it became more and more intense as time went on.

Second, the occurrence of pain was succeeded after a time by the appearance of definite areas of anesthesia in the cutaneous distribution of the twelfth thoracic and second lumbar nerve roots, showing that there must have been some injury to the nerves in the region of the spine, inducing anesthesia in their area of distribution. These two conditions—pain of the character mentioned and radicular anesthetics—are among the commonest and most characteristic signs of an abdominal aortic aneurysm that encroaches upon the spine.

Third, the presence of a mass in the upper abdomen in which there is strong, expansile pulsation, felt on bimanual palpation—one hand over the epigastrium and the other over the back—is very characteristic of abdominal aneurysm. The most common site for aneurysm of the abdominal aorta is the epigastric region, the aneurysm arising at the level of origin of the arteria cœliaca.

Fourth, the absence of anything else, either in the history of the case or in the physical signs, that could adequately account for the features I have just described.

In my opinion, the evidence is, then, very strongly in favor of the existence in this patient of an aneurysm of the abdominal aorta, though it would be unwise absolutely to rule out the presence of a very vascular pulsating neoplasm. I think, however, that the evidence is strongly against neoplasm, for the pulsatile expansion is greater than in an angiosarcoma.

The difficulties of diagnosis in abdominal aneurysm are well illustrated by statistical figures. Thus Dr. Osler says that in 54 cases cited by him a correct diagnosis during life was reached in only 18 cases. In these 54 cases abdominal tumor was present 21 times; pulsation, 35 times; and expansile pulsation, only 8 times. Roentgenography, helpful as it is in the diagnosis of intrathoracic aneurysm, cannot be relied upon in the diagnosis of abdominal aneurysm.

Such an abdominal aneurysm as this patient presents is of great interest, for it is a very rare condition. Dr. Osler states that on analysis of 18,000 admissions to his wards, there were only 16 cases of aneurysm of the abdominal aorta, the ratio of abdominal to thoracic aneurysm being as 1 : 10. The statistics collected by Bryant for Guy's Hospital, during the period between 1854 and 1910, showed 325 aortic aneurysms out of 18,678 necropsies, of which only 54, or 16 per cent., were situated in the abdominal aorta. I am inclined to doubt whether in a larger series the proportion would be quite so large, but you perceive that, in any case, aneurysm of the abdominal aorta is an exceedingly rare condition. This man must, I think, have had lues and a luetic mesaortitis involving the upper part of the abdominal aorta, and at this site a large aneurysm has developed and is now eroding the spine and compressing the roots of the spinal nerves.

Subsequent History of Case I (John S.).—The patient was kept at rest in bed on light diet until the bronchitis subsided and the circulation improved. In addition, the treatment included iodid of potash, gr. v, given three times a day, and inunctions of mercurial ointment, 1 dram each. A little later the patient had a course of digitalis and theocin. He was discharged from the hospital on April 4th as "greatly improved." At that time there was no dyspnea and the edema had disappeared. The pulse was distinctly collapsing

in character, but otherwise not remarkable. The liver edge was palpable just below the costal margin. There were still a few crackling râles to be heard at the bases of the lungs.

About one month later he was readmitted because of a return of symptoms of circulatory insufficiency. The Wassermann reaction was quadruple plus. On Karel diet and digitalis therapy he again improved, and was discharged at the end of a month's stay.

Subsequent History of Case II (John B.).—In this case 0.2 gm. of diarsenol was administered intravenously. It was followed by no reaction. On April 1st the patient had an attack of pain, which was controlled quickly by the use of nitroglycerin. After this he became very irritable and unreasonable. His condition, otherwise, remained practically unchanged, except that under rest and antiluetic treatment he had no further attacks of pain up to the time of his discharge on April 4th.

Subsequent History of Case III (Frank C. C.).—This patient remained under observation in the medical ward for about three weeks, at the end of which time his condition was practically unchanged. He was then transferred to the surgical service, where he was kept under study for about two weeks, with a view to operative interference.

Operation was performed on May 3d, five weeks after the clinic was held, by Dr. George Heuer. An incision was made over the eighth rib, and parallel to it, after which longitudinal segments, each about 6 inches long, were removed from the seventh and eighth ribs. Each segment extended back nearly to the edge of the M. latissimus dorsi. Before opening the thoracic cavity the parietal pleura was freed and stripped away for a considerable distance; after the pleura was incised the lung collapsed. There were some adhesions between the left lower lobe and the upper part of the diaphragm at the point where bulging and pulsation due to the aneurysm could be seen. After these adhesions were freed the lung fell back and the descending thoracic aorta was exposed. An aluminum band of No. 43 metal, about $\frac{3}{4}$ cm. wide, was placed around the aorta, and then rolled until a definite thrill could first be felt and later be perceived to weaken. The amount of constriction employed was estimated as amounting to about two-thirds of the diameter of the aorta. Definite pulsations could still be felt in the aorta below after the application of the band, but the operator was unwilling to employ further constriction. The aneurysm could be easily seen on lifting the diaphragm, and pulsation

was observed in it after the application of the band, though it was not so marked as before. The fascia around the aneurysm was secured by interrupted silk sutures. The layer of fascia seemed to afford pretty good protection to the band, so that it was not thought advisable to take a piece of fascia and place it around the band, a procedure that had previously been considered. The wound was closed by means of interrupted sutures of coarse or of fine silk. After closure of the skin a large trocar was introduced into the left thoracic cavity, and by means of strong suction sufficient air was removed, it was thought, to make the lung expand. No definite bruit could be heard on listening over the aorta or over the back after the operation.

At first the patient did very well. Six days after the operation the wound was perfectly healed and the stitches were removed. After this the patient began to suffer a great deal of pain on the right side, similar in character to that which he had had on the left side before the operation. An *x*-ray examination made on May 27th showed a thickened left pleura, with some fluid in the left lung, and partial collapse of the lung, due to pneumothorax. About ten days later the patient complained of constant pain on deep inspiration in the left chest. Examination showed an area of dulness, extending up to the inferior angle of the scapula in the back and to the fourth intercostal space in front. The breath sounds were feeble over this area and pectoriloquy was pronounced. A friction-rub, synchronous with respiration, could be heard at a point situated at about the middle third of the incision. Two days later the physical signs were unchanged, though the pain in the left chest was somewhat less. Examination of the blood showed the white corpuscles to be 15,960. Thoracentesis was performed and a reddish fluid removed, that showed:

White blood-cells (almost all mononuclears).....	2,000
Red blood-cells.....	60,000

A culture from the pleural fluid was negative. The character of the fluid suggested the probability that a slight leak had occurred about the band.

After the thoracentesis the patient's condition grew steadily worse. He became very anemic and extremely weak. On June 8th he had an attack of agonizing pain in the lower part of the back on the right side, requiring large doses of morphin for its relief. Next day

(June 9th) he had a pulmonary hemorrhage; the lungs seemed to fill up with blood, the expectorated fluid was frothy, and he died in about ten minutes.

Autopsy.—It was found that the band at its upper edge had cut entirely through the wall of the aorta, except for a strip about $\frac{1}{2}$ cm. wide, posteriorly. At the lower edge it had cut through at one or two places, anteriorly. The connective tissue and the vessel sheath had formed a new wall that had dilated, forming a false aneurysmal sac around the band. This had held the blood for a time, but, eventually, blood from the false sac leaked into the pleural cavity and then into the left lung. About 3 liters of blood-stained fluid containing large blood-clots was present in the left pleural cavity. The left lung contained a large blood-stained cavity communicating with the false sac. This lung cavity had ruptured into a bronchus, causing the final, sudden, fatal hemorrhage.

The aorta, both above and below the band, seemed to be normal until the level of the aneurysm was reached. There were, in reality, two aneurysms, one of them diffuse, the other sacculated. The diffuse dilatation involved the abdominal aorta at the level from which the celiac artery arises; the aortic wall here showed puckering suggestive of lues, though the aorta higher up, even the ascending arch, showed no evidence of it. The sacculated aneurysm arose from the posterior wall of the aorta directly opposite the origin of the celiac axis, and communicated with the aorta through a neck no larger than the aortic lumen. It was of large size, and was entirely filled with an adherent, antemortem blood-clot. This aneurysm had eroded the bodies of the eleventh and twelfth thoracic vertebræ, had extended into the spinal canal on its left side, and had dissected along the lumbar muscles as far as the crest of the ilium. The intervertebral cartilages were but very little affected, and there was less erosion of the vertebral bones on the right side than on the left. It was thought that the application of the band had caused the clotting in the posterior sac and would probably have cured the aneurysm eventually, if the patient had not had the unfortunate accident of the cutting through of the band, causing fatal hemorrhage.

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VI. SUBACUTE BACTERIAL ENDOCARDITIS OR ENDOCARDITIS LENTA

A MIDDLE-AGED, OBESE, LUETIC, PANHYSTERECTOMIZED COLORED WOMAN, WITH AN EARLIER HISTORY OF RECURRING TONSILLITIS AND ACUTE RHEUMATIC FEVER WITH MITRAL INSUFFICIENCY, COMPLAINS OF FEVER, CHILLS, SWEATS, WEAKNESS AND PAINS IN THE CHEST, SHOWS SIGNS OF CIRCULATORY INSUFFICIENCY, AND IS FOUND TO HAVE AN ENLARGED SPLEEN, A MARKED SECONDARY ANEMIA AND A VIRIDANS BACTERIEMIA; SIGNS OF EMBOLISM OF THE SPLEEN AND OF THE BRAIN APPEAR; DEATH IN COMA; AUTOPSY.

DR. BARKER: The patient whose condition is to be discussed today is very ill. She is so orthopneic that she is being brought into the room in a wheel chair. We shall have the history of the case first, then we shall make a brief examination of the patient before you, after which she may return to the ward and we can go on with the discussion of the condition in her absence.

Mr. Andrus, will you please tell the class the history of the patient up to the time of admission to the hospital.

STUDENT: The patient, Laura W., a colored married woman, by occupation a cook, entered Ward O of this hospital on November 6th complaining of weakness, of shortness of breath, and of pains in the chest.

Her *past history* is of considerable interest. Although she is only thirty-seven years of age, she has had many severe illnesses, having been admitted to this hospital on five different occasions before the present admission.

Thus, in 1905 she was admitted in the month of February suffering from acute rheumatic fever with polyarthrititis, acute tonsillitis, adenoids, mitral insufficiency, and secondary anemia.

In June of the following year, 1906, she was admitted for the second time with another attack of acute articular rheumatism.

In December, 1908 she was admitted for the third time with a third attack of acute articular rheumatism, acute tonsillitis, lobar pneumonia, and cardiac decompensation. After her condition had improved her tonsils were removed; unfortunately, after the operation, there was a secondary hemorrhage and her hemoglobin was

reduced to 55 per cent. She had to remain in the hospital for a time until the condition of the blood improved.

In 1911 she was admitted to the gynecological service of this hospital on account of a pelvic abscess, which was punctured; and later in the same year she was admitted for the fifth time, suffering from chronic pelvic inflammatory disease and chronic appendicitis. An operation was done on the gynecological service, the appendix being removed as well as the uterus and adnexa.

Subject to frequent sore throats before 1908, she became free from these after the tonsillectomy of that year, and she had no further attacks of rheumatism.

On inquiring into her earlier history, she states that she had several of the commoner diseases of childhood, that she has often suffered from nosebleed, that she has had a good deal of trouble with her teeth and gums, and that she has suffered more or less from dizzy spells during the past fifteen years.

She began to menstruate late, the first period occurring at the age of seventeen. After this, however, she menstruated regularly, though the discharge was profuse during the first two days of each period. Menstruation, of course, ceased at the time of the pan-hysterectomy.

She has had several venereal infections. Thus, at the age of twenty-three, she had a gonococcal urethritis and, at about the same time, multiple venereal sores on the external genitals. She states that at about this time there was also a bubo, that her hair fell out, and that sores appeared over the surface of her body. It seems fairly clear that during this period she must have had a syphilitic infection as well as multiple soft chancres and gonorrhoea. For many years past she has had to rise several times at night to pass urine.

During recent years she has worked when well enough as a cook, but, since her attacks of rheumatism, involving also the heart, she has been much handicapped at times by shortness of breath and swelling of the ankles. She admits using beer and whisky, but denies excess.

Questioned regarding her *family history*, she states that both her father and mother suffered from rheumatism, that 2 of her sisters have also had rheumatic attacks, and that 1 of them has heart trouble. One of her sisters died of tuberculosis at the age of sixteen. One

brother died of tuberculous meningitis in this hospital in the year 1904. Her father suffered from severe recurring epistaxis.

The patient dates her *present illness* from an attack of mumps from which she suffered last June. Since then she has been far from well. She has had some fever from time to time, has grown paler, and has suffered much from shortness of breath. She has also gradually grown weaker, and states that she has had pains of variable severity in the chest. During the past few months she has noticed night-sweats frequently, and from time to time also chilly sensations. Recently she has noted tingling in the hands and feet and her fingertips have felt sore on waking in the morning. There have also been some vague pains in the joints. Her appetite was fairly good until three weeks ago, since when she has found it difficult to eat owing to anorexia. Since last June she has been able to do almost no work, the shortness of breath and the pains in the chest and legs having incapacitated her.

During the night of November 5th she was suddenly wakened with a severe pain in the lower part of the chest. When asked to locate this pain with her hand, she pointed to the lower margin of the ribs on the left side. This pain she says was violent, and she decided to enter the hospital for observation and treatment.

DR. BARKER: Would you give us an epitome of the positive findings on admission?

STUDENT: Soon after admission she was examined both by the house officer, Dr. Friedenwald, and by the resident physician, Dr. Mason. Her temperature was 102° F., the respirations 30 to the minute, and the pulse 110. The radials were palpable, but fairly soft, the blood-pressure was 134 systolic, 80 diastolic. The dyspnea was so marked that she was compelled to sit up in bed. There was marked pallor of the mucous membranes and a little general glandular enlargement. There was moderate pyorrhea alveolaris and there were some suspect teeth. She was coughing a little and producing some mucopurulent sputum. The lips were dry and fissured and the tongue coated.

In the chest the percussion note was a little impaired at both bases; there were crackles in both lower lobes and the voice sounds were somewhat distant at the right base. The heart was enlarged, especially to the left, the apex being in the fifth interspace, 13 cm from the median line. There was a palpable thrill at the apex. A

loud blowing systolic murmur was audible in the mitral area and was well transmitted to the axilla. The pulmonic second sound was accentuated. There were no diastolic murmurs. The retrosternal dulness was a little increased. She complained of some tenderness in the precordial area and over the sternum.

A little edema could be made out, the ankles pitting on pressure and also the tissues over the sacrum. On the left lower eyelid a small petechia could be made out, but this has disappeared since admission. The fingers were not markedly clubbed, but the finger-nails were definitely in-curved.

The patient was abdominous. The liver was enlarged, the dulness beginning above at the fifth rib and extending two fingerbreadths below the costal margin in the right mammillary line, where the edge could be palpated. The spleen also was enlarged on percussion and its lower border could be felt two fingerbreadths below the costal margin. The patient complained of tenderness in the left hypochondrium when the spleen was being palpated. No friction-rub, however, was audible over the spleen.

The pupils reacted normally, the eye-grounds were negative, and the deep and superficial reflexes were normal. Mentally the patient was clear and well oriented.

There were no evidences of endocrine disturbance except the slight protrusion of the eyeballs and obesity.

DR. BARKER: If you will bring the patient in we can check up some of these points.

(To the patient): As you are not feeling very well today, we shall not keep you long in the clinic. Have you any pain now?

PATIENT: No, the pain in the chest is better, but it hurts me here (pointing to the abdomen) when they press on it.

DR. BARKER: The general malaise of the patient is obvious, and even at a distance you can, I think, see the pallor of her lips and tongue and observe the obvious shortness of breath. She is breathing now about 30 times per minute, and though the respirations are shallow, they are evidently labored. Her pulse-rate is 108. There is now no sign of the petechia on the lower eyelid. There is still a little edema of the ankles. The heart's apex is about in the anterior axillary line. The apex-beat is forcible and rather diffuse. The thrill is not very marked at present. A loud blowing systolic murmur is audible in the precordial area and can be heard well out into the axilla, as well as

at the base of the heart. Just medial from the mamillary line, in the fifth space, the first sound can be heard and is rather thudding and brusque. I should not be surprised if there were a little narrowing of the mitral orifice here, in addition to the insufficiency. I can hear no diastolic murmur. The signs at the back of the chest are about the same as on admission. The abdomen is, as you see, still very tender, for attempts to palpate the liver and spleen make her wince. But the liver edge and the spleen edge are palpable at about the same levels as on admission, namely, two fingerbreadths below the costal margin. We shall not keep the patient longer, but shall permit her to return at once to her bed in the ward.

(To student): What laboratory tests have been made in this case?

STUDENT: The blood and urine have been examined. On admission the *blood-findings* were as follows: Red blood corpuscles, 2,456,000; hemoglobin, 40 per cent (Sahli); white blood count, 13,480. A smear of the blood was fixed, and stained with Wilson's stain. The differential count showed 76.3 per cent. polymorphonuclear neutrophils, 0.3 per cent. polymorphonuclear eosinophils, 0 basophils, 20 per cent. small mononuclears, 2.6 per cent. large mononuclears, and 0.6 per cent. transitionals. No nucleated red cells were seen. There was moderate anisocytosis, but no poikilocytosis. There was no basophilia. The platelets were normal in number.

The *urine* contained albumin, a few casts, and a few white blood corpuscles. No red blood corpuscles were seen and the guaiac test was negative. The specific gravity varied between 1008 and 1012. The urine contained neither sugar nor bile.

DR. BARKER: Has a Wassermann test been made? You will recall that there is a history of an earlier luetic infection.

STUDENT: Blood was drawn from a vein at the bend of the elbow on November 6th both for a Wassermann test and for a blood-culture. The Wassermann test was positive. Blood-cultures were made on blood-agar plates.

DR. BARKER: Have any bacterial colonies appeared on the blood-agar plates?

STUDENT: No colonies were visible at the end of twenty-four hours, but since then a number of colonies have developed. They seem to be characteristic of *Streptococcus viridans*.

DR. BARKER: Yes. Here is the blood-agar Petri dish. You see a number of colonies that present the characteristic appearances.

Note especially the absence of any hemolytic zone about the individual colonies. If this were the *Streptococcus hemolyticus*, each colony would have a clear zone about it. The *Streptococcus viridans*, on the other hand, is non-hemolytic, or, if hemolytic at all, very slightly so. Several additional differential tests must still be applied to these colonies, but it seems almost certain that they are colonies of *Streptococcus viridans*.

(To student): What is your general conception of the condition in this patient?

STUDENT: She has, I think, a fresh endocarditis due to infection with the *Streptococcus viridans*. This has developed upon the basis of an old rheumatic disease of the mitral valve.

DR. BARKER: Yes, I think every one would agree with you in this conclusion. What do you think was the cause of the violent pain that woke her during the night before her admission?

STUDENT: The pain was evidently in the region of the spleen. I think an embolus from the heart was carried through the splenic artery to the spleen and caused infarction.

DR. BARKER: Yes, that is very probable. Embolic phenomena are very common in this disease. What other arteries are often the sites of emboli in this form of endocarditis?

STUDENT: Emboli may cause a stoppage of any artery in infectious endocarditis, but the clinical signs are most pronounced in the so-called terminal arteries.

DR. BARKER: Yes, the emboli that lodge in the branches of the splenic artery, the renal arteries, the coronary arteries, and the cerebral arteries are those that most often give rise to symptoms. Sudden and violent pain in the region of the spleen, hematuria, stenocardiac attacks, and signs of focal cerebral lesions are not at all uncommon in the course of this malignant malady. What do you think gives rise to the petechiæ in the mucous membranes and in the skin of such patients?

STUDENT: They are probably due to minute emboli in the small arterioles of the mucous membranes and of the skin.

DR. BARKER: Yes, the emboli may consist either of masses of bacteria or of minute vegetations, consisting of bacteria and blood-platelets, swept off from the diseased endocardium.

It is interesting that thus far you have not been able to demonstrate red blood corpuscles or even occult blood in the urine of this

patient. These patients very frequently develop an embolic, hemorrhagic glomerulonephritis. Minute emboli lodge in single capillaries of the glomeruli and lead to slight hemorrhages. This condition in the kidneys has been very carefully studied by Dr. G. Baehr, of New York. He, with Dr. Lande, has recently shown that in some of these cases, besides the focal changes in the glomeruli, there are diffuse, universal glomerulotubular change, very much like those seen in scarlatinal nephritis, or in nephritis after tonsillitis. Sometimes this diffuse glomerulotubular nephritis obscures the typical focal glomerular lesions and their clinical phenomena. When these diffuse glomerular changes occur there is often general edema, elevation of the blood-pressure, and increase of the blood nitrogen. In this patient it would seem that neither the focal nor the diffuse glomerular changes are marked as yet; either may develop later. The albuminuria and cylindruria now present may depend upon the chronic circulatory insufficiency, though I think it likely that at least some damage has been done to the glomeruli by the streptococcus infection. Do you think that this patient has syphilis now?

STUDENT: Yes, the Wassermann reaction is positive.

DR. BARKER: She undoubtedly still has syphilis; the infection has been present during the past fourteen years. The secondaries appeared, apparently, in 1906, when her hair fell out and she noticed sores over the surface of her body. Do you think that the syphilis has anything to do with the circulatory condition?

STUDENT: That is hard to say.

DR. BARKER: It is difficult to be sure. You will recall how common it is in the colored race to have the aorta involved in syphilis; luetic aortitis is especially common in the negro. The retrosternal dulness is somewhat increased here, but there are no definite signs of aneurysm or of marked diffuse dilatation of the aorta. Has a roentgenoscopic examination of the chest been made or a teleroentgenogram taken?

STUDENT: No, she has been in the hospital only a few days and has been so ill that she has not been sent to the x-ray laboratory.

DR. BARKER: We know that she has syphilis, but just where the spirochetes that are keeping up her positive Wassermann reaction are located we do not really know. It would seem that the cardiovascular symptoms in this patient could be sufficiently accounted for

by the old rheumatic infection and by the *Streptococcus viridans* infection.

What do you think the enlargement of the spleen is due to in this case?

STUDENT: It is common to have an enlarged spleen in this form of endocarditis owing to the infection. It may be that infarction of the spleen has increased its size also.

DR. BARKER: Yes, one of the most characteristic findings in subacute infective endocarditis, or endocarditis lenta, of the adult is enlargement of the spleen. The spleen is usually rather firm, much firmer than that of the ordinary acute splenic tumor of infection, but it is, as a rule, not quite so firm as the spleen in chronic malaria. The enlargement of the spleen and the occurrence of chills often lead to the false diagnosis of malaria in these patients. The recurring fever and the night-sweats also often lead to the false diagnosis of pulmonary tuberculosis. The marked anemia and the sallow tint occasionally mislead a physician to think that a pernicious anemia is present; the blood findings, however, in this slow form of endocarditis are characteristic of secondary rather than of primary anemia. The sudden sharp pain felt in the region of the spleen by the patient and the tenderness that has persisted there since are strong evidence in favor of the view that infarction of the spleen has occurred.

What do you think is the most important diagnostic criterion in this form of endocarditis?

STUDENT: The demonstration, by culture, of the presence of *Streptococcus viridans* in the blood in a patient known to have an old endocarditic valvular lesion.

DR. BARKER: Yes, the demonstration of the existence of a viridans bacteriemia clinches the diagnosis. An experienced clinician will, however, feel pretty sure of the diagnosis in a case of this sort even before the reports of the blood-culture are known. A patient with an old valvular lesion who develops a low fever, night-sweats, and chills, or chilly sensations, with petechiæ in the skin or mucous membranes, splenomegaly, marked anemia, and general weakness is likely to have the *Streptococcus viridans* in his blood.

The whole subject of the clinical diagnosis of subacute infectious endocarditis, or endocarditis lenta, was discussed at length at the Cambridge meeting of the British Medical Association (1920). Sir Thomas Horder opened the discussion and Dr. E. Libman, of

New York, who has made the most important contribution to our knowledge of this subject in the United States, also participated. You will find a full report of the papers read and of the remarks made by several clinicians in the *British Medical Journal* of August 24, 1920. I hope that some of you will find time after the clinic to look up this discussion. You will find it interesting reading.

Let us now summarize the results of the diagnostic survey made of this patient. We may say that she is now suffering from endocarditis lenta due to infection with the *Streptococcus viridans*. Superimposed upon her old valvular cardiopathy (mitral lesion) due to the earlier tonsillitis and rheumatic infection she now has the signs of a subacute infection (fever, night-sweats, chilliness, tachycardia, secondary anemia, streptococcus bacteriemia, nephropathy, petechiæ, and splenomegaly). There is enlargement of the heart due to both the hypertrophy and dilatation, and there has been a long period of chronic circulatory insufficiency, more pronounced at present with signs of chronic passive congestion in the lungs, liver, kidneys, and subcutaneous tissues. She has had a splenic infarction. The patient also still has signs of her old luetic infection, as shown by the positive Wassermann reaction. Besides the severe secondary anemia, with hemoglobin reduced to 40 per cent. (Sahli), there is a slight leukocytosis, with relative increase in the polymorphonuclear neutrophilic elements. Finally, there is a moderate degree of obesity and a history of recurrent epistaxis, possibly familial.

(To student): What, in your opinion, is the outlook for this patient?

STUDENT: The outlook is grave.

DR. BARKER: Our experience at this hospital, so far as the treatment of viridans endocarditis is concerned, is very discouraging. When an adult has had heart murmurs, a viridans bacteriemia, enlarged spleen, fever, chills, and sweats the result has been uniformly fatal. I have observed more than 30 of these cases myself, and every one of the patients has died. Dr. R. H. Major has reviewed the histories of the patients who had suffered from the disease in this hospital up to 1912. You will find his paper in the *Bulletin of the Johns Hopkins Hospital* for that year. And our experience has been no more encouraging since his publication. Professor Thayer is this year reviewing the whole subject of endocarditis and our experience with it here, and will report the results of his analyses. Dr.

Libman, of New York, has brought evidence that proves, I think, that now and then a patient with endocarditis lenta does recover. but recovery must be exceedingly rare, at any rate when the full-fledged syndrome, as you have seen it today, is met with. This woman, who has just gone back to the ward, will, in my opinion, not recover. Just how long she will live I cannot tell you. Perhaps a few weeks, possibly a few months from now, she will die.

In this hospital and in private practice in the series of cases I have mentioned I have made use of most of the various therapeutic measures that have been recommended in subacute bacterial endocarditis, including autogenous vaccines, sensitized vaccines, antistreptococcus sera, intravenous collargol injections, intravenous salvarsan, etc., but all without avail. I am, I fear, a poor therapist in this disease, for I feel so hopeless regarding the prognosis, once the syndrome is full-fledged, that I fear my countenance must betray my hopelessness to the patient. We must not, however, permit our despair to prevent us from further experimentation in the therapy of this malady. We may yet find some form of chemotherapy or of immunotherapy that will be successful.

I remember a very sad case in consultation practice last year. A young physician came back from France stating that he had had recurring fever while at work at the front. He had had an old mitral lesion that he had known about for years. When I saw him he had just had a chill, with a temperature of 102° F., followed by profuse perspiration. He was sallow and anemic. A loud blowing murmur was audible in the mitral area and a large, rather firm spleen could be palpated. From the history he gave and the condition in which I found him I at once feared that he was a victim of a viridans infection, and this supposition was confirmed by means of repeated blood-cultures that showed the existence of a viridans bacteriemia. He was a well-informed internist and knew the serious nature of the disease, but notwithstanding the bad prognosis, which I frankly expressed, he determined to fight the infection vigorously and he urged his medical friends to leave nothing undone that might possibly be of help. He first had some infected teeth extracted and had his gums put into good condition, but the fever, chills, and sweats continued. As he had had a good deal of pain in the right hypochondrium and had difficulty in digesting food, he felt sure that he had an inflamed gall-bladder and insisted upon operation by a surgical col-

league. At the operation many gall-stones were removed and the gall-bladder was drained; the wound healed, but the fever, chills, and sweats continued. As I had no hope for his recovery myself, I was loath to subject him to the additional torture of prolonged vaccine therapy or even serotherapy, since in my experience these had never benefited. One of his medical friends, a general practitioner, had great faith, however, in antistreptococcic serum and urged its use in very large doses. Despite my lack of faith in the efficacy of the serum, I consented to its use, since the patient seemed inclined to try it. He suffered violent reactions (fever, chills, urticaria) and, after a few administrations, he himself saw that, instead of being benefited, he was being injured by the injections, and he asked that they be discontinued. A few weeks later he succumbed.

I have seen one patient with a viridans bacteriemia who recovered, but he did not, in my opinion, have an endocarditis. The man was an army officer, who had entered the private ward for treatment for sinus disease. One antrum was filled with pus. The antrum was repeatedly washed out, but as the suppuration continued, a radical operation was done by Dr. S. J. Crowe. After the operation the patient had intermittent fever for several days and, as is our custom when fever persists, we made a blood-culture and were astonished to find that he had a viridans bacteriemia. Though there were no heart murmurs and the spleen was not palpable, I feared, of course, that he might be developing a viridans endocarditis, and I told his wife of my anxiety. In the course of a week or two, however, the temperature became normal, the bacteria disappeared from the blood, and no signs of endocarditis developed. The patient has remained well since. He had, it seems to me, a most fortunate escape. If he had had an old mitral lesion he might not have got off so easily.

A pathetic side of the disease is the comparative well-being of the patients in its early stages and the continuance, in most cases, of an unclouded consciousness up to or until near the end. It is often very difficult to convince physicians who are not well acquainted with the disease of its gravity, and the patients themselves and their families are for a long time sure that the trouble must be trivial. Even after the diagnosis has definitely been made and the family has been told of its serious nature, it is difficult for them to believe that a patient who seems so little disturbed can, in reality, be suffering from an almost inevitably fatal disease. In some instances there are even

afebrile periods and the patient feels sure that he is getting well, but the fever sooner or later returns, chills and sweats recur, and embolic phenomena become observable.

After Schottmüller had shown us how to differentiate the *Streptococcus viridans* from other varieties of streptococci by means of blood-agar plates and had demonstrated its presence in the blood in this slow form of endocarditis, he expressed the hope that, particularly in this form of streptococcal infection, it might be possible to secure favorable results by means of serotherapy, but thus far his hopes have not been realized. The most that we can do, at present, as therapists is on the prophylactic side. We must endeavor to prevent the development of this form of endocarditis and this bacteriemia in patients suffering from rheumatic valvular cardiopathy. In this direction much, I believe, can really be done. Persons suffering from valvular heart disease should take extraordinary precautions to avoid contracting infections and should exercise especial care in getting rid of focal infections. We have tried to emphasize this in the clinic here, and Dr. Libman in New York has repeatedly drawn attention to the importance of such prophylactic measures. Focal infection in the head deserves special attention—pyorrhœa alveolaris, periodontal granulomata, infected tonsils and adenoids, and diseases of the paranasal sinuses are the forms of focal infection to which I especially refer.

Though our therapeutic efforts in endocarditis lenta, once the infection is established, have thus far been fruitless, these failures should only spur us on to greater endeavors to find a cure. We may still find it, as I have hinted, in some form of improved vaccine therapy or serotherapy. I have the feeling, however, that there may be greater hope in the direction of chemotherapy. The effects of ethyl hydrocuprein upon pneumococcal infections and the benefits derivable in the treatment of colon bacillus infections of the urinary tract with mercurochrome make experimental research for a chemical cure of streptococcus infections seem well worth while.

In the few minutes of the clinic still remaining to us I should like to draw your attention to some other studies of viridans infections that interest me greatly. These are certain studies the results of which are difficult to correlate with our experience here with endocarditis lenta in adults. The studies I refer to are: (1) those of Oille, Graham and Detweiler, of Toronto, published in the *Journal of the American*

Medical Association in 1915, and (2) those of von Funke and Falus, reported at the German Medical Society in Prag and cited in an article by E. Münzer, in the *Zentralblatt für innere Medizin* in April, 1920. The Toronto investigators, in whose technic I have entire confidence, found a non-hemolytic streptococcus, usually producing a green color on blood-agar, in the blood of some 26 cases of endocarditis, investigated by a modification of Rosenow's culture method. The majority of these patients had a very mild endocarditis with anemia, joint pains, and fever, but the malady was not accompanied by progressive emaciation, weakness, or marked anemia. Most of the patients were children or young adults, and the majority of them recovered.

Von Funke and Falus reported, subsequent to the work of the Toronto investigators, that they had demonstrated the presence of the *Streptococcus viridans* in the blood of a large number of very mild and benign cases of endocarditis, cases that would ordinarily be described as instances of rheumatic endocarditis.

In these two groups of cases, studied apparently entirely independently of one another, the European investigators apparently being ignorant of the work of the Canadian investigators, the clinical picture and the outcome were totally different from those of ordinary endocarditis lenta with viridans bacteriemia in adults. In these mild cases there were no chills, there was often no history of rheumatism, there was no marked tachycardia, the spleen was only slightly enlarged if at all, and the patients recovered, despite the fact that bacteriological studies in the Toronto cases and in the Prag cases demonstrated the presence in the blood of an organism that showed the characteristics of *Streptococcus viridans*!

If the *Streptococcus viridans* is actually present in the blood of these mild cases ending in recovery, then, as Münzer has pointed out, the diagnostic and prognostic significance of viridans bacteriemia associated with endocarditis must be valued in a wholly different way from hitherto. According to these newer studies, the mere presence of the *Streptococcus viridans* in the blood in endocarditis need not necessarily mean a grave or fatal malady. Only when, in addition to the endocarditis with viridans bacteriemia, such signs as chills, night-sweats, splenomegaly, petechiæ, anemia, and progressive weakness are also present, dare we, from now on, decide that the prognosis is grave.

In the light of these important studies from Toronto and Prag, it will be necessary to investigate anew the relationship between acute articular rheumatism, rheumatic endocarditis, and endocarditis lenta. I cannot yet bring myself to believe that ordinary rheumatic endocarditis is due to the *Streptococcus viridans*. It may, of course, turn out to be so, in which event we shall have to determine whether or not the *Streptococcus viridans* of the endocarditis lenta of malign prognosis is the same organism as the *Streptococcus viridans* of benign infections, or is a different strain. Some years ago Dr. Arthur Bloomfield, in this clinic, made use of Rosenow's method of blood-culture in a number of benign endocarditis cases and benign arthritis cases. Streptococci were occasionally found, but no constant relationship could be established.

If *Streptococcus viridans* is really present in both benign and malign cases, new studies of differences in the virulence of the micro-organism and of differences in the resistance of the hosts will be in order. In this connection I would draw your attention to a recent article by Morgenroth and his colleagues on what is called "super-infection and depression immunity."

The hour is now up and these matters may not be further discussed at this time, but a whole series of new problems present themselves for attack, and some of you will, I know, be interested in following these questions further. The first chief of the medical clinic of this hospital, Professor Osler, did more, perhaps, than any other single man to familiarize the profession with the clinical features of subacute infective endocarditis. Beginning with his Goulstonian lectures in 1885, and continuing with a series of papers throughout his clinical career, Dr. Osler reiterated the characteristic features of this peculiar slow form of endocarditis until the profession generally recognized them. If you have not already read his papers on the subject you should do so at the first opportunity.

Subsequent History of the Case.—The patient underwent a marked change for the worse on December 13th, about a month after the clinic. She became comatose, exhibiting most of the time a peculiar form of periodic breathing. There was evidence of a cerebral embolism on the right side, for on the night of December 13th flaccidity of the left arm and leg appeared along with marked facial asymmetry, with obliteration of the nasolabial fold on the left side; on the following day the patient passed into deep coma, the respiration, although

rapid, became more regular. The temperature rose to 105° F. Death occurred on the next day.

Autopsy Report, Professor W. G. MacCallum, December 15, 1920.—“Chronic mitral endocarditis with insufficiency. Acute mural and valvular endocarditis (*Streptococcus viridans*), affecting the mitral, aortic, and tricuspid valves, the wall of the left auricle, and the chordæ tendineæ. Myocardial degeneration; mural thrombi; pericardial adhesions. Chronic passive congestion of the viscera. Renal and splenic infarctions. Acute nephritis. Panhysterectomy.”

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VII. STOKES-ADAMS' SYNDROME AND PAGET'S DISEASE

HEART-BLOCK WITH COMPLETE DISSOCIATION BETWEEN THE ATRIUM AND THE VENTRICLES, SYNCOPAL ATTACKS, PECULIAR ATRIAL ARHYTHMIA, AND PROBABLY PARTIAL SINO-ATRIAL BLOCK IN A MAN OF SIXTY-SIX SUFFERING ALSO FROM PAGET'S DISEASE OF THE BONES (OSTEITIS DEFORMANS), ATHEROSCLEROSIS WITH CALCIFICATION OF THE ARTERIES, AND CHRONIC FIBROID PULMONARY TUBERCULOSIS.

DR. BARKER: Though this patient sitting in his wheel-chair does not look very ill, he will be found on examination to present a whole series of pathological conditions involving especially the cardiovascular, pulmonary, and skeletal domains. I shall ask the clinical clerk, Mr. Sun, to tell you of his history.

STUDENT: The patient, Worthington J., is a white married man, sixty-six years old, a demonstrator in the use of machinery in a factory. He was admitted to Ward F of the Medical Service of this hospital on February 10, 1921, complaining of shortness of breath, aching around the heart, and chronic catarrh.

Previous History.—In childhood he had mumps, scarlet fever, whooping-cough, and measles. During adolescence, between the ages of fourteen and twenty-three, he suffered frequently from what he calls "chills and fever." The attacks occurred, as a rule, during the summer, and were believed to be malarial attacks, though he states that he was not ill enough to be confined to bed. At the age of twenty-three he spat up a good deal of blood on three successive days, and it is possible that his febrile attacks were not malarial in origin, but were symptoms of a pulmonary tuberculous infection. He married at the age of twenty-three. His wife and one child are living and well, though his wife has had three miscarriages. He denies having suffered from venereal disease of any sort. He gives no history of typhoid or of pneumonia. In early life he had frequent attacks of tonsillitis, but he states that he has been free from sore throat during the past thirty years. He has been deaf in his right ear since childhood. He has never had acute rheumatism; at the age of fifty-nine, however, he began to have pains in his feet, which he speaks of as "rheumatic pains," though there has never been any enlargement or redness in the joints themselves. From the age

of thirty on, except for occasional headaches, he seems to have been practically free from all symptoms of disease, at any rate, as far as he has recognized them. His habits have been good as regards the use of alcohol and tobacco.

During the past ten years he has noticed that he has gradually grown shorter in stature. His height was formerly 5 feet, 1 inch. He is now only 4 feet, 11 inches tall. At the age of fifty he suffered for about six months with what he calls "nervous indigestion"; during this period he had occasional vomiting.

Present Illness.—He dates the onset of what he regards as his present illness to three years ago, when he began to feel weak and to have less endurance than formerly. In May, 1919 he became breathless and his legs easily gave way under him. He found that he could not run, and that it was difficult for him even to walk. He consulted a physician, who prescribed digitalis and rest in bed, telling him that he suffered from "a leaky heart." Despite the physician's advice he continued to work, but he found himself growing ever more breathless on exertion. On December 28, 1919, when turning suddenly, he felt very dizzy and had a sensation of choking in his throat. He was, however, able to walk across the room, but fell upon a chair, uttered a gurgling sound, and lost consciousness for a minute or two.

DR. BARKER (to patient): Did those who saw you notice any jerking while you were unconscious?

PATIENT: They said there was a little twitching of the eyelids and face; nothing else.

STUDENT: On the morning after this attack the patient noticed palpitation of his heart, and was very short of breath. He then went to bed and remained there for several weeks. By February, 1920 he had improved somewhat and was able to be up and about again. In May he suffered a second syncopal attack, and in July a third similar one.

On December 22, 1920 he applied to the medical dispensary of this hospital for examination and treatment. He was there seen by Dr. Mayo, who studied his heart condition and observed the skeletal changes to be referred to later. In the dispensary it was noticed that he had marked arteriosclerosis; that there was some enlargement of the heart with myocardial insufficiency, a blowing systolic murmur at the apex, and apparently a heart-block. A Wassermann

test was made and was reported negative. An electrocardiogram was also made at this time in the heart station (Dr. E. P. Carter).

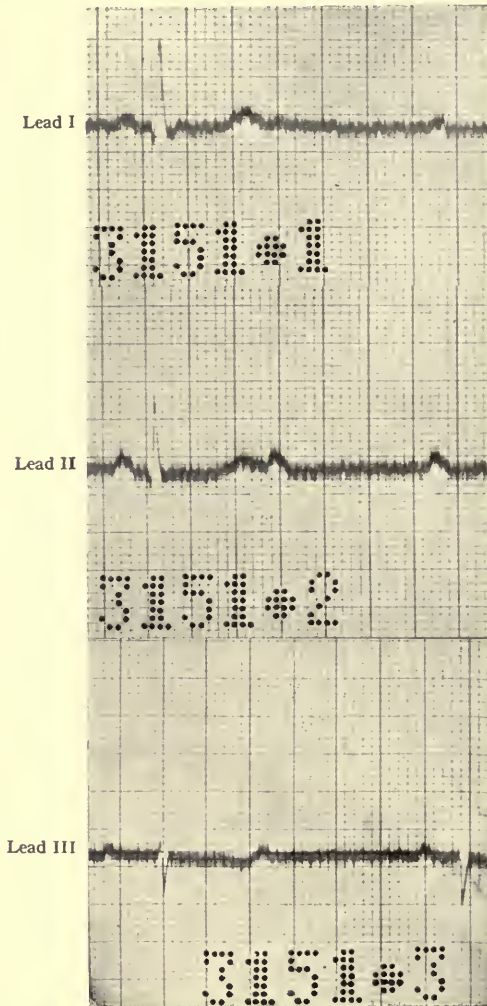


Fig. 7.—Electrocardiogram of the patient when seen in the out-patient department, January 5, 1921. Rate (ventricular, 44; auricular, 88). Rhythm, regular. The P. R. interval varies from 0.15 to 0.26 second. Remarks: Every other P wave lacks a ventricular response. Diagnosis: 2 to 1 heart-block with varying conduction time.

It is stated that it indicated a 2 to 1 heart-block with varying conduction time (Fig. 7).

DR. BARKER: I have just seen this electrocardiographic tracing, and the number of P-waves is about double that of the R-waves. Why did the patient enter the hospital?

STUDENT: On February 1, 1921, while riding in a street car, he felt very weak and uncomfortable; he feared that he was about to have another attack of fainting. Returning to his home, he remained quiet for a week, but despite the rest, had by February 9th grown much worse; he had marked dyspnea on exertion, and found that, on attempting to walk, he had to stop frequently to get his breath. He suffered also from dizziness, pain over the eyes, earache, and thumping of the heart. He therefore decided to enter the hospital ward for treatment.

DR. BARKER: What were the physical findings on admission?

STUDENT: The first physical examination was made by the house officer, Dr. Telinde. The patient's temperature was 98.6° F.; the respiration-rate 20, and the pulse-rate 44. The patient's mind was clear. He was somewhat undernourished and his musculature was flabby. The radial arteries were palpably thickened and beaded from calcification. The blood-pressure was 178 systolic and 70 diastolic.

DR. BARKER: Please note the large pulse pressure in this case; the difference between the systolic pressure and the diastolic pressure is unusually great. This is a feature often met with in heart-block.

STUDENT: There were some interesting skeletal changes. The right clavicle showed an exaggerated curving and its medial half was markedly thickened and nodular. The femurs and the tibiæ were markedly curved, so that the lower extremities were bowed forward and lateralward. The tibiæ especially were much thickened and felt rough on palpation. The skull was triangular in shape and the cranial skull rather overdeveloped in contrast with the facial skull. The facial expression, however, was normal. There was some congestion of the conjunctivæ. The extraocular movements were normal. The pupils reacted to light and on accommodation. There was marked impairment of hearing in the right ear; air conduction was better than bone conduction in both ears. Marked pyorrhea alveolaris was observable, as well as many dead teeth. The tonsils were small. An examination of the eye-grounds revealed tortuosity of the arterioles, but no exudates or hemorrhages were visible. The percussion note was somewhat impaired over the apices of both lungs;

moist râles were audible at both bases, more on the left than on the right.

The apex-beat of the heart was palpable in the fifth interspace about 11 cm. to the left of the median line, and was forceful. A harsh murmur, continuous through systole, could be heard at the apex and was audible also in the axilla; it was followed by a fairly loud second sound. These pairs of sounds occurred at intervals that correspond to the radial pulse-rate. In the long interval between each pair of sounds a small sound could sometimes be heard, apparently due to contraction of the atria without contraction of the ventricles. The pulmonic second sound was accentuated and split. No diastolic murmur could be heard. The abdomen was negative except for a palpable liver edge two fingerbreadths below the costal margin. The deep and superficial reflexes were normal. The testes were small. Rectal examination was negative.

Dr. Telinde made a preliminary diagnosis of arteriosclerosis, chronic arterial hypertension, cardiac hypertrophy and dilatation, myocardial insufficiency with relative mitral insufficiency, chronic nephropathy, heart-block, and Paget's disease.

The patient was also examined by Dr. H. M. Thomas, Jr., who observed what appeared to be isolated *a* waves between the *a-c-v* cycles in the venous pulse, and arranged for the making of phlebograms and electrocardiograms to decide whether or not there was a partial heart-block with 2 to 1 rhythm, or a complete heart-block simulating a 2 to 1 rhythm.

DR. BARKER: Will you now give us the results of the various laboratory examinations that have been made?

STUDENT: Blood examination: R. B. C., 5,840,000; hemoglobin, 102 per cent.; W. B. C., 5360. Differential count in the stained smear: Polymorphonuclear neutrophils, 59 per cent.; polymorphonuclear eosinophils, 7 per cent.; polymorphonuclear basophils, 0.7 per cent.; small mononuclears, 21.3 per cent.; large mononuclears and transitionals, 12 per cent. No pathological white cells seen.

DR. BARKER: There was evidently a slight polycythemia; a relative decrease in the polymorphonuclear neutrophils, a relative increase in the large mononuclears and transitionals, and a rather striking eosinophilia. Has this eosinophilia as yet been explained?

STUDENT: No parasites were found in the feces, nor is there any skin eruption to account for the eosinophilia. The patient has a

bronchitis and dyspnea, but has not complained of asthmatic attacks. The cause of the eosinophilia is not quite clear.

DR. BARKER: Has another Wassermann test been made?

STUDENT: Yes; it is reported negative.

DR. BARKER: How about the urine?

STUDENT: The specific gravity was 1025; the specimens examined have contained a faint trace of albumin and a very few casts; urobilin has been present and some white blood-corpuscles; otherwise the urine has been negative.

DR. BARKER: How has the pulse-rate and the blood-pressure behaved since the patient has been in the hospital?

STUDENT: The pulse-rate has varied between 35 and 45 per minute. The systolic blood-pressure has varied between 134 and 175 mm.; the diastolic pressure between 70 and 83 mm.

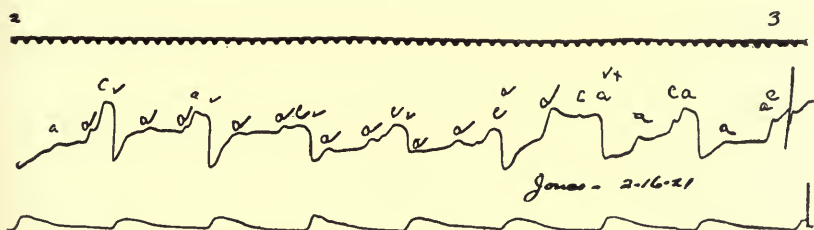


Fig. 8.—Phlebogram and arteriogram of the patient while in Ward F., February 16, 1921. Radial pulse, regular rate, 35 per minute. Jugular pulse, *c*-waves regular, rate 35 per minute; *a*-waves not constantly spaced in relation to *c*-waves, rate 78 per minute. Diagnosis: Complete heart-block.

DR. BARKER: What did the phlebogram show?

STUDENT: Tracings from the jugular vein show the presence of about twice as many *a*-waves as *c*-waves, and there is no constant relation of the *a*-waves to the *c*-waves. The phlebogram indicates the existence of a complete heart-block (Fig. 8).

DR. BARKER: Has the patient been examined since entrance to the hospital by Dr. Carter in the heart station?

STUDENT: Yes, here are the electrocardiograms that were taken by him on February 10th. The atrial rate is 79; the ventricular rate 36. There is no constant relationship, in the electrocardiogram, of the P-waves to the R-waves. Dr. Carter reports "complete atrioventricular dissociation." Here is another set of electrocardiograms (Fig. 9) made yesterday. They show similar conditions.

DR. BARKER: These electrocardiograms are very interesting. There can be no doubt, I think, of the fact that there is complete dissociation; in other words, complete heart-block now exists. The ventricles are beating entirely independently of the atria. The R-R

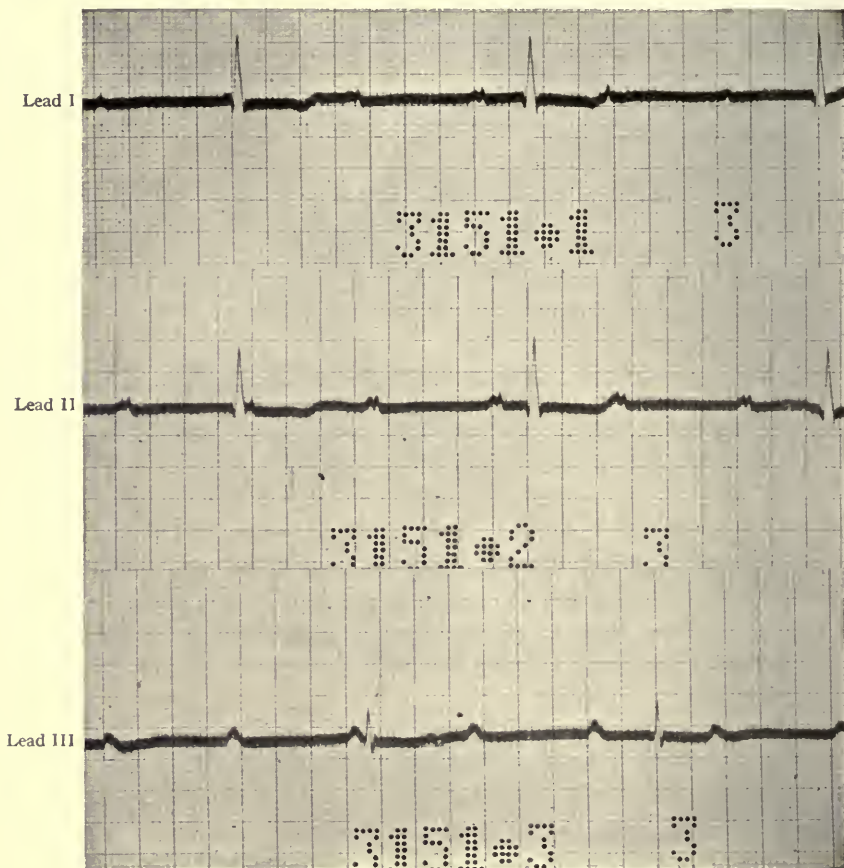


Fig. 9.—Electrocardiogram of the patient while in Ward F., February 14, 1921. Rate: Ventricular, 35; atrial, 84. Rhythm, regular. There is no conspicuous relationship between any two P and R waves. Remarks: P_I and P_{II} are conspicuously notched. T_I and T_{II} are negative. Diagnosis: Complete heart-block.

intervals seem to be equal. On measuring the P-P intervals, however, I find that they are not always equal. There is an atrial arrhythmia here to be accounted for. It is rather striking that the P-P interval in which a ventricular complex appears is sometimes shorter than the other P-P intervals.

Wilson and Robinson, in their paper on "Heart-block" in the *Archives of Internal Medicine* for 1918, called attention to a similar, or identical, disturbance of the atrial rhythm in heart-block. They also found that the interatrial period during which the ventricular systole falls is shorter than those that follow it. In some way or another the ventricular systole seems to be capable of influencing the formation of impulses in the atria.

It is interesting to speculate as to the possible causes of such an atrial arrhythmia in heart-block. Wilson and Robinson have referred to the idea advanced by Erlanger and Blackman (1909), who suggested that the vagus tonus is increased with each arterial pulse-beat. Wilson and Robinson also noticed that in complete heart-block, when the systole of the atrium is superimposed upon that of the ventricle, an ectopic atrial systole sometimes occurs; and it has been assumed that a direct mechanical stimulation of the atrium by the ventricular systole results in such ectopic beats. In some instances the time relations of all the atrial systoles to the ventricular systoles are so influenced by the ventricular rhythm that a fictitious appearance of partial block (2 to 1 rhythm) is brought about. I have wondered whether or not the 2 to 1 rhythm reported to exist when the patient was in the dispensary may have been a simulated partial block when, in reality, complete block existed. But Dr. Carter, who has re-examined the electrocardiogram made at the time, assures me that a partial, not a complete, block existed then.

Thomas Lewis, in association with P. D. White and J. Meakins, has studied complete block simulating partial block in experimental animals. I would refer you to their paper on this subject in the fifth volume of *Heart* (1913-14). You will find an excellent description of the electrocardiographic features of heart-block in the important book by Dr. Thomas Lewis, entitled, *The Mechanism and Graphic Registration of the Heart-beat* (1920). Those of you who are especially interested in the cardiovascular system ought to own this book. It is by far the best treatise that I know of on the newer methods of studying the circulation clinically. You will do well to consult also this volume by Dr. Arthur Hirschfelder, which gives both the older and newer methods of studying the circulatory apparatus. (To student): What do you think is the cause of the heart-block in this patient?

STUDENT: The atrioventricular bundle must have suffered an

injury that prevents impulses passing from the atria to the ventricles.

DR. BARKER: Yes. Can you suggest anything regarding the nature of the injury?

STUDENT: The patient has taken a lot of digitalis.

DR. BARKER: You mean that you think that his atrioventricular bundle has been poisoned by the digitalis?

STUDENT: I think that heart-block of such origin does occur.

DR. BARKER: Yes, undoubtedly. Since electrocardiographic studies have gained vogue we have been made tolerably familiar with digitalis heart-block. Strophanthus and squills can also cause block. After the administration of an excess of any one of these drugs a partial block may appear. Sometimes complete dissociation between atria and ventricles follows digitalis poisoning, even in normal persons. Such toxic block due to digitalis is much more common, however, in patients whose atrioventricular bundles are already diseased. Block due to digitalis poisoning does not, as a rule, persist; if the administration of digitalis be stopped, the block soon passes off. Sometimes a digitalis block can be made to disappear quickly by administering atropin in full doses to paralyze the vagus. This is not always possible, however. When a digitalis block passes off after an atropin injection we may assume that the digitalis has stimulated the vagus and caused a vagotonic heart-block. In the cases in which the digitalis block continues after full doses of atropin it may be assumed that the digitalis has acted directly upon the junctional tissues (Ebedens, 1911; Humes McKenzie, 1910-11). In asphyxial states a toxic heart-block sometimes occurs.

Though prolonged digitalis therapy may cause heart-block, there are reasons for thinking that the heart-block in this patient is not due to digitalis poisoning. Can you think of any other possible cause?

STUDENT: Syphilis sometimes causes heart-block and gummata have been found postmortem in the atrioventricular bundle in such cases.

DR. BARKER: That is true; but this man's Wassermann reaction has been negative on two occasions and there is no history of syphilis.

STUDENT: His wife had three miscarriages.

DR. BARKER: Yes; nevertheless, I do not think it likely that syphilis is the cause of the heart-block in this man. Syphilis is not the only cause of miscarriages. What other cause can you think of?

STUDENT: He has an advanced arteriosclerosis with calcification of the palpable peripheral vessels. He may have coronary sclerosis or an atherosclerotic patch on the endocardium involving the His bundle.

DR. BARKER: Yes; I think that atherosclerotic change is a probable cause. Certainly this man has a diseased myocardium, for he has shown signs of myocardial insufficiency for some time. He has an enlarged and dilated heart with a relative mitral insufficiency. His peripheral vessels are so calcified that we can feel the "beading" with our fingers in the radials and we can see the shadows due to calcified areas in the arteries in x -ray plates made of his legs. Please note how prominently the arteries stand out in this roentgenogram owing to the calcified areas in their walls. It is quite possible that the atrioventricular bundle of His has suffered from an atherosclerotic process.

Another possible cause of this patient's block worthy of consideration is chronic myocarditis. You will recall that this patient had many attacks of tonsillitis in earlier life. He has a mitral insufficiency that may be due to an earlier endocarditis of the mitral valve, though we cannot be sure of this, as a relative insufficiency due to weakness of the heart muscle without actual endocarditic lesion of the valves could cause a similar systolic murmur. It is possible that he has had myocarditic foci with gradual sclerosis of the myocardium, though of this we cannot be sure.

In most cases of heart-block that come to autopsy extensive changes throughout the myocardium are demonstrable. It is only occasionally that the myocardial lesions are limited to the A-V bundle. Usually the involvement of the A-V bundle is merely incidental—a part of a general myocardiopathy. In this article (that I pass around) by Boenniger and Moenckeberg, in the *Deutsche medizinische Wochenschrift* for 1908, you will find the organic lesions associated with heart-block well described. In Dr. Thomas Lewis' *Mechanism of the Heart-beat*, 1911, p. 100, you will also find a careful analysis of the cases in which postmortem examinations had been made in heart-block cases. His list is very valuable for reference.

Workers in the medical clinic here in Baltimore have been especially interested in heart-block, since the fundamental, experimental investigations of Erlanger were made in Dr. Howell's Laboratory in 1906. You should, if possible, read Erlanger's paper some time

during the coming week. You will be impressed by the ingenuity of the experiments by means of which he made his important contribution to our knowledge of pathological physiology.

There is another interesting feature of the electrocardiogram recorded from this patient to which I desire to draw your attention. On looking for the regular recurrence of the P-waves you will notice that now and then a P-wave seems entirely to drop out, or that a totally altered P-wave, one entirely different from the others, makes its appearance. Sometimes instead of an ordinary P-wave there is a deviation that is so slight that one would at first think that the P-wave was really absent. What could be the cause of this?

STUDENT: I do not know.

DR. BARKER: Well, I am not sure either. But I should not be surprised if we had here to deal with a sino-atrial block, which partially or even completely suppresses a P-wave occasionally. According to Dr. Thomas Lewis, sino-atrial block is not so very infrequent as a consort of atrioventricular block, and he has recorded tracings that seem to favor this view.

Evidently, then, we have to deal with complex conditions in this man's heart. The disturbance of the dromotropic or conductive function is less simple than it might at first sight appear; for there is not only complete atrioventricular block, but there is also a variation in the intervals between the atrial excitation impulses as shown by the atrial arrhythmia, and there is occasionally entire suppression of the atrial excitation impulse, or a very marked modification of it, suggesting a possible sino-atrial block of slight degree. I shall enjoy discussing the exact analysis of these tracings with our expert in electrocardiography, Dr. Carter. He will doubtless be able to make clear some of the points that are puzzling to those of us who are less familiar with electrocardiagnosis. It will be desirable, too, to make more electrocardiograms from this patient from time to time in order to establish the constancy or inconstancy of these peculiarities.

The patient's heart is distinctly enlarged judging by the physical examination. Has a teleroentgenogram of the heart been made in this case?

STUDENT: Yes; it is on the illuminating shaft.

DR. BARKER: Yes; here it is. You see that the heart is somewhat enlarged, though rather less so than might have been expected. The measurements are M. R. 5.5; M. L. 8.8. You get a good idea of the

exact form of the cardiac shadow in the plate. The apex of the heart looks full and rounded. It will be interesting to examine this heart under the fluoroscope. I dare say it will be possible on roentgenoscopy to observe (1) that the atrial contractions are about twice as numerous as the ventricular contractions and (2) that there is complete dissociation of the rhythm of atria and ventricles.

This teleroentgenogram, though helpful for judging the size and shape of the cardiovascular stripe, is not satisfactory for information regarding the lungs. Has a lung plate been made?

STUDENT: Yes; here is the chest plate, made especially for the lungs.



Fig. 10.—Roentgenogram showing shadows at the lung apices (chronic fibroid tuberculosis) and the changes of Paget's disease in the clavicles.

DR. BARKER: This plate (Fig. 10) is very interesting. You see that the apices of both lungs are clouded and that there are irregular shadows in both upper lobes below the clavicle, more marked upon the right than upon the left. These changes in the lungs could be due to scarcely anything other than chronic fibroid tuberculosis. I dare say that these shadows represent the scars of the tuberculous process that was associated with hemoptyses and with chills and fever when this man was in his twenties. The shadows in the lower lobes are of entirely different character from those at the apices and in the upper

lobes. It is probable that these alterations in the lower lobes are due either to chronic passive congestion or are the residuals of a non-



Fig. 11.—Roentgenogram showing changes of Paget's disease in the lower end of the femur and in the tibia.

tuberculous inflammatory process in the lower lobes. The patient now shows, clinically, a chronic bronchitis.

Let us examine next the roentgenograms of the femora and of

the tibiæ (Fig. 11). These roentgenograms of the long bones show the characteristic changes of osteitis deformans, or so-called Paget's disease. The process is a rarefying osteitis. The changes are not so marked, however, in these bones as they often are in Paget's disease. The changes are, moreover, more striking in the tibiæ than they are in the femora. In this roentgenogram of the leg, alongside of the tibia, the shadows due to calcification of the arteries are exquisitely visible. Notice, too, the marked changes in the right clavicle in this chest plate. They also are typical of Paget's disease.

The roentgenogram of the skull of this patient shows only slight changes, however, suggestive of Paget's disease. I have placed beside it the skull from another patient who had Paget's disease in a more marked degree. You will notice the strikingly fuzzy appearance of the bones of the skull—an appearance that has been compared to loose cotton wool. When you see such shadows presented by the bones of the skull you can be sure that the patient is the victim of Paget's disease. It is possible that the patient under study today will later on develop more marked changes in his skull.

The pathological process in Paget's disease is sometimes limited to a single bone. Hurwitz has reported such cases from this clinic. It is not uncommon, for example, to find a single metacarpal bone, a single metatarsal bone or a single clavicle, showing the characteristic alterations of Paget's disease. When in doubt as to the existence of Paget's disease in a patient you should always resort to roentgenography as an aid in diagnosis. I am sure that our roentgenologist, Dr. F. H. Baetjer, has more than once called your attention to this fact.

I am surprised that this patient has not developed a more marked kyphosis than he exhibits, for kyphosis usually appears rather early in the course of Paget's disease. Doubtless, the kyphosis will become more marked later on. The kyphosis, together with the calcification of the costal cartilages and the rigidity of the thorax common in this disease, leads to emphysema, to chronic bronchitis, and to myocardial insufficiency—all common findings in Paget's disease. The lower aperture of the thorax is usually widened in Paget's disease. A "violin shape" of the trunk is also one of the characteristic features.

The measurements made of the head and of the lower extremities of the patient are of considerable interest. They are as follows:

MEASUREMENTS OF SKULL AND LOWER EXTREMITIES

Head.

Occipitofrontal circumference.....	54.25	cm.
Occipitofrontal diameter.....	18.25	"
Occipitomenal diameter.....	17.5	"
Biparietal diameter.....	15.5	"
Suboccipitobregmatic diameter.....	15.5	"
Suboccipitobregmatic circumference.....	50.5	"
Bitemporal diameter.....	13.25	"
Vault from meatus to meatus.....	36.5	"

Lower Extremities.

	Right.	Left.
Anterior superior spine to medial malleolus.....	74.5	75.5
Umbilicus to medial malleolus.....	75	76
Anterior superior spine to medial condyle of femur.....	41	42.25
Circumference of thigh 20 cm. above midpatella.	38.25	39
Circumference of calf 20 cm. below midpatella..	24.75	24.25
Circumference of ankles above malleoli.....	12	12
Distance between medial condyles of femora when heels are put together and knees are brought as close together as possible.....	6	"

Time will not permit further discussion of the case at this time. I hope, however, that the conditions you have observed in this patient will stimulate you to read, for there are many points of interest in the patient, both in connection with his heart-block and with his Paget's disease, that should make you desirous of consulting the literature.

Subsequent History of the Case.—The patient remained in the hospital between two and three weeks, during which time he was quite comfortable and improved steadily. He had no shortness of breath after the fifth day from his admission, and on the last two days before his discharge he was able to be up and about the ward without dyspnea. Examination of his heart, made after he had been in the hospital a week, is recorded as follows: "A third sound appears at fairly regular intervals, in one instance split. This third sound varies constantly in its relation to the other sounds, which are regular in rhythm."

The patient was discharged as "improved" on February, 28, 1921, with precise directions as to the use of digitalis.

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DISEASES OF THE BLOOD AND BLOOD-MAKING APPARATUS

VIII. HODGKIN'S DISEASE

ENLARGEMENT OF THE CERVICAL AND AXILLARY LYMPH-GLANDS WITH SPLENOMEGALY, FEVER, CHILLS AND SWEATS, AND WITH A BLOOD PICTURE AND LYMPH-GLAND PUNCTATE CHARACTERISTIC OF HODGKIN'S DISEASE IN A BOY OF TWELVE.

DR. BARKER: This boy looks very pale and has dark rings under the eyes. Mr. F., will you tell us the history of this patient?

STUDENT: The patient, Joseph B., is a white schoolboy, twelve years of age, who was admitted to the hospital six days ago, complaining of swelling in the neck and a lump under the left arm.

His mother states that in February, 1920 a lump was noticed behind and below the left ear the size of an egg, but there was no other swelling elsewhere in the body. A physician examined the boy and, in addition to the swelling mentioned, found, in an x -ray picture, that there were enlarged glands inside the chest. The nose and throat were negative and the blood count normal according to the report made at that time.

A consultant was called in, who advised x -ray treatment monthly. After the patient had two of these treatments the swelling on the right side of the neck markedly diminished in size. Two weeks later, however, a swelling appeared on the right side of the neck. As the x -ray treatments were continued it was noticed that the swellings would diminish in size for about two weeks subsequent to each treatment, but would then again increase in size. It seems that he has had, in all, some four or five of the x -ray treatments.

One week before applying to this hospital for treatment he suffered from "a severe spell of vomiting," and had what was called "a fainting spell," though he did not lose consciousness completely.

The boy has grown progressively weaker and paler since last February. Since that date he has also suffered from chills, fever, and night-sweats. He has gradually become emaciated, the body weight having decreased from 97 to $83\frac{1}{4}$ pounds.

The family history contains nothing of great significance, though one sister had an enlarged gland in the neck that was removed after scarlet fever some thirteen years ago, and another sister died of influenza at the age of fourteen.

The boy himself has had good health up to the time of the present illness, except for measles, whooping-cough, diphtheria, and frequent colds. He has also suffered frequently from epistaxis, this nosebleed following trauma sometimes, at others occurring spontaneously.

As improvement did not seem satisfactory under *x*-ray treatment for the "swellings," the boy was brought to the Out-patient Department of the Johns Hopkins Hospital where he was first seen by Dr. Maurice Pincoffs, who advised that one of the glands in the neck be removed for histological examination in order to make the diagnosis certain. With this test in view he was admitted first to the surgical ward of the hospital and was thence transferred to the medical ward for a general diagnostic survey and for treatment.

DR. BARKER: Would you give us a summary of the physical findings on admission to the medical ward?

STUDENT: The house officer, Dr. Rienhoff, dictated a note on the physical examination, a summary of which is as follows: Marked anemia; undernutrition, 15 pounds; apathetic. Skin very white; no exanthem, cyanosis, edema, or petechiæ. Muscular and osseous systems negative. Tonsils slightly hypertrophied. Trachea deflected somewhat to the right.

Large lymph-glands in the anterior and posterior triangles of the neck on both sides, more marked on the left than on the right. Enlarged glands in the left axilla. Moderate enlargement of the subinguinal glands on the right. These enlarged glands are firm, discrete, and not tender; they are freely movable and the skin over them is unaffected. In size they vary from that of a pea to that of a pigeon's egg.

Thyroid negative. Lungs negative except, perhaps, for slight impairment of the percussion note over the left upper front. Breath sounds everywhere normal. Some retromanubrial dulness and paramanubrial dulness, the latter extending 1 cm. to the right and 4 cm. to the left.

Moderate tachycardia. Heart not enlarged. Soft systolic murmur at the apex and in the pulmonic area, with slight accentuation

of the pulmonic second sound. Blood-pressure, 100 systolic, 70 diastolic. Abdomen negative, except for palpable spleen two finger-breadths below the costal margin. Genitals negative. Secondary sex characters undeveloped. No hirci; no crines. Reflexes normal.

DR. BARKER: The class will, of course, be very much interested to hear the reports of the laboratory examinations that have been made in this case. Mr. F., will you tell us of the findings in the blood?

STUDENT: The red cell count was 3,224,000; hemoglobin, 55 per cent.; white cell count, 7960; Wassermann reaction negative. Differential count of the white corpuscles in the stained smear: polymorphonuclear neutrophils, 66 per cent.; polymorphonuclear eosinophils, 1 per cent.; small mononuclears, 13 per cent.; large mononuclears, 13 per cent.; transitional forms, 6 per cent.

DR. BARKER: I understand that Dr. Frank Evans, of the clinical laboratory, made a special note on the smear of the blood in this case. What did he report?

STUDENT: Dr. Evans' report is as follows: Red cells slightly paler than normal; total white count not increased; differential formula shows an increase in cells of the large mononuclear and transitional type; no eosinophilia; an occasional pathological lymphocyte seen; platelets increased in number; many large forms of platelets present. His impression was that the blood picture was that of an early stage of Hodgkin's disease and corresponded very closely to the blood picture described by Bunting, of the University of Wisconsin.

DR. BARKER: Yes; these findings are very characteristic for Hodgkin's disease. I think one could almost make the diagnosis upon the blood picture alone, namely, the moderate anemia, the relative and absolute lymphopenia, the increase in the large mononuclear elements and the transitionals, and the increase in number and size of the blood-platelets. The lymphopenia here helps to differentiate this form of lymphadenopathy from tuberculous and luetic lymphadenopathies in which there is usually a lymphocytosis. It also differentiates this lymphadenopathy from the leukemic and the aleukemic lymphadenoses, in which the lymphocytes are also absolutely or relatively increased. This lymphopenia indicates a diminution in lymphadenoid leukopoiesis, and is just what we should expect from the histological changes that take place in the lymphadenoid tissue of the body in Hodgkin's disease. I shall refer to these changes later.

To what does the increase in the large mononuclear cells and the transitional elements, so-called, point?

STUDENT: I think to an increased activity of the bone-marrow.

DR. BARKER: There has been some dispute as to the origin of the large mononuclear elements and the so-called transitional forms. I went over the whole literature some time ago and gained the impression that these cells do really have their origin in the bone-marrow, though there are some hematologists who assume that they have their origin in the spleen or from endothelial elements in different parts of the body. I see Dr. Guthrie here. Dr. Guthrie, has this point regarding the origin of these cells, in your opinion, been settled?

DR. GUTHRIE: There may still be some doubt as to their origin, but, in the opinion of the majority of those who have worked on the subject, they arise from the myeloid tissue and not from the spleen.

DR. BARKER: I remember that that was Naegeli's view, and, if I recall aright, it was also the view of Dr. Frank Evans, who studied these cells and their origin carefully.

Is there anything else in the blood picture that points to a changed activity of the bone-marrow?

STUDENT: The increase in the number and size of the blood-platelets.

DR. BARKER: Yes. Since the studies of Dr. Homer Wright, of Boston, we have known that the blood-platelets arise through the pinching off of little bits of the protoplasm of the megalokaryocytes of the bone-marrow. An interesting feature of Hodgkin's disease is that the platelets are increased in number and that many platelets of larger size appear in the blood. Sometimes quite large masses of the protoplasm of the megalokaryocytes are found free in the circulating blood. It would be interesting to stain a smear of this blood with iron-hemotoxylin, since the iron-hemotoxylin stain brings out very beautifully the structure of the protoplasm of the megalokaryocytes.

What it is that determines this pinching off of larger masses of the protoplasm of the megalokaryocytes in Hodgkin's disease we do not know. Certain it is, however, that myeloid leukopoicis and myeloid activity in the production of blood-platelets is somewhat disturbed in this patient.

In the later stages of Hodgkin's disease it is quite common to

find an outspoken increase in the total white count. Sometimes there are 20,000 to 60,000 white cells per cubic millimeter. When the white cell count is thus increased there is usually also a marked increase in the polymorphonuclear neutrophils; they sometimes amount to 80 per cent. of the total white count. In most cases, too, though not in all, there is a marked eosinophilia. In some instances the eosinophil count is very high. In one case I recall that we saw an eosinophil count of 35 per cent., and in another case in this hospital there was an eosinophil count in Hodgkin's disease of 65 to 70 per cent. of the total count. I think Dr. Clough will recall that case.

DR. CLOUGH: Yes. As I recollect it, the eosinophil percentage was over 65.

DR. BARKER: This marked increase in polymorphonuclear neutrophils and in eosinophils, sometimes met with in Hodgkin's disease, points to a great increase in the activity of myeloid leukopoiesis, since both the polymorphonuclear neutrophils and the eosinophils are of myeloid origin. One may say, therefore, that it is characteristic of the early stage of Hodgkin's disease to see a depression of lymphadenoid leukopoiesis and, at least, slight changes in myeloid leukopoietic activity. In the late stages there is often an outspoken increase in myeloid leukopoiesis, with evidence of overproduction of polymorphonuclear neutrophils and eosinophils.

STUDENT: The Wassermann reaction was negative.

DR. BARKER: That is an important point. When the lymph-glands are enlarged it is always necessary to rule out syphilis before deciding that some other form of lymphadenopathy is present.

This patient has had fever, chills, and sweats. How has the temperature ranged?

STUDENT: Since the boy was admitted to the hospital his temperature has ranged between 101° and 103° F.

DR. BARKER: You said that the boy had a soft systolic murmur at the apex, that the pulmonic second sound was accentuated, that his tonsils were somewhat hypertrophied, and that the spleen was enlarged. These signs, together with the existence of a secondary anemia with marked pallor, and the occurrence of chills and sweats, would make one think of some general infection.

STUDENT: One of the assistant physicians suspected the existence of endocarditis lenta, and a blood-culture was made, but there has been no growth in the blood-agar Petri plates.

DR. BARKER: In every case of continuous fever, especially if there be chills, sweats, anemia, and splenomegaly, it is highly desirable to make a blood-culture. I am glad that one has been made in this instance. It might be well to make one or more blood-cultures later on, for sometimes a first blood-culture is negative, whereas later cultures are positive. Even if you are sure that Hodgkin's disease exists, it is desirable to rule out a complicating bacteriemia.

What other laboratory tests have been made?

STUDENT: The urine and feces have been examined. The urine is negative except for the presence of a little urobilin. The stool is normal.

DR. BARKER: The crucial test in the differential diagnosis of Hodgkin's disease of the lymph-glands from other lymphadenopathies lies in the histological examination of the lymph-gland excised for diagnostic purposes. You all remember the so-called "Dorothy Reed lesions" in the lymph-gland of Hodgkin's disease. I have often been able to make a positive diagnosis of Hodgkin's disease from the histological examination of an excised gland when the diagnosis otherwise would have remained in doubt. Has a lymph-gland been excised from this patient?

STUDENT: Dr. Pincoffs suggested that one be excised, but the surgeons felt that the lymph-glands now enlarged lie rather deep, and that it might be better to wait for a time before excision of a gland for the test. Dr. Guthrie has, however, made an exploratory puncture of one of the deep lymph-glands with a needle of rather wide caliber, and has examined a smear made from the punctate.

DR. BARKER: I shall be very much interested to know what Dr. Guthrie found. Certainly examinations of lymph-gland punctates can be very valuable for diagnosis. For example, in African sleeping sickness it is often possible to demonstrate the trypanosomes in punctates of the cervical lymph-glands, and in tuberculous and luetic lymph-glands it may sometimes be possible to demonstrate the etiological agents, the *Bacillus tuberculosis* in the one instance and the *Treponema pallidum* in the other. Would you read us Dr. Guthrie's report?

STUDENT: In the stained smears of the punctate of a gland Dr. Guthrie found cells of several types:

1. Lymphocytes, the small type predominating, though larger ones are also present.

2. Eosinophils, both mononuclear and polymorphonuclear, in great numbers.

3. Occasional mast cells.

4. Large cells of two general types: (a) Cells with large round or oval nuclei, the nucleus being two or three times the size of a small lymphocyte, the protoplasm clear and abundant, the entire cell being from two to ten times the size of an ordinary eosinophil; and (b) cells with nuclei similar to the above, but with protoplasm that stains a pale blue tint; in these large cells mitotic figures were occasionally observable.

5. Some enormous cells were also present, but no definite multinucleated giant-cells were encountered.

Dr. Guthrie felt that the findings in these smears indicated definitely the existence of Hodgkin's disease.

DR. BARKER: That is a very interesting report, indeed, and I think Dr. Guthrie is fully justified in concluding that Hodgkin's disease is present from those findings alone. Eosinophilic infiltration of the lymph-glands does, it is true, sometimes occur in other lymphadenopathies, for example, in the enlargement of the lymph-glands in diphtheria; but the total picture he describes could scarcely emanate from any lymph-gland that was not affected by Hodgkin's disease.

It will be interesting for a time to make parallel examinations of lymph-gland punctates and of sections of lymph-glands excised for histological examination. Of course, exploratory puncture of the lymph-glands is even simpler as a diagnostic procedure than lymph-gland excision and histological examination.

The histological changes that occur in the lymph-glands in Hodgkin's disease are, as you know, very characteristic. Most histologists look upon these changes as inflammatory in nature, though the character of the inflammatory process is certainly peculiar. There are, as a matter of fact, some histologists who look upon the changes as neoplastic in nature, but I cannot accept their view. In the early stages of Hodgkin's disease there is a temporary lymphadenoid hyperplasia, a proliferation of the endothelial cells upon the reticulum, and fibroblasts soon begin to appear. The process, however, rapidly changes the whole appearance of the histological section of the lymph-gland. Thus, a reduction in the number of small mononuclear elements in the lymph-gland quickly occurs, a change that probably accounts for the lymphopenia in the blood. As the fibroblastic pro-

liferation continues sclerotic changes gradually occur in the lymph-glands. After a time some of the endothelial cells on the reticulum become transformed into giant-cells; some of these have large round nuclei, whereas others may have lobulated nuclei or even complex nuclear forms not unlike those seen in the megalokaryocytes of the bone-marrow. A striking feature of the histological section of the affected lymph-gland in the well-developed disease is a marked infiltration with eosinophilic leukocytes and sometimes, also, with polymorphonuclear neutrophils and basophils. Focal necroses in the lymph-glands are not uncommon, and might mislead the tyro into thinking that he was dealing with tubercles in the gland. The general appearance of the sections of the lymph-glands has given rise to the terms "lymphogranulomatosis" or "malignant lymphoma." In the later stages the sclerosis of the gland becomes very marked; indeed, in certain instances, it may be so pronounced as to mislead the histologist into thinking at first that he is dealing with a neoplasm (spindle-celled sarcoma or endothelioma).

It is interesting that these changes may occur in any of the lymph-adenoid tissues of the body, not only those of the lymph-glands but also those of the lymph-follicles that are met with in the mucous membranes in the several viscera and in the bone-marrow.

It would appear that we have in Hodgkin's disease to deal with what may be called "a tissue disease" or "a histiopathy." The noxa, whatever it is, shows a predilection for lymphadenoid tissue everywhere in the body. The changes in this tissue in the spleen, in the liver, in the lungs, in the perivascular sheaths, and in the serous membranes are sometimes very marked. As yet we do not know just what determines the predominant involvement of certain parts of the lymphadenoid tissue in one patient and certain other parts of it in another.

What do you think is the cause of this disease?

STUDENT: The cause is unknown, though a diphtheroid bacillus has been described as often being present in the diseased tissues.

DR. BARKER: Yes; the bacteriological studies that have been made in Hodgkin's disease are most interesting. As far back as 1910 Fränkel and Much treated some of the glands by the antiformin method and observed a bacillus that resembled the tubercle bacillus in its morphology, but was not so acid-fast. Later on Negri and Mieremet described the presence of a pleomorphic diphtheroid organ-

ism in the glands in Hodgkin's disease. Similar organisms have been observed in the affected tissues by Bunting and Yates (of Wisconsin), by Rosenow (of Chicago), and by Arthur Bloomfield (here). These diphtheroid bacilli can be seen sometimes in smears of the lymph-glands. They can also be grown from the lymph-glands by cultural methods. Bunting has recovered this bacillus no less than eight times, from a single patient, during a period of five years. He believes that, with an appropriate technic, this bacillus can be recovered from 100 per cent. of the cases. Rosenow asserts that he has grown the bacillus in cultures made from the blood during acute exacerbations of the disease.

The constant association of diphtheroid bacilli with the lesions of Hodgkin's disease is certainly a very striking fact. I remember a case in which a man, who had enlargement of the lymph-glands of the neck, suffered also from an inflammation of the gums. In this gingival exudate a bacillus having a morphology resembling that of the diphtheria bacillus was found. It was at first supposed by his attending physician that the whole process was due to the Klebs-Löffler bacillus, and the patient was accordingly treated with antidiphtheria serum, and his children, who had been in contact with him, were given prophylactic injections of serum. Later on the man developed all the signs of Hodgkin's disease, and it became evident that what had been thought to be the diphtheria bacillus was, in reality, this diphtheroid organism to which I have referred.

Great skepticism still exists, however, regarding the relationship of this diphtheroid bacillus to the etiology of Hodgkin's disease. Similar diphtheroid organisms have been recovered from other lymphadenopathies, and a number of investigators believe that, since the finding of such diphtheroid organisms is so common in various diseases, no stress dare be laid upon its presence as an etiological factor. It must be admitted, I think, that its presence is, however, more constant in Hodgkin's disease than in any other condition. Some time we shall probably know what this constant, or almost constant, association of a diphtheroid bacillus with the Hodgkin lesions means. At present it is probably wise to hold our minds open, and to regard the infectious agent in Hodgkin's disease as still in doubt.

There are certain other points in the etiology of Hodgkin's disease that should be kept in mind. Thus, the disease is twice as common in males as in females. Furthermore, it shows a certain predilection

for certain ages; though the disease may occur at any age, it is met with most often between the ages of fifteen and thirty-five, though it is also quite common between the ages of five and ten. It has even been observed in children during the first year of life and in men and women over sixty.

The disease does not seem to be contagious. It is often preceded, however, by a history of focal infection. Thus far it has not been possible to reproduce the disease in experimental animals.

Do you think this boy is suffering from a severe form of Hodgkin's disease?

STUDENT: Yes. I should think so. The fact that the first symptom was noted in February, 1920, and that, in spite of therapy, the boy's condition grows pretty steadily worse, points in that direction. The rather high fever with chills and sweats also indicates a grave infection.

DR. BARKER: Yes; I think so, too. The disease has been progressive and has quickly become generalized in this boy. The great clinician Trousseau, a very acute observer, described the disease as passing through three stages: (1) a latent period; (2) a period of progress and generalization, and (3) a period of cachexia.

What is the first symptom, as a rule, to attract attention?

STUDENT: Usually an enlargement of one or more lymph-glands, most often on one side of the neck.

DR. BARKER: Yes, enlargement of the cervical lymph-glands is the first symptom in at least half of the cases. In Bunting's series it was the first symptom in three-fourths of the cases. Next in frequency the enlargement appears first in the axillary glands; next to that in the inguinal and subinguinal glands. It is rarer to have the glands in the mediastinum, the glands in the abdomen, or the spleen first enlarged.

When Hodgkin's disease is suspected it is very important to make an x -ray of the chest, even if there be no demonstrable retro-manubrial or paramanubrial dulness. One is often surprised to find marked changes in the x -ray plates pointing to involvement of the mediastinal glands, the bronchial glands, or the lung tissue when the signs pointing to the chest have been slight.

Were x -rays made of the chest of this boy?

STUDENT: Yes. As far back as last February, that is, nine months ago, a roentgenogram of the chest showed definite shadows in the

region of the arch of the aorta and to the left of the sternum, which made the roentgenologist strongly suspect the existence of Hodgkin's disease of the glands in the mediastinum.

DR. BARKER: Has an x -ray of the chest been made since the boy entered this hospital?

STUDENT: Yes. I have the plate here.

DR. BARKER: Let us examine this roentgenogram. Evidently there is a marked contrast between the present condition of the chest plate and that seen last February. No shadows of retromanubrial masses are present now. There are, however, shadows in the hilum of the right lung and some soft shadows still further to the right in the lung substance. There are a few shadows also on the left side in the region of the hilum of the left lung. These do not look like the shadows of a tuberculous process, which are usually irregular if there has been caseation, or very dense if there has been calcification. I think that no one could make a certain diagnosis of Hodgkin's disease, however, from this plate alone, though from the plate made in February the roentgenologist is reported as having strongly suspected the existence of the disease.

Let me call your attention to a paper by Wessler and Greene, of the Mt. Sinai Hospital, published in the *Journal of the American Medical Association* of this year. I shall pass the number of the journal containing the paper around the class. These investigators have analyzed all the x -ray plates of the chest made in their Hodgkin's cases, and have given us the results. They are very interesting. You will be surprised, I think, to find how frequent intrathoracic changes, as revealed by the x -ray plates, were in their cases of Hodgkin's disease. Wessler and Greene describe several different types of "intrathoracic Hodgkin's," including: (a) mediastinal tumor in 8 of 25 cases; (b) infiltrative type, invading the lung like a neoplasm from the hilus, in 4 cases; (c) isolated nodules in the lung looking like metastases, but in reality autochthonous foci, in 4 cases; (d) discrete nodules at the root of the lung showing as faint shadows in 17 cases, and (e) enlarged paratracheal nodes revealed as shadows just to the right of the manubrium, below the clavicle, in 50 per cent. of the cases.

Apparently, the paratracheal glands on the right have been involved in our boy, judging from the description of the x -ray plates made nine months ago.

I advise you to study this paper by Wessler and Greene very carefully, and to make use of it when you are examining roentgenograms of the chest made in Hodgkin's suspects.

Is there anything characteristic about the fever in Hodgkin's disease?

STUDENT: In certain types of the disease it is very characteristic.

DR. BARKER: What types have you in mind?

STUDENT: One type especially, in which the relapsing fever of Pel and Ebstein appears.

DR. BARKER: Yes; the periods of pyrexia in this type have been very well described by MacNalty. The fever is often of low grade at first; or the temperature may be normal or subnormal for a time, after which there is a steady rise for from two to four days, when a temperature of 103° or even 105° F. may be reached. The temperature may remain at this higher level for, say, three days, and then fall by lysis during another period of three days, after which it again becomes subnormal. There then follows an afebrile period of ten days, two weeks, or more, and this is followed by another period of pyrexia. Such a relapsing fever may continue for months. I remember one case, which Dr. Osler often referred to, in which the fever lasted exactly fourteen days in several successive paroxysms; during these paroxysms the lymph-glands became more enlarged and were hot and tender. This relapsing fever of Pel and Ebstein may occur in cases in which the accessible lymph-glands are not enlarged, though there is involvement of the internal lymphadenoid tissue of the viscera.

You will see by looking at the temperature chart of this boy that his temperature range is now between 101° and 103° F. The fever is almost continuous in type, being only slightly remittent. It will be interesting to follow the course of the temperature and to see whether or not definite intermissions of the pyrexia occur.

The boy has a marked tachycardia at present, the pulse-rate varying between 110 and 140 to the minute. There is also moderate tachypnea, the respiration rate varying between 24 and 40 per minute. We shall now permit the patient to return to the ward. (*Patient removed from the amphitheater.*)

(To student): What is the outlook for this boy?

STUDENT: Not very good.

DR. BARKER: He will die, in my opinion, certainly die of the disease unless some intercurrent malady cuts him off sooner. We

may be able to secure a remission through energetic treatment, but even if we do, I feel sure that there will be a relapse, or relapses, and that he will die. I have now followed a large number of these cases, and I have never seen one get well and remain well. It is seldom that these patients live over two or three years after the first lymph-gland enlargement is seen. A few patients do live as long as six or eight years, but this is exceptional. One always makes the diagnosis

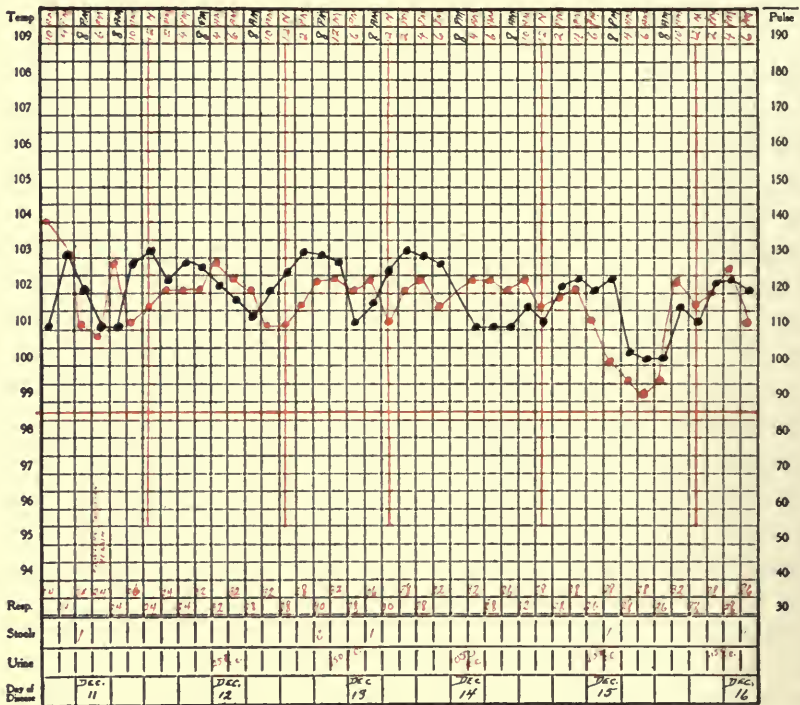


Fig. 12.—Temperature (black) and pulse-rate (red) in a boy suffering from Hodgkin's disease.

of Hodgkin's disease with real regret now that we know that it is inevitably fatal. I shall, in a few moments, refer to the forms of treatment that have helped most, but I may say at once that no treatment has yet been discovered that prevents the ultimate fatality. Let us go on trying, however, to discover some forms of treatment that will be successful. None will be found unless investigators are active in making trials of new forms of therapy.

On what points would you lay greatest stress as regards diagnosis in the present case?

STUDENT: Progressive enlargement of the lymph-glands, the splenomegaly, the fever, the characteristic blood-picture, the characteristic smear of the lymph-gland punctate, and the roentgenogram of the chest.

DR. BARKER: Yes; you have, I think, mentioned the most important points.

With what diseases is Hodgkin's disease most likely to be confused?

STUDENT: With other infectious granulomata of the lymph-glands, such as tuberculosis or syphilis; with the leukemias and the aleukemic lymphadenoses; and with lymphosarcoma or other tumors of the lymph-glands or mediastinum.

DR. BARKER: Yes; you might add to your list certain of the more obscure infectious processes, say, endocarditis lenta, in the febrile cases with chills and sweats, and diphtheria, as in the case to which I have already referred, though the confusion with diphtheria should be only temporary. In the rare instances in which Hodgkin's tissue compresses the superior or inferior vena cava, the condition might easily be confused with tumors pressing upon the vena cava. If you will keep in mind certain points, however, in addition to the salient diagnostic criteria that you have mentioned, you will rarely have difficulty in making the differential diagnosis satisfactorily.

Confusion with tuberculosis of the lymph-glands is not uncommon. Tuberculosis is the commonest cause of progressive enlargement of the lymph-glands in young people, though Hodgkin's disease comes next in frequency. But in tuberculosis the glands are usually matted together, areas of necrosis and softening occur in the gland, and the inflammation extends to the periglandular tissues, often involving the skin, and sometimes, as you know, breaking down with fistula formation. Moreover, in tuberculosis there is usually relative or absolute lymphocytosis, signs of tuberculosis elsewhere in the body, and a positive tuberculin reaction. The histology of an excised gland or the examination of the lymph-gland punctate may decide the diagnosis. Unfortunately, tuberculosis and Hodgkin's disease sometimes coexist, and then the difficulties of diagnosis may be greatly increased. Even then the skilful histologist may recognize both processes in a section of an excised gland.

In later life it is commoner to mistake Hodgkin's disease for

leukemia or for lymphosarcoma; but when routine examinations of the blood are made, and especially when careful differential counts are recorded, there should be but little difficulty in arriving at a correct diagnosis. The blood-pictures of lymphadenoid and myeloid leukemia are characteristic. Greater difficulties may be experienced in differentiating the aleukemic lymphadenoses and the aleukemic myeloses from Hodgkin's disease; but here again there is lymphocytosis rather than lymphopenia. In lymphosarcoma there is usually a less generalized process than in Hodgkin's disease, the lymph-gland enlargement remaining localized in one group of glands for a longer time, but here the crucial test lies in the histological examination of an excised gland.

(To student): What treatment is most efficacious in Hodgkin's disease?

STUDENT: I have heard that the gland swellings can be made to disappear by applying x -rays.

DR. BARKER: Yes, the glandular enlargement in Hodgkin's disease may often be made to disappear under x -ray treatment, under radium treatment, or under arsenical treatment. Probably the quickest disappearance occurs with radium treatment. Dr. Curtis F. Burnam has reported his experiences with radium treatment in Hodgkin's disease in *Surgery, Gynecology, and Obstetrics*. I have referred a number of cases to him for radium treatment and have been gratified to observe the rapid disappearance of the glandular swellings, the diminution in the size of the spleen, and the marked increase of the general health and well being of the patient. Unfortunately, however, the benefit is only temporary. After a few months, or a year or two, these patients have returned, and several of them are already dead. I think that they will all die of the disease.

x -Rays exert an effect similar to that of radium, though somewhat less rapidly. If they be resorted to, one must be very careful to avoid x -ray burns. I remember one patient who, some years ago, received a very severe x -ray burn of one side of his neck while being treated for Hodgkin's disease of the cervical lymph-glands. Of course, now-a-days, roentgenologists, having had larger experience regarding the dosage, rarely permit a burn to occur.

Arsenic has exerted a beneficial effect in many cases. Formerly we used Fowler's solution. Of late it has been customary to administer arsenic in the form of salvarsan or some similar preparation.

It may, if desired, be used in association with the application of *x*-rays or radium, or in the intervals between treatments by radiation.

Bunting and Yates have strongly recommended early excision of all accessible diseased tissue as well as of any foci of infection that may be discoverable, applying afterward also *x*-rays or radium to lesions inaccessible to surgery and making use of such dietetic-hygienic measures as may increase the resistance of the patient. Yates reports that he has some patients who have lived over ten years since subjection to this surgical treatment.

Billings and Rosenow have made a trial of vaccines prepared from diphtheroid organisms, and though, at first, they thought they saw benefit, their later reports indicate that this method is of little, if any, value. Attempts to prepare immune sera against the diphtheroid organism and to apply them in the treatment of Hodgkin's disease have also thus far been futile.

You will gather from this brief review of the therapy that we do not, as yet, know of any really satisfactory way of treating Hodgkin's disease. Unless we can discover something more efficacious than has thus far been tried we must admit that we are practically powerless as far as permanent arrest is concerned, though we can compel the swellings temporarily to recede, and can, for a time, ameliorate the patient's condition.

Subsequent History of the Case (June 30, 1921).—On December 17th the patient was treated with *x*-rays. There was no apparent reaction. The temperature gradually fell after this, and then rose again (daily elevations to 99.4° to 100° F.). During the patient's stay in the hospital he exhibited an irregular fever. Later he received a second *x*-ray treatment, with no apparent results. He was discharged on December 30th, his condition being practically unchanged. The glands were of approximately the same size as they were on admission. The patient was advised to return, later on, for further treatment, but he failed to do so. A letter of inquiry was sent to his physician, but no reply has been received.

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IX. HEMOLYTIC JAUNDICE

CHRONIC HEREDITARY AND FAMILIAL HEMOLYTIC JAUNDICE WITH SPLENOMEGALY AND HEPATOMEGALY, ANEMIA, DECREASED RESISTANCE OF THE RED CELLS TO HYPO-ISOTONIC SALT SOLUTION; ELEVEN KNOWN CASES OF SPLENOMEGALY IN THE FAMILY IN TWO GENERATIONS. PECULIAR ULCER ON THE LEFT LEG WITH OSTEOPERIOSTITIS OF THE FIBULA. CONVALESCENCE FROM ACUTE NEPHRITIS.

At one of the earlier clinics of the present session I showed you a patient with chronic hemolytic anemia of the Addison-Biermer type and discussed the relationships of this anemia to the reticulo-endothelial-metabolic apparatus of the hepato-lienal system. Today I am able to show you a patient from Ward F, who also suffers from anemia (though of a different type), who has marked enlargement of the spleen and of the liver, and decreased resistance of his red blood corpuscles to hypotonic salt solutions; he has a so-called hemolytic icterus, with urobilinuria, but without bilirubinuria. This disease, too, is probably related to the hepato-lienal system and its reticulo-endothelial-metabolic apparatus. I shall ask Mr. Shaw to give you the history of the patient.

STUDENT: The patient, Harvey S., a married white teamster from West Virginia, thirty-two years of age, was recently admitted to the public ward of the hospital complaining of "attacks of indigestion" and of "kidney trouble." On questioning him, his indigestion seems to have consisted chiefly of gaseous eructations with occasional vomiting and abdominal discomfort. His urinary symptoms at present consist of polyuria and nocturia, which are the residues of an acute attack of renal disease following tonsillitis a little over a month ago.

Previous History.—The patient states that he has had a large spleen since childhood, and that his father, two of his uncles, three brothers, and three sisters all have enlarged spleens. His family physician states that these spleens were not enlarged from malaria, and that there is no malaria in the district in which he lived.

The patient's habits have been good as regards alcohol and tobacco, but he has been an excessive eater.

He enjoyed good health until 1918, when he suffered from a severe attack of influenza with prolonged convalescence. He states that he has not felt well since this attack. After the influenza he began to have "spells of gas on the stomach" after eating heartily, and occasional vomiting with abdominal discomfort, but without severe pain.

In January of this year, 1921, he suffered from a severe sore throat (tonsillitis), and shortly afterward the quantity of urine passed was greatly diminished and was of a high color; he then began to have swelling of the ankles and of the face. These symptoms lasted about a week, when they disappeared, but since then he has noticed an increased quantity of urine in the daytime and has had to rise several times to pass urine at night.

The patient has suffered from several accidents. Some six years ago he states that he barked his shin, that the wound became infected and remained sore for some three months, after which it healed; about two years ago it broke down again, and on the front of the left shin he has had an ulcer that has gradually increased in size. This ulcer is now about the size of a 25-cent piece and is surrounded by pigmented skin. About three years ago the patient was kicked in the nose and suffered a fracture of the nasal bone. Three years ago he fell, injuring his coccyx.

The patient has never been operated upon. He has been married three years. His wife is healthy, but has not been pregnant.

One other point in the past history may be of some importance. The patient became deaf in early childhood, more in the left ear than in the right. For the past two years he has had a suppurative otorrhea on the left side.

History of Present Illness.—The patient had not thought of connecting his present trouble with the enlargement of the spleen. He is concerned chiefly regarding his attacks of indigestion (with gas on the stomach) which he says soda will relieve. He asserts that he did not suffer from these attacks of gaseous eructations with abdominal discomfort until after his influenzal attack in 1918. Since then, at irregular intervals, he has had these paroxysms of digestive disturbance. During the first year after the influenza nausea and vomiting not infrequently accompanied the attacks, but during the past year vomiting has not occurred. He states that there has been a little tenderness on pressure below the rib margins on each side of the upper abdomen. Overeating seems, as a rule, to have precipitated the attacks. Other causal factors have not been recognized by him. His only other complaints are (1) increased quantity of urine and (2) rising at night to pass urine; these symptoms have been present since the attack of acute renal disease followed his tonsillitis of last January.

DR. BARKER: Let us examine the patient. You see that he is a fairly well-nourished, muscular man, whose lips are pale and whose skin presents a peculiar earthy tint, not unlike that seen in some forms of cirrhosis of the liver. The skin is somewhat sallow, but I do not think you would say that the skin looks yellow. The scleræ, it is true, have a slight subicteric tint, but not more than one often sees in the ward and ignores. The temperature is normal. The pulse-rate is slightly accelerated, 92 to the minute, and the breathing is quiet, at the rate of 20 per minute.

Here on the left leg is the ulcer that you have already heard of. You see it is about the size of a quarter, presents a granulating surface covered by a little purulent discharge, and the skin, for a considerable area about it, is thickened and of a brownish-blue color. There are no varicose veins in this leg, otherwise one might think of a varicose ulcer. I can feel no nodes on the tibia, but there are interesting x-ray findings in the bones, as we shall see a little later. When I was in India in 1899 I saw some patients suffering from what was known there as "Delhi sore." This ulcer reminds me very much of the

kind of sore that was thus described. Delhi sore, as you know, is a form of cutaneous leishmaniasis. As far as I know cases of Delhi sore do not occur in the United States, though a similar sore due to *Leishmania* has been described in Panama and South America. It would be a simple matter to make smears from this ulcer and stain them for *Leishmania*. A small piece of the margin of the ulcer might also be excised for histological examination. Syphilis should be thought of also in connection with this sore, though it would be surprising to have this single ulcer present as a sign of syphilis. Has the Wassermann test been made in this patient?

STUDENT: Blood has been taken for the Wassermann test, but the result of the test has not yet been reported.

DR. BARKER: The patient's arteries are soft. His blood-pressure in the ward was 130 systolic, 80 diastolic. The head is negative except for the bilateral deafness, the suppurative otorrhea on the left, a coated and tremulous tongue, and some pyorrhea alveolaris and dental caries. The tonsils are small and ragged and show but little evidence now of the recent acute tonsillitis. There is, however, slight enlargement of the glands at the angle of the jaw.

The thorax is negative except for slight enlargement of the heart and a soft systolic murmur audible at the base and apex. The aortic second sound is louder than the pulmonic second sound. The lungs are entirely negative.

On examining the abdomen one finds, on palpation, the edge of the spleen some three or four fingerbreadths below the costal margin. The spleen is very hard. It descends on inspiration and I can press it backward. Evidently this spleen is fairly movable. He has a little tenderness at times about the spleen, but just now there is no marked tenderness. If there has been perisplenitis here it does not seem to have caused adhesions that limit the mobility of the spleen. This would be an important matter if surgical interference were to be decided upon.

On palpation of the liver edge, I find that it is one and one-half fingerbreadths below the costal margin in the right mammillary line. Percussion corroborates this position for the lower margin of the liver. The patient complains of a little tenderness in the right upper quadrant as I palpate. I am unable to feel a distended gall-bladder. Physical examination of the abdomen otherwise is negative.

This would be a very suitable case for the application of the

method of pneumoroentgenography of the peritoneal cavity. A little air or, better still, some carbon dioxid gas could be injected into the peritoneal cavity and roentgenograms taken. We could then see the exact size and position and form of the spleen and of the liver. We could tell whether or not accessory spleens are present, and we might be able to judge still better of the mobility of the spleen and of the existence or absence of perisplenic adhesions. The cautious injection of carbon dioxid gas into the colon would also permit of the making of a roentgenogram that would tell us much about the spleen and the liver. The results from such colon distention and roentgenography are, however, less satisfactory than the results of pneumoperitoneal roentgenograms.

Notice the horizontal line limiting the crines pubis above in this patient. He has so-called "transverse crines" or the "feminine type" of disposition of the hairs. That is sometimes a sign of status thymicolymphaticus. When I see transverse crines I always look for other signs of status thymicolymphaticus and, especially, I examine the teeth to see if there is a great discrepancy between the size of the upper medial incisors and the upper lateral incisors. In this case the medial incisors are large, but the lateral incisors are also fairly large. I should say that the discrepancy was not so marked here as it usually is in a status thymicolymphaticus. Moreover, transverse crines may occur in hypogenitalism independent of a status thymicolymphaticus.

A rectal examination was made in the ward. It revealed enlargement of the left side of the prostate and induration of the left seminal vesicle. This patient has evidently had a chronic prostatitis and chronic seminal vesiculitis.

Neurologically, the patient presents nothing abnormal. The pupils react to light and accommodation. The eye-grounds are negative. The deep and superficial reflexes are all normal.

There is marked bilateral flat-foot.

Summarizing these regional findings on physical examination, we have here bilateral deafness, left otorrhea, oral sepsis, chronic tonsillitis, general pallor, earthy tint to the skin, subicteric tint to the scleræ, slight enlargement of the heart with systolic murmur, splenomegaly, hepatomegaly, chronic prostatitis and seminal vesiculitis, chronic ulcer of the left leg, and flat-foot.

Would you tell us of the laboratory tests that have already been made?

STUDENT: The blood examination showed: R. B. C., 4,240,000; hemoglobin, 50 per cent.; W. B. C., 7520. The differential count of the leukocytes showed polymorphonuclear neutrophils, 46 per cent.; polymorphonuclear eosinophils, 1 per cent.; polymorphonuclear basophils, 1 per cent.; small mononuclears, 40 per cent.; large mononuclears and transitionals, 10 per cent. A few normoblasts were seen. There was marked anisocytosis and poikilocytosis. The blood-platelets were increased, the count being 1,200,000 instead of the normal 250,000 to 400,000. The resistance of the red blood-corpuscles to salt solutions was tested. Hemolysis began at 0.5 per cent. and was complete at 0.24 per cent. salt solution.

DR. BARKER: The red count is evidently not much diminished, but the hemoglobin percentage is greatly diminished. You see that the color-index is about 0.6, a low index indicating a secondary anemia. In most hemolytic anemias the color-index is around 1 or higher than 1. You observed that the other day in the patient who suffered from the Addison-Biermer type of anemia.

An analysis of the differential formula in this patient of today indicates a relative diminution of the polymorphonuclear neutrophils, a relative increase of the small mononuclear elements, and a relative increase of the large mononuclears and transitionals. It looks as though the neutrophils were either not being produced in normal numbers, or were being destroyed in more than normal numbers. The opposite is true of the small mononuclear elements and of the large mononuclears and transitionals. The increase in the blood-platelets indicates either that the megalokaryocytes in the bone-marrow are producing more blood-platelets than normal, or that fewer blood-platelets are being destroyed than normal. One might link up the lymphocytosis with the transverse crines, if there is, or has been, a status thymicolymphaticus in this patient. One might link it up with the ulcer of the leg if the latter should turn out to be luetic in origin.

The nucleated red corpuscles in the blood indicate an active bone-marrow. The erythropoietic tissue in the marrow is giving off unripe cells to the blood. Were any myelocytes seen?

STUDENT: We did not make out any in the stained smear.

DR. BARKER: In some cases of chronic hemolytic jaundice there

have been marked blood crises with large numbers of nucleated red corpuscles and sometimes a tremendous increase in the white count with the appearance of myelocytes in the blood. Doctors Allan and Leinbach, of Charlotte, North Carolina, have reported a case of this sort, and there are other interesting cases in the literature.

There is a special method of searching for unripe red cells in the blood—the “vital staining method,” introduced by Widal, Abram, and Brulé. Has this test been applied?

STUDENT: Not yet, but it will be done today or tomorrow.

DR. BARKER: Have the stomach contents been examined?

STUDENT: Yes. We found, after a test breakfast, free hydrochloric acid, 30 acidity per cent.; total acidity, 39 acidity per cent. There was no occult blood, nor was there any lactic acid in the stomach contents.

The feces contained bile and urobilin.

DR. BARKER: There has been no intestinal acholia here then. How about the urine?

STUDENT: The urine was of a dark, orange-brown color, and had a specific gravity of 1020. It contained, on admission, much albumin and many casts, together with a few white blood-cells and a few red blood-corpuscles. Urobilin was present, but there was no bilirubin in the urine.

DR. BARKER: Has any marked change occurred in the urine since admission?

STUDENT: The albumin has almost entirely disappeared, though there is still a faint trace, and the casts have diminished in number. The dark color persists and the increased urobilin content also.

DR. BARKER: It is interesting that there is urobilinuria, but no bilirubinuria. Chronic hemolytic jaundice, though an acholuric jaundice, is a urobilinuric jaundice.

Have you tested the blood-serum for bilirubin?

STUDENT: That test has not yet been made.

DR. BARKER: There are now available some very delicate tests for the presence of bilirubin in the blood-serum. Indeed, we have not only qualitative tests but also very good quantitative tests for bilirubinemia. There is a little bilirubin, a very minute amount, in normal blood, but in chronic hemolytic jaundice the bilirubin in the blood is increased above the normal.

It is interesting that bilirubin is one of the threshold substances for the kidneys. You know when there is any urea in the blood there will always be some in the urine; in other words, urea has no threshold. With sugar, however, and with sodium chlorid a certain percentage has to be exceeded in the blood before these substances appear in the urine. There is, accordingly, a threshold for sugar and for sodium chlorid. Now there seems to be a threshold also for the excretion of bilirubin in the urine, and unless this threshold is exceeded a bilirubinemia does not lead to a bilirubinuria.

There is some evidence that the threshold for bilirubin may be increased in chronic hemolytic jaundice, but there may be another reason for the non-occurrence of bilirubinuria. An interesting hypothesis regarding the occurrence of bilirubinemia without bilirubinuria has been advanced by Blankenhorn. His most recent article appeared last month in the *Archives of Internal Medicine*. From his own studies, and those of Professor Hoover, he concludes that bilirubin in the blood may be either dialyzable or non-dialyzable. Dialyzable bilirubin in the blood passes over into the urine. Non-dialyzable bilirubin does not. The non-dialyzable bilirubin seems to be attached to the protein constituents of the blood-plasma by absorption just as a dye is attached to a colloid. He found that by precipitating the proteins of the blood he precipitated the bilirubin with it. This bilirubin can be removed from the protein to which it is attached by alcoholic extraction, but it cannot be removed by extraction with ether, dilute acids, or dilute alkali. This is an interesting observation and may ultimately throw some light upon the pathological physiology of chronic hemolytic jaundice.

It was long thought that the yellowish discoloration of the skin and of the scleræ in chronic hemolytic jaundice was due to urobilin staining of the skin and scleræ. Thus, Gerhardt introduced the term "urobilin icterus" for this form of jaundice. The studies of Quincke are very interesting in this connection. He made spectrophotometric examinations of the skin in such cases and found the spectrum of bilirubin present, but could not obtain the spectrum of urobilin. It would seem, therefore, that the jaundice in these cases is a true bilirubin jaundice rather than a urobilin jaundice.

The amount of urobilin in the blood in chronic hemolytic jaundice seems to be small, though urobilinogen, or some polymeric form of urobilin, may be present in larger amounts. Recent studies indicate

that there are several varieties of urobilin, but this discovery of the biochemists can scarcely be valued as yet clinically.



Fig. 13.—Osteoperiostitis of the fibula in a patient with ulcer of the leg and chronic hemolytic jaundice.

Have any *x*-ray examinations been made?

STUDENT: Yes; an *x*-ray of the left leg has been made, and also a gastro-intestinal series after a contrast meal.

DR. BARKER: Let us put them upon the illuminating screen. Here are the bones of the left leg in the x -ray plate (Fig. 13). The tibia shows very little change, but this fibula is markedly altered. You see these several elevations along the course of the fibula. There has been an osteoperiostitis here. It certainly suggests the possibility of a luetic process. We shall await with interest the result of the Wassermann test.

But even if the Wassermann reaction should turn out to be positive in this patient, we should not lay too much stress upon it, for it is sometimes positive in cases of jaundice in the absence of syphilitic infection. Dr. Sydney Miller has told me of a case recently observed in which there was a chronic hemolytic jaundice and in which there was also a 4+ Wassermann reaction, verified by three laboratories. The patient was a man whose statement, it was believed, could be trusted, and he denied any history of syphilitic infection. There were no other signs of syphilis to be detected on physical examination or in the anamnesis. Moreover, he was given several doses of salvarsan without any effect whatever upon the positive Wassermann reaction. The salvarsan injections caused an exacerbation of his jaundice.

The gastro-intestinal series of x -ray plates points to adhesions in the right upper quadrant. Gall-stones are very common in cases of hemolytic jaundice, but they rarely show in x -ray plates. These plates also indicate that both the spleen and the liver are considerably enlarged. There is no sign of ulcer or of neoplasm of the stomach or intestine, and there is no very marked intestinal stasis.

We cannot yet report to you upon the findings in the duodenal contents nor upon the condition of the bile itself obtained by duodenal intubation. The patient, as you see, now has *in situ* a small tube that has been passed through his stomach into the duodenum. It was not feasible to complete this Meltzer-Lyon test before bringing him into the clinic. We hope, however, to be able to report to you later the results of the examinations of the duodenal contents and of the A, B, and C fractions of bile.

We are safe, however, in prophesying that this man will show a pleiochromia, that we shall find high figures for the bile pigment in the duodenal contents, as J. T. Schneider has done in similar cases, and I expect that the bile will be thicker and darker in color than normal. Sometimes minute fragments of bile thrombi have been demonstrable in the bile secured from these patients.

Has this patient had any itching?

STUDENT: No, he has not suffered from pruritus. There has been no bradycardia and there is no xanthelasma.

DR. BARKER: Of course, he has practically no visible jaundice, but it is characteristic, any way, of chronic hemolytic jaundice not to have pruritus, bradycardia, and xanthelasma associated, whereas in acute obstructive jaundice these signs are very common accompaniments of the icterus.

Do you think, though, that it is certain that this patient has a chronic hemolytic jaundice?

STUDENT: Though the jaundice is very slight the whole picture makes the diagnosis certain, I think.

DR. BARKER: Yes; I think we can feel very sure that we are dealing here with a chronic, hereditary and familial, hemolytic, and acholuric jaundice. The splenomegaly and hepatomegaly of the patient, the subicteric tint of the scleræ, the anemia, the urobilinuria without bilirubinuria, and, above all, the decreased resistance of the red blood-corpuscles to hypotonic salt solution make the diagnosis certain. It is supported also by the report of at least eleven splenomegalic cases in the family.

Here is a chart (Fig. 14) which Mr. Shaw has prepared of the hereditary and familial conditions as regards enlargement of the spleen and jaundice (see p. 171).

There are certain points, however, that might make you doubt the validity of the diagnosis of chronic hemolytic jaundice in this case. Thus: (1) It is unusual to have such a low color-index in chronic hemolytic jaundice. Usually the color-index is around 1 or above 1; here it is about 0.6, the hemoglobin percentage being reduced out of all proportion to the reduction in red cells. (2) Though the resistance of the red cells to hypotonic salt solution is decreased, it is not markedly decreased. When hemolysis begins around 0.5 rather than with a greater strength of salt solution, the normal is approached. The test for resistance should be made in cases like this with washed red corpuscles rather than simply with defibrinated blood. When the test is made with washed corpuscles the hemolysis often begins at a higher level. Do not forget that the demonstration of decreased resistance of the red cells to hypotonic salt solution, or so-called increased fragility of the red cells, is a very important item as a diagnostic criterion in hemolytic jaundice, though there are

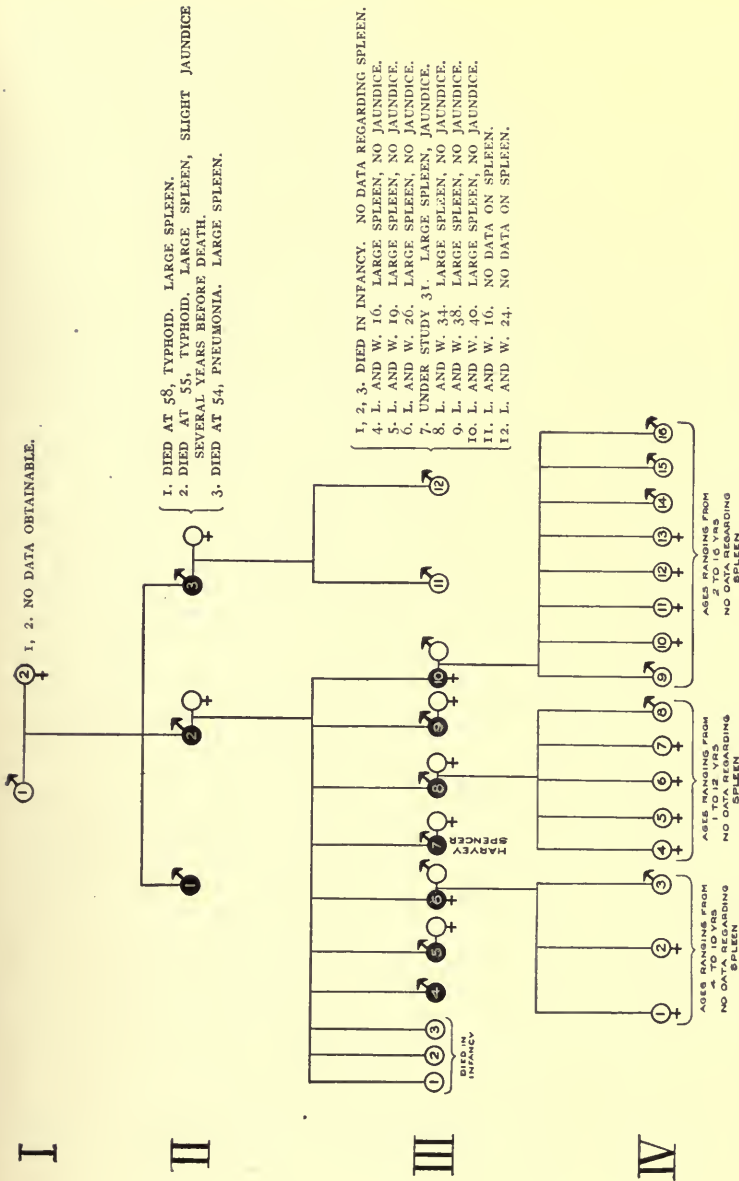


Fig. 14.—Patient under study, Harvey S., III, 7. Patient says all his brothers and sisters with their families live within a radius of 10 miles. His cousins, III, 11 and 12, live 60 miles away. L. and W. means "living and well."

cases of undoubted hemolytic jaundice in which there is no decrease in the resistance of the red cells or in which there may even be an increased resistance. Still, in such cases one must be very careful to rule out simulating disorders, like splenomegalic cirrhosis of the

liver and pernicious anemia. This patient certainly has not a chronic hemolytic anemia of the Addison-Biermer type. The color-index in the blood is against it, as is the degree of anemia. Moreover, the nucleated red cells present are normoblasts and not megaloblasts. Again, there is no leukopenia and no reduction in the number of blood-platelets. All these points militate against the diagnosis of the Addison-Biermer type of anemia.

Splenomegalic cirrhosis of the liver should, of course, be kept in mind. We have learned a good deal of late years about the splenomegalic cirrhososes. We know a group in which there is splenomegalic cirrhosis without jaundice. We know, further, a group with jaundice, and finally, also a group with jaundice and with severe anemia. When jaundice is present it is partially of hemolytic origin, partly of obstructive origin. All the recent evidence points to the reticulo-endothelial apparatus of the hepato-lienal system as responsible in the pathogenesis of these several forms of splenomegalic cirrhosis. Let me refer you to this interesting volume by Eppinger and Ranzi (1920), entitled *Die hepato-lienalen System*. You will find an excellent collective review of the facts in this book together with a full discussion of all the current theories. The French literature on the subject is original and illuminating; I have placed references to some of the best articles on the blackboard.

Workers in the United States and Canada, too, have done much in connection with chronic hemolytic jaundice. One of the first cases to be recognized in this country was presented at a meeting of the Interurban Club in Toronto (1910). In the United States Tileston and Griffin (1910) called the attention of American workers to the importance of the subject. In this clinic Thayer and Morris (1911) made an exhaustive report of 2 cases, and I would call your attention to the excellent bibliography appended to their article. Careful metabolic studies upon a few cases have been made by Goldschmidt, Pepper, and Pearce (1915), and by McKelvy and Rosenbloom earlier in the same year. The importance of the endothelium of the blood-vessels in hemolytic jaundice was emphasized by Whipple and Hooper in the *Journal of Experimental Medicine* as early as 1913; and, in the same year, McPhedran and Orr made a metabolic study of a case in Toronto. Levy and Kantor (1916) called attention to the frequency of enlargement of the heart and of arterial hypotension in this malady.

The value of splenectomy in the treatment of this disease, recog-

nized by European investigators, has been confirmed by several American surgeons. For the technical surgical details I would refer you to the articles by Thalpoor and by W. J. Mayo.

The effects of α -ray and of radium upon the spleen in this disorder have also been studied by both American and European observers. It would be fortunate, of course, if intensive radiation would make it possible to avoid splenectomy. Unfortunately, the changes in the spleen in the disease consist chiefly of hyperemia and of changes in the endothelial apparatus. If we had to deal instead with a lymphadenoid hyperplasia there would be a greater likelihood, I think, of effective radiotherapy. In any case thorough radiotherapy would seem to me worthy of trial.

The articles of H. Z. Giffin (1917), of the Mayo Clinic, and of J. P. Schneider (1919), of Minneapolis, are well worthy of careful study, since they contain careful analyses of the newer facts concerning chronic hemolytic jaundice. You will be interested, too, in the publications of the Cleveland School (Hoover and Blankenhorn) on dissociated jaundice, on dialyzable and non-dialyzable bile pigment in the blood, on the relations of bilirubin to the proteins of the blood, and on the effect of the bilirubin-protein combination upon the bilirubin threshold to which I have already referred.

One observation upon the patient presented to you today, which has interested me particularly, merits an additional word. The observation I refer to is the occurrence of a peculiar and unexplained leg ulcer in association with chronic hemolytic jaundice. I have sought in vain for similar instances in the literature, with one exception. Dr. J. I. Johnson, of Pittsburgh (1919), mentions in his paper that one of his patients had a large leg ulcer, which began as a small pustule a few years before the patient was seen, and later broke down, the ulcer enlarging to 2 cm. in diameter. Dr. Johnson thought that possibly this ulcer was a varicose ulcer, following phlebitis in typhoid, or that it might have resulted from a varicosity due to pressure of the large spleen upon the iliac vein. Now our patient, as you see, has a peculiar ulcer of the left leg, but he gives no history of phlebitis and shows no signs of varicose vein. The ulcer of our patient reminds me very much of the ulceration seen in cutaneous leishmaniasis. It would be interesting to inquire carefully into the occurrence of leg ulcers in other patients with chronic hemolytic jaundice. It may be that such ulcers have occurred more frequently than we suppose,

but that they have been considered accidental associations and have not been reported. The ulcer in our patient may be a mere coincidence due to lues or some other not ascertained cause. But let us not dismiss it too lightly as a separate and distinct lesion; we may later find out that certain ulcers of the leg stand in nearer relationship to chronic hemolytic jaundice.

Let us turn for a moment to the patient's nephropathy. Do you think he will entirely recover from it?

STUDENT: Yes, I think so. The albumin has almost disappeared and the casts are fewer in number. The oliguria and edema have disappeared.

DR. BARKER: What form of renal disease do you think he has had?

STUDENT: I think he had an acute nephritis following his acute tonsillitis.

DR. BARKER: Yes, I think there can be but little doubt that this man has had an acute glomerulotubular nephritis. Acute tonsillitis is most often due to the streptococcus. Whether or not the nephritis was due to streptococcus toxins, or to metastatic infection with actual streptococci, we cannot be sure. I should not be surprised, however, if we dealt with a metastatic infection. It cannot have been very severe, however, and I trust that he is not in for a chronic hydropsical glomerulonephritis. The edema has disappeared and the urinary findings now are favorable; these facts make it seem fairly clear that we deal with an acute, rather than a chronic, process. The blood-pressure is not increased; that is another good sign.

From what I have said you will recognize that there is room still for a great deal of study in this case. The patient has been here only a short time, but I hope that he will remain long enough to permit of a thorough investigation of some of the mooted points.

Subsequent History of the Case.—The patient was discharged nine days later (on March 17th) in good condition, with instructions (1) to stay in bed at home until the urine became clear in examinations made by the local doctor; (2) to make use of a diet low in proteins and salt; and (3) to return to the hospital later on for tonsillectomy and for treatment of the leg ulcer. He had not returned up to June 30, 1921, and a letter to his physician had remained unanswered up to that date.

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DISEASES OF THE DIGESTIVE APPARATUS

X. CHRONIC STARVATION, EXTREME EMACIATION, AND EXHAUSTION PSYCHOSIS

AN EXTREMELY EMACIATED COLORED WOMAN WITH AN EXHAUSTION PSYCHOSIS, SECONDARY MENTAL ANOREXIA, OLD PULMONARY TUBERCULOSIS, ORAL SEPSIS, GASTRIC ULCER, ACHYLIA GASTRICA, PARTIAL PYLORIC STENOSIS, AND SECONDARY ANEMIA.

THE patient before us today presents a combination of symptoms and signs both unusual and interesting. The outspoken feature is emaciation, an emaciation so extreme that on seeing the patient for the first time one is forcibly reminded of the description of the Ass in Peter Bell:

"How gaunt the creature was, how lean,
Yea, wasted to a skeleton."

The patient is a colored woman, forty-six years old, named Mary E. C. She comes from Virginia, and was admitted to the Johns Hopkins Hospital some three months ago.

The scanty information that could be elicited concerning the previous history of the case is practically negative. During childhood the patient had measles, mumps, and pertussis, besides an attack of malaria. Otherwise her general health has always been good, except that, according to her own account, she has had "night-sweats and dysentery." She has always been a hard worker, and she is accustomed to the use of alcohol in moderation. She denies having had lues. She was married for twenty-five years and has had seven children, three of whom are living and well.

The patient's present illness, according to her own account and that of her friends, began in March, 1917, with numbness in the hands, arms, and legs, accompanied with "aching pains." Because of these symptoms she consulted a doctor, who, she says, treated her for "rheumatism," and the pains were soon completely relieved. A little later, to use her own words, she "broke out in splotches all over her body." She went to the doctor again and he prescribed some

"blood medicine," after which the spots healed. Following this treatment she became constipated and when the bowels moved she passed what she describes as "lumps of flesh." Finally, between four and five months ago, she became unable to eat on account, she says, of pain and vomiting that came on after eating. When brought to the hospital she had become so weak that she could not walk. For some little time before this her family and friends had noticed that she was "excitable and flighty."

Physical examination on admission to the hospital showed the extreme emaciation that, as I have said, is one of the most noteworthy features of the case. There was marked atrophy of fat and muscle; scattered over the skin were pigmented areas within which were unpigmented centers. There was some slight general glandular enlargement. For the first six weeks that she was in the hospital she showed irregular elevations of temperature, accompanied with tachycardia. Since then her temperature has, for the most part, been subnormal, with a relative tachycardia. At present her temperature and pulse-rate are practically normal. There was a slight ptosis of the eyelids, more marked on the left side, but otherwise there were no ocular palsies. The fundi of the eyes were normal. Her teeth, except for a few bad snags, were all gone. The lungs showed slight changes. There was slight impairment of the percussion note at both apices and slight dullness in the right interscapular region, but the percussion note was otherwise remarkably clear throughout. The breath sounds also were clear. Have any râles been heard over the lungs since she has been in the ward?

DR. SANGER: From time to time there have been a few râles, but it is a difficult case to examine carefully, because the patient declines to co-operate. We were, of course, suspicious of the lungs because of the irregular fever and the great emaciation.

DR. BARKER: The abdomen was scaphoid in appearance. The recti muscles were held somewhat rigidly. No abnormal mass was palpable in the abdomen. The liver and spleen could not be felt and the liver dullness was not increased. The tone of the anal sphincter was poor. The extremities showed marked emaciation and out-spoken flexion contractures. Was there any sign of organic nervous disease?

DR. SANGER: No; except difficulty in eliciting the deep reflexes

DR. BARKER: How about Babinski's sign?

DR. SANGER: It was negative. There seemed to be no muscular disturbance except extreme atrophy, but the reflexes could not be elicited.

DR. BARKER: What did she weigh?

DR. SANGER: Before the present illness she weighed 110 pounds. She began to lose flesh about six months ago, and she now weighs only 45 pounds!

DR. BARKER: How tall is she?

DR. SANGER: Four feet, 11 inches.

DR. BARKER: Then she is about 60 pounds below her calculated ideal weight. That is an extreme degree of emaciation. She has suffered very much from anorexia and says she sometimes goes three days without eating. At present she has a bun in her hand that she gnaws as though she had some desire for food.

PATIENT: I don't eat nothing at all.

DR. BARKER: Does she eat in the ward?

DR. SANGER: At times she will eat and at others she will not. Sometimes she will eat what is given her by the doctors and will refuse food given her by the nurses, because, she says, the nurses want to poison her, and the food they offer her contains Paris green.

DR. BARKER: Notice how she babbles to herself all the time. Before we take up the case from the physical side let us examine cursorily her mental condition. (To patient): What is your name?

She gives it correctly enough, but her voice is so low that she can scarcely be heard. Notice that there is no delay in her response to questions. (To patient): Where do you live? She says at Hamptom, not far from Norfolk. You perceive there is no retardation in her replies. That is an interesting point. Now we will test her capacity for orientation—first, for place. (To patient): What place are you in now?

PATIENT: I'm in a small ward.

DR. BARKER: But in what building is it? She says in Ward I. That is correct. At first she was in Ward O, but she became so noisy that she was moved to Ward I, where there are several small rooms. (To patient): Are you at home or in a hospital? She says she is where there are lots of doctors. (To patient): Do you know what city this is?

PATIENT: Baltimore.

DR. BARKER: Quite right. Next let us test her orientation as regards time. How long have you been in this place?

PATIENT: Four years.

DR. BARKER: When did she come into the hospital?

DR. SANGER: On July 27th of this year.

DR. BARKER: Just three months ago. (To patient): What year is this? Do you know?

PATIENT: No sir, I don't. I've had so many nerve sicknesses I don't keep no track of time.

DR. BARKER: Do you think it might be the year 1917? She says she won't undertake to tell us. Notice how quickly she answers.

(To patient): What time of the year is it?

PATIENT: The fall.

DR. BARKER: Quite right. Now can you tell me what day of the week it is?

PATIENT: Wednesday.

DR. BARKER: Are you quite sure about that? She says she is quite sure. (To patient): You are wrong then. What time of day do you think it is? She says that, according to her calculations, it is about eleven o'clock. It is really about half-past twelve. You see she is not very well oriented as regards time. Next let us test the orientation for persons. (To patient): Who is that standing at the foot of your bed?

PATIENT: Dr. Sanger.

DR. BARKER: Yes; that is right. Now who is the lady in the white uniform beside you?

PATIENT: Don't know that lady.

DR. BARKER: We may also test her memory for recent events. What have you been doing today?

PATIENT: I've been in bed.

DR. BARKER: Why have you been in bed? (No reply.) What did they offer you for breakfast?

PATIENT: I didn't eat any breakfast.

DR. BARKER: Whom did you see yesterday?

PATIENT: I don't know.

DR. BARKER: Now let us test her for the presence or absence of the commoner pathological ideas. First, we may ascertain whether or not she harbors hypochondriacal ideas. (To patient): Are you sick?

PATIENT: I'm quite well, except I can't walk.

DR. BARKER: That does not sound like the reply of a hypochondriac. We may now search for melancholic ideas. Do you feel unhappy? Do you feel sad about anything?

PATIENT: Yes; because they wants to kill me.

DR. BARKER: This reply reveals the presence of ideas of persecution rather than of melancholy. Who wants to kill you, Dr. Sanger? She says it isn't the doctor who wants to kill her, but sometimes he talks to "the other ladies" and they are going to kill her. (To patient): Tell us about it. She is talking to herself now about the medicines she has taken. In the ward she has had the idea that her fingers and toes were going to be cut off. Did she have any other delusions?

DR. SANGER: She has had definite auditory hallucinations, seeming to hear voices. She thinks that someone she calls "Ole Mose" is trying to attack her and is under her bed.

DR. BARKER: Let us follow that up. (To patient): What is "Ole Mose" trying to do to you? She says he is going to kill her and that she knows he has killed two or three people already. Dr. Sanger, she says, wants her toes. (To patient): Does anyone else try to harm you?

PATIENT: I know they do.

DR. BARKER: Are you quite sure of that? She says she is convinced of it. Evidently the persecutory ideas are firmly fixed.

DR. SANGER: If she is contradicted in regard to any of her hallucinations or delusions she begins to argue vehemently.

DR. BARKER: From the history and our questioning thus far we see that she has evidently some disturbance of orientation as to time and has had auditory hallucinations. She has no hypochondriacal ideas, but she has certainly ideas of persecution. (To Dr. Sanger): Did you say she has also had ideas of grandeur?

DR. SANGER: Yes. She once told us that she had been left \$30,000,000 and was paying \$60 a week for board. She also said she owned the ward and was going to pay us all large salaries.

DR. BARKER: Then, obviously, megalomaniac ideas are present. Her mental symptoms are a mixture of ideas of persecution with ideas of grandeur and auditory hallucinations. She has no marked melancholic ideas. She smiles frequently and does not seem unhappy. There is no psychomotor retardation. Nor, aside from the refusal

of food, does there seem to be any negativism. The patient is "accessible." There is no grimacing, no stereotypy of movement, and no verbigeration.

Now let us examine quickly into her present physical condition. The loss of fat and flesh is really remarkable (Figs. 15, 16). Her eyes seem prominent, but that is largely due to the emaciation. The bones of the skull are painfully evident; the malar bones look as though they were actually pushing through the skin. Note the



Fig. 15.—Anterior view of patient exhibiting extreme emaciation.

hollow cheeks beneath the zygomata. Her upper extremities are almost literally nothing but skin and bone. Notice how plainly evident is the groove between the radius and the ulna. You can see the tendons in the arms and almost nothing else between the skin and the bones. On examination of the thorax the clavicles are so prominent that it seems as one could almost pick them up. Each rib can be almost as plainly seen as in a skeleton. The breasts are atrophic, but there are otherwise no gross abnormalities in them.

There are no hirci in the axilla. It would be interesting to know if there ever were any. The epigastric angle is acute. When we come to examine her back we see that the scapulae are so prominent that they are almost "winged." One gets the same impression of being almost able to pick them up that one does with the clavicles. Notice also how clearly visible is the spinous process of each vertebra. I would call your attention to another feature, namely, that you can



Fig. 16.—Lateral view of patient exhibiting extreme emaciation.

also see the outline of the bony pelvis quite clearly. It is not often that emaciation proceeds so far as to make that possible. The abdomen is truly boat-shaped, owing to the extreme undernutrition. Even the false ribs are seen in relief. It looks as though at some time or another she has had a bed-sore which has left a scar over the right trochanter.

PATIENT: I didn't have no bed-sore.

DR. BARKER: What was it then?

PATIENT: A man beat me.

DR. BARKER: There was some edema of the feet and ankles on admission, but that has for the most part disappeared. You observe that the thigh is practically nothing but a femur covered with skin. The hamstring muscles (what is left of them) show extreme atrophy. There is, of course, no calf at all. The whole effect is more like an x-ray picture of a lower extremity than a living specimen. The foot does not give the impression of such excessive emaciation as we get from the upper part of the lower extremities, probably because there is so little soft tissue there to be lost. The patient still exhibits a little scattered papular eruption over the extremities and also considerable leukoderma. Her hands, however, are not at all rough nor dry. Of course, anyone examining a patient from the South with such a history as we have here would look at once for the signs of pellagra. But there seem to be no definite signs of that disease in this patient.

Examination of the lungs, made on admission, showed, as has been said, some slight dulness at the apices and in the right interscapular region, but the percussion note was remarkably clear elsewhere and the breath sounds also were everywhere clear. Just now the note is, I think, still a little higher pitched than normal in the right interscapular region. There are no râles at present, so far as I can make out, but the patient does not co-operate well. It is quite possible that there have been tuberculous lesions here, but there is little, if any, activity now.

Examinations of the heart have been negative except for a soft systolic murmur at the apex, and that is still audible. The blood-pressure is 110 systolic, 90 diastolic.

I can make out nothing abnormal on physical examination of the abdomen except the extreme degree of emaciation, and perhaps a little tenderness on pressure in the epigastrium. A pelvic examination made in the ward was negative and need not be repeated here. You will recall that there was some relaxation of the tone of the anal sphincter, but there has been neither incontinence nor retention of feces or urine.

Let us turn to the nervous system. You perceive that there is a distinct tendency to ptosis, especially on the left side. The patient says that she was "born with an ill-formed eye." Among the important points for us to check up in this case is the condition of the reflexes. First, as to the knee-jerks, the contractures make it almost

impossible to test these reflexes satisfactorily. I am unable to get any knee-jerk on either side. The same is true of the ankle-jerks. I fail to obtain any of the deep reflexes in the lower extremities. I wonder whether there is enough muscular tissue left there to contract. There is a note in the history, however, stating that at one period since she entered the hospital the deep reflexes were active. Plantar stimulation yields plantar flexion of the great toe on each side, so Babinski's phenomenon of the toes is negative, thus ruling out pyramidal tract lesion. I fail also to get any response on testing for the deep reflexes in the upper extremities.

Have these muscles been tested electrically for reaction of degeneration?

DR. SANGER: That has not yet been done.

DR. BARKER: The pupils respond actively to light and on accommodation. The eye-grounds are negative. The abdominal reflexes cannot be obtained. No objective sensory disturbances can be made out.

Summing up our general physical and psychical examination, the essential features thus far made out include: Undernutrition (60 pounds); extreme atrophy of all voluntary muscles and of the subcutaneous tissues; flexion contractures in the lower extremities; loss of the deep reflexes of the extremities; loss of the abdominal reflexes; oral sepsis; signs of old lesions in the lungs, but without evidence of present activity; moderate pallor; slight general glandular enlargement; slight tenderness on pressure in the epigastrium; asthenia; slight exanthem and pigmentation of the skin; slight mental disorientation with impairment of the recording faculty, auditory hallucinations, delusions of persecution, delusions of grandeur, and profound anorexia.

We may now turn to a consideration of the results of the laboratory tests that have been made. How about the blood?

DR. SANGER: The examination made on admission showed a marked secondary anemia:

Red blood-cells.....	2,544,000
White blood-cells.....	3,000
Hb.....	45 per cent.

DR. BARKER: It is interesting that with such extreme emaciation the anemia is not even more marked. One reason for this is

probably the concentration of the blood. There was only slight anisocytosis and poikilocytosis. The patient drinks very little water. There is a rather marked leukopenia. The polymorphonuclear percentage (84 per cent.) was higher than normal, whereas the small mononuclear percentage was rather lower than normal.

How about the eosinophils in the differential count?

DR. SANGER: There were none to be seen.

DR. BARKER: No eosinophilia; instead an eosinopenia. We want to ascertain the presence or absence of animal parasites in order to settle the question of diseases caused by them. The absence of eosinophilia is important because it helps us to exclude tapeworm, hookworm disease, amebic dysentery, and trichinosis. Did the stools contain any occult blood?

DR. SANGER: No.

DR. BARKER: How about the analysis of the stomach contents?

DR. SANGER: There was no free HCl in the stomach contents. The total amount of acid was 5 acidity per cent. The HCl deficit was 35 acidity per cent. There were streaks of pus and numerous long bacilli present on microscopic examination. No red blood-corpuses were seen and the guaiac reaction was negative. There was no lactic acid with Uffelmann's test.

DR. BARKER: You say there was no free HCl, that the total amount of acid was 5 acidity per cent., and that the HCl deficit amounted to 35 acidity per cent. This shows that a condition of achlorhydria for some reason or another is present. You say there was no occult blood.

DR. SANGER: No; but there was some pus.

DR. BARKER: Pus may appear in the stomach contents under different circumstances. Thus it may be swallowed (purulent sputum; pus from oral sepsis or from a nasopharyngitis). Oral sepsis we know to be present in this case. Again, pus may be found in the stomach contents when there is an ulcer (benign or malignant) of the stomach wall, or a suppurative gastritis, or when an abscess from outside the stomach has perforated its wall.

What was shown by the *x*-ray examinations?

DR. SANGER: The *x*-ray of the chest showed some opacity at both apices probably due to old tuberculosis of both apices. A gastrointestinal series of *x*-ray plates showed a definite fifteen-hour reten-

tion. The roentgenologist, Dr. F. H. Baetjer, thought there was ulceration at the pylorus.

We will take a look at the *x*-ray plates now. You perceive at once that the stomach is dilated and has not emptied itself at the end of fifteen hours; besides, the duodenal cap is not emptied. This indicates a pathological disturbance of gastric motility. Now we have to ask, Is this disturbance of motility of benign or malignant origin? If it be benign, it may be caused by ulceration (simple, tuberculous, or luetic); or by a fibroma, a myoma, or any other benign growth. If it be malignant, it may be due to carcinoma or, perhaps, to sarcoma. The slight filling defect at the pylorus is highly suggestive of either a benign or a malignant ulcer there.

DR. BARKER: How about the feces? Was there any occult blood in the stools?

DR. SANGER: No.

DR. BARKER: What test was employed?

DR. SANGER: The guaiac test.

DR. BARKER: Did you use the benzidin test as well?

DR. SANGER: Yes.

DR. BARKER: I lay some stress upon this point, for when there is an active benign ulcer or an ulcer due to carcinoma of the stomach, occult blood can usually be demonstrated in the stool on making the guaiac test. The presence of occult blood in the feces on a meat-free diet does not, however, always signify malignant disease, for occult blood may be present in the feces in chronic gastric ulcer, in duodenal ulcer, in ulcer of the colon or rectum, in hookworm invasion, in severe mucous colitis, in dysentery, etc. The fact that there is no free HCl in the stomach contents and that Oppler-Boas bacilli are present is suggestive of carcinoma ventriculi. Has the Wolff-Junghans test been tried?

DR. SANGER: Yes. It was negative.

DR. BARKER: I attach some importance to this test also, for it is usually positive in carcinoma of the pyloric end of the stomach.

How about the Wassermann reaction?

DR. SANGER: The Wassermann reaction for the blood was negative. Lumbar puncture revealed a clear fluid under no increase of pressure, with only 8 cells. The Wassermann reaction for this fluid (made by Dr. C. A. Neyman) was negative; and the globulin test and the gold-sol tests also were negative.

DR. BARKER: If the Wassermann test was negative for both the blood and the spinal fluid and there has been no history of syphilis, lues can, I think, be positively excluded. We may be sure, I think, that the scaly eruption that she says was caused by medicine given her early in her illness was not luetic in origin. It is helpful to rule out syphilis in a case like this not only on account of the cutaneous lesions but also because of the gastric and nervous symptoms.

Now let us examine the *x*-ray plates of the chest. The cardiovascular stripe looks normal. The apices of both lungs are a little cloudy. There is slightly more opacity at the right than at the left apex. Still, in the absence of râles and of fever, I should not lay much stress upon these *x*-ray findings in the lungs in a woman of forty-six, even though she is a colored woman and is much emaciated.

Were any other *x*-ray examinations made?

DR. SANGER: No.

DR. BARKER: Were there any examinations of special domains made?

DR. SANGER: Yes. Besides the laboratory tests and the *x*-ray tests, Dr. Augusta Scott, of the Phipps Psychiatric Clinic, made a special report on the mental state of the patient.

DR. BARKER: What conclusion did she reach?

DR. SANGER: She came to the conclusion that the case may be classed under the head of "infective-exhaustive-psychosis."

DR. BARKER: That is interesting. Please read to us her report in full.

DR. SANGER: Dr. Scott's report is as follows:

Copy of Dr. Scott's Report on Mary E. C. made September 17, 1917.

General Behavior.—Lies quietly in bed and answers questions promptly and fairly relevantly. Spontaneous talk consists of complaints of pain in legs and side and requests to be left undisturbed.

Orientation.—Correct only for place. At times correct for time. Variable. Patient has been seen three times and has not been oriented for time. She recognized the examiner and knows she is at the Johns Hopkins Hospital, but at times locates this at Fairfield, Va.

Delusions, Hallucinations, etc.—She speaks of having been on the floor or in a different bed. Only once has she mentioned any grandiose ideas. She said she had been left \$30,000,000; that she paid \$60 a week here. She was not hallucinating during the examination,

but, from history, has been. She believes her "sister's brother-in-law" is shooting at her.

Mood.—Unstable; cries easily; affective states not prominent.

Recent Memory.—Confused. Once said she came here in August; then she said it was last spring.

Remote Memory.—Difficult to test. Cannot give dates or calculate. She says she is forty-five; married at twenty-five; has been married twenty-six years, and has a daughter aged thirty-six. Two other children, ages ten to seventeen.

Speech and Intellectual Functions.—Tests not reliable.

On Admission.—There is a history of hallucinations with clear orientation and these seem to be limited to "being killed." This condition is most frequently seen in chronic alcoholism. Patient asks nurses for "whisky straight," but present psychosis is more complicated than that of an alcoholic hallucinosis and more profound than an ordinary toxic-delirious state.

If patient's condition permits would suggest lumbar puncture to rule out a luetic psychosis and to obtain a culture.

Impression.—Infective-exhaustive-psychosis.

DR. BARKER: We have now collected the data that we may use to define and to locate our diagnostic problem in this patient. The more important facts will already have stamped themselves upon your minds. A colored woman of forty-six, with a history of moderate alcoholism, began six months ago to complain of soreness and aching pains in the extremities. She was treated for "rheumatism" and the pains soon disappeared, but under treatment a skin eruption was noticed. Later she had gastro-intestinal symptoms, including abdominal pains after eating, vomiting, and probably blood in the stools. She starved herself, lost weight and strength rapidly, became unable to walk, and began to manifest disturbing mental symptoms. She entered the hospital just three months ago complaining of stomach trouble, weakness, and inability to walk. In the hospital she has refused to eat, and has had auditory hallucinations along with ideas of persecution and of grandeur. She presents a profound degree of emaciation with extreme atrophy of the fatty and muscular tissues, muscular contractures, and areflexia. She weighs only 45 pounds, though her normal weight is 105 pounds. She has oral sepsis, signs of an old (inactive?) tuberculous process in the lungs, a soft systolic

murmur at the apex of the heart with arterial hypotension, a marked secondary anemia with leukopenia (but with relative polymorphonuclear increase), and eosinopenia, and slight general enlargement of the lymph-glands, achylia gastrica, pyloric stenosis with slight filling defect, pus-cells in the stomach contents and delayed emptying time of the stomach, and transitory edema of the ankles. For a time she had slight fever and tachycardia which gradually disappeared. During her stay in the hospital she was noisy and had to be removed to the isolation ward. She refused nourishment, stating that the nurses were trying to poison her, and continued to lose weight. For a week in August she suffered from diarrhea and abdominal pain, but these symptoms passed off after the administration of subcarbonate of bismuth and a little paregoric. From these data we have to try to arrive at ideas of solution of our diagnostic problem.

The emaciation with muscular atrophy is so extreme that we may first turn our attention to it. Now an interesting point regarding the muscular atrophy in this patient is the equal involvement of all the voluntary muscles of the body. The wasting of the face, neck, and trunk muscles has occurred in just as great degree as the wasting of the muscles of the extremities. Moreover, in the muscles of the extremities the atrophy is general, not local; it is not more marked proximalward than distalward, nor more pronounced distalward than proximalward; nor is the atrophy any more distinctly shown in any one group of muscles than in another—there is no “peripheral nerve topography” nor any “radicular or segmental topography” to the muscular wasting. This universality of the atrophy of the muscles helps us much in ruling out certain causes of muscle wasting. Thus, all the unilateral and asymmetrical atrophies due to poliomyelitis or to localized neuritis are at once ruled out. Again the progressive atrophic myopathies of all types (Landouzy-Dejerine, Duchenne, etc.) can be excluded as inconsistent with the topography of the atrophy in this patient, as can also, in my opinion, the progressive (central) muscular atrophies and the muscular atrophies due to peripheral neuritis. One type of muscular atrophy due to polyneuritis should, however, be carefully considered before we exclude it as a cause of the general muscular wasting in this patient. I refer to what has been described as “generalized bilateral neuritic muscular atrophy due to a toxic or infectious neuritis.” In the latter condition

the neuritic atrophy may develop either rapidly or more slowly, and the peripheral nerves are usually sensitive to pressure. But even in this generalized atrophy the process nearly always involves the lower extremities earlier than the upper; and besides, the paralysis and atrophy are much more marked in the distal portions of the extremities than in the proximal. Moreover, in a polyneuritis involving motor nerves so widely there is always involvement of the sensory fibers of the peripheral nerves as well with resultant objective disturbances of cutaneous and deep sensibility. You have seen that, in the patient before us, the topography of the atrophy is general and equal, not more pronounced distalward than proximalward in the extremities. It is true that the patient has used alcohol to some extent, and that she has had some infectious process with fever and tachycardia. It is also true that when she was first taken ill she complained of pains and aches in the extremities, diagnosed as rheumatism. Furthermore, we have seen that her calves were rather tender on pressure, that she had transitory edema of the ankles (not uncommon in polyneuritis), and that there is diminution or loss of the deep and superficial reflexes, and finally, in considering a toxic-infectious polyneuritis as a possible cause of the generalized muscular atrophy, we must not forget that this patient has exhibited the mental symptoms of a psychosis in which there has been some disorientation as regards time, auditory hallucinations and delusions of grandeur, and of persecution. You will at once recall that the so-called Korsakoff's psychosis is frequently associated with a polyneuritis, and I have no doubt that you are now comparing in your minds the clinical picture of a typical Korsakoff's psychosis with the mental state presented by the patient before you. If so, you have probably already realized that though there is resemblance there is not identity, for in Korsakoff's psychosis the memory disturbance is peculiar and striking; there is such marked impairment of the recording faculty that the patient forgets most new and recent impressions and works up his older memories into so-called pseudo-reminiscences or memory falsifications so that he describes amazing experiences and adventures that have no basis in fact. Our patient's mental state, as Dr. Scott has emphasized, seems rather to be that of an exhaustion psychosis such as is not infrequently seen in convalescence after a prolonged toxic or infectious process. This form of psychosis, sometimes described as collapse-delirium, is characterized by dream-like confusion,

hallucinations and illusions, and sometimes by delusions and by lively motor excitement. The generalized muscular atrophy in our patient, accompanied as it is by loss of all the subcutaneous fat and by exhaustion psychosis, must really be due to a general process of undernutrition of the body as a whole. The patient has catabolized her own fatty and muscular tissues and has failed to anabolize them. In a sense she may be said then to have been "auto-anthropophagous," if we dare coin such a word.

When a person starves himself for any reason, his combustion processes continue nevertheless; the oxygen consumption continues and the heat production rarely falls below 30 calories per kilo of body weight. Though in chronic undernutrition the nitrogen output falls markedly, still a certain amount of protein must be catabolized each day even when there is no protein intake, and this protein is derived from the patient's own tissues, especially the muscles. The decrease in weight in chronic starvation is due chiefly to loss of water and to a reduction in the weight of the adipose tissues and the muscles. There is some reduction in the weight of the skin, the bones, the blood, and the abdominal viscera. Strange to say, there is very little reduction in the weight of the heart and of the central nervous system, though the physiological activities of the circulatory and nervous systems may be markedly disturbed owing to the deficiency of nourishment. The patient before us presents the picture of chronic starvation with extreme wasting; she weighs only 45 pounds.

Now what is the explanation of the starvation in this case? Has it been due to an insufficient intake of food (as in anorexia nervosa); is it because she has been unable to utilize the food she has ingested (as in diabetes); or has there been an abnormal acceleration of the metabolic processes in her case (as in Graves' disease, in carcinoma, in tuberculosis, and in other cachectic states)? It looks to me as though several factors may have been operative. Early in her illness she suffered from nausea, vomiting, abdominal pain, diarrhea at times, and possibly from melena. She found that the ingestion of food aggravated her symptoms, and doubtless on this account restricted her food intake. The x-ray examination now reveals pyloric stenosis. At times she vomited some of the food ingested. During the periods of diarrhea she may have passed unassimilated food in the stools. Later she suffered from an exhaustion psychosis, thought the nurses were poisoning her, and refused all nourishment (secondary mental

anorexia). She had fever and tachycardia for some time (whether from pulmonary tuberculosis or some other cause we are not sure), and during this period there may have been an acceleration of her metabolic processes, with so-called "toxic destruction of protein." Obviously, then, there are several reasons why this woman should have undergone the extreme emaciation that she exhibits.

Her gastro-intestinal symptoms next deserve special mention. The nausea, vomiting, abdominal pain, and possible melena have to be explained. She has an achylia gastrica, a filling defect at the pylorus, and partial pyloric stenosis with motor insufficiency of the stomach. One cannot help but think of a gastric ulcer, benign or malignant. Chronic cholecystitis and pericholecystitis with peripyloric adhesions causing a pyloric distortion and partial stenosis of the pylorus ought also to be kept in mind. The achylia gastrica, with pus-cells and Oppler-Boas bacilli in the stomach contents, and filling defect at the pylorus, in an emaciated woman of forty-six, who has had, or may have had, melena are certainly suggestive of carcinoma ventriculi, but there is no lactic acid in the stomach contents, the Wolff-Junghans test is negative, there is now no occult blood in the stool, no abnormal mass is palpable in the epigastrium, and there are no evidences of metastases in the liver or in the Virchow-Troisier lymph-gland above the left clavicle. Achylia is uncommon in benign gastric ulcer, but by no means incompatible with it; it or subacidity is, however, more common in association with gall-bladder diseases than with ulcer. It may be that the alcoholism and the oral sepsis may have contributed to the achylia by causing a chronic gastritis. We could not without an exploratory laparotomy be sure of the exact nature of the process at the pylorus, but I am inclined to think that we are dealing with a benign ulcer there with cicatrix formation causing partial stenosis.

We may next turn to the consideration of the anemia. It is of the secondary type, as shown by the low color-index and the relative polymorphonuclear increase in the differential count of the white blood-corpuscles. We can, I think, rule out a so-called pernicious anemia despite the leukopenia and the association with oral sepsis and with achylia gastrica. Were it not for loss of water the blood count would probably be lower. The infection and the prolonged undernutrition are sufficient, I think, to account for the impoverishment of this patient's blood.

Coming, finally, to an interpretation of the nervous and mental symptoms in this patient, I should like to refer briefly, first to the areflexia, and second, to her psychosis.

The loss of reflexes together with outspoken muscular atrophy without fibrillary twitchings, but with a history of "rheumatic pains," made one think seriously of polyneuritis; but I have already shown why we cannot view the muscular atrophy of our patient as neuritic in origin. I think it quite probable, nevertheless, that the peripheral nerves in this patient have undergone a slight toxic-degenerative change due perhaps to the oral sepsis or other infections, to the prolonged gastro-intestinal disorder, and the extreme undernutrition. Experienced clinicians have long been familiar with the fact that the superficial and deep reflexes may be abolished, or markedly diminished, at an advanced stage of any grave general disease that leads to emaciation or cachexia even though they have been slightly exaggerated at an earlier stage.

As to the psychosis presented by our patient, it seems probable that it should be regarded as a true exhaustion psychosis due to the profound and prolonged undernutrition. It has not the earmarks either of the Korsakoff's psychosis or of the paranoid state of the chronic alcoholic; it has nothing to do with a paralues; it is not the picture of dementia præcox, though in certain of its features it may suggest it. It is sufficiently accounted for, I believe, by the undernutrition and the toxic-infectious process from which the patient has suffered.

Summing up our diagnostic findings, we may then conclude that we are dealing here with:

1. Chronic starvation and extreme undernutrition.
2. Exhaustion psychosis.
3. Secondary anemia with leukopenia.
4. Ulcer of the pylorus with cicatrix formation, partial pyloric stenosis, and achylia gastrica.
5. Oral sepsis.
6. Old pulmonary tuberculosis.

As to the planning of a suitable therapy you will at once see certain difficulties in the way. We desire to nourish this patient, but her mental state is such that it is almost impossible to induce her to swallow food. Were it practicable to isolate her, in charge of special nurses who would be constantly with her, it might, with the authority

of a physician, especially if he could gain her confidence, become possible to induce her to swallow milk every two hours of the day and, later, solid food. But could her stomach retain the food, digest it, and pass the chyme into the duodenum for further elaboration and absorption? With conditions at the pylorus such as the x-ray shows them to be, and with an achylia, this is doubtful. The stenosis at the pylorus is, it is true, only a partial, not a complete, obstruction. And we could give HCl to help digest any food that was swallowed or that was introduced through a stomach-tube. Were the general nutrition of the patient less involved, and were the mental state normal, I should advise a laparotomy at once in the hope that the surgeon would find a benign lesion at the pylorus and could relieve the partial pyloric obstruction. As she is, she is a very poor surgical risk, for her resistance to infection must be low; moreover, there is no telling what she might do to an abdominal wound after operation so long as her psychosis continues. I should be inclined to try to improve her nutrition, at least for a short time, (1) by inducing her to eat, (2) by gavage, (3) by nutrient enemata, and (4) by administering HCl with, or after, food. But I should not wait too long before turning her over to a surgeon. If she cannot be made to gain at all, or even if we can make her gain a little, her best chance for recovery lies, I think, in surgical operation that will relieve the pyloric obstruction. Carcinoma ventriculi may, of course, be found at operation; if so, the outlook is entirely hopeless. But if at operation a benign condition be found that is corrigible, and if she survive the operative procedures, then it might be possible very rapidly to improve the general nutrition, and later on to observe a mental recovery. The emaciation has, however, advanced to such a stage in this patient that sanguine prophecies are but too likely to go unfulfilled.

[*Subsequent History of the Case.*—Three days after the clinic the patient was sent to Bayview Hospital, having been discharged from the Johns Hopkins Hospital as “unimproved.” Her condition was practically unchanged from that on admission three months earlier except that she was holding her own in the matter of weight. She left the hospital in good spirits, indulging in grandiose ideas, and assuring everyone that she had two private nurses waiting for her at Bayview who would provide her with “lots of grub and stewed chicken.”

After her removal to Bayview she improved for a time, took

more notice of her surroundings, and gained 7 or 8 pounds in weight. At the end of a few weeks, however, the improvement ceased, and though she remained at Bayview until May 19th of the following year, her nutrition remained at about the same level.

Nevertheless, her mental state gradually became more normal. A note made at the time of her discharge from Bayview states that she was "clear mentally, though with some slight ideas of grandeur." She had occasional febrile disturbances that were believed at Bayview to be due to exacerbations of her pulmonary tuberculosis. Apparently, no operation was performed.]

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XI. ADENOCARCINOMA OF ASCENDING COLON

CHRONIC INTESTINAL OBSTRUCTION IN A COLORED MAN OF THIRTY-ONE WITH HISTORY OF RECURRENT COLIC AND DISTENTION OF THE RIGHT SIDE OF THE ABDOMEN; CLINICAL AND x -RAY SIGNS POINTING TO A MASS CONSTRICTING THE LUMEN OF THE COLON ASCENDENS AT ITS JUNCTION WITH THE HEPATIC FLEXURE. DIFFERENTIAL DIAGNOSIS BETWEEN OBSTRUCTIONS OF INFLAMMATORY AND OF NEOPLASTIC ORIGIN

THE patient before you this morning exhibits symptoms and signs that point to some chronic process within the abdomen. The case is a very instructive one not only on account of several features in the history but also because of the opportunity it gives us for the discussion of the differential diagnosis among several possible conditions that might be thought of as explaining the phenomena.

The patient was admitted to the medical ward about a month ago, but has recently been transferred to the surgical service for operation. In the absence of the clinical clerk to whom the case was allotted during his stay in the medical ward, I shall ask Dr. Dorsey to give us a summary of the history and of the physical findings.

DR. DORSEY: The patient, George P. C., a married colored man, thirty-one years of age, by occupation a postal clerk, was admitted to the medical service (Professor Thayer) on December 2, 1920, complaining of "attacks of pain below the navel, of troublesome diarrhea, and of poor blood."

The family history was unimportant. The patient himself has been married for eight years. His wife is living and well, has given birth to two children (living and well), and has had one miscarriage.

Except for the present illness the patient has, in general, enjoyed good health. Of the infectious diseases of childhood, he suffered from measles, pertussis, mumps, and chickenpox. Some twelve years ago he had a single attack of tonsillitis, without complications. About fourteen years ago he had a soft chancre, but he denies having had other venereal diseases. His habits as regards tobacco and alcohol have been good. He has never undergone any surgical operation.

Questioned regarding the present illness, he states that up to the spring of 1916 he had been very well and kept regularly at work. During the year preceding he had been employed in a chemical

plant, where he was exposed to benzol, chloroform, ether, and methyl-alcohol. He gave up this work in March of 1916 and became a postal clerk.

His *present illness* dates from the same month, when he began to suffer from dull aching pains in the hypogastric region. These pains were not related in any definite way to meals or to urination. During the next year there were recurring attacks of the pain, which seemed to be colicky in nature. Occasionally these pains were so severe as to prevent him from sleeping. In the spring of 1917 he began to suffer from diarrhea, having from four to seven movements of the bowels each day. With the diarrhea there was some tenesmus, but he never noticed the presence of any blood or mucus in the stools. This diarrhea has continued ever since, though during the past month, under medication, it has practically ceased.

The pains grew progressively worse from the time of the onset of the trouble until August, 1920, when they were at their maximum. Since that time medical treatment has relieved them to a certain extent.

His appetite has been good throughout his illness, but he has hesitated to take food because of a heavy feeling that followed. This heavy feeling occurred no matter what kind of food he ate.

When his illness began he weighed 200 pounds, being at that time about 68 pounds above calculated ideal weight for his height of 5 feet, 4 inches. With the gradual loss of weight there has been progressively increasing weakness.

During the past two years he has suffered off and on from abdominal distention, localized always in the right half of the abdomen. The distention, however, occurred in attacks of brief duration.

Recently he has noticed that he has grown very pale, and it is probable that he has become gradually more anemic during the past two years. He had to stop work about two years ago on account of weakness, shortness of breath on exertion, and persistent diarrhea. He has noticed a little dizziness and some tinnitus at intervals for about two years. Some two weeks before admission he had a fainting spell, when he felt particularly weak.

Aside from the symptoms mentioned he has had nothing to complain of. He states that he has not suffered from nausea or vomiting at any time during his illness.

DR. BARKER: It is interesting that his illness set in just after his

year of work in the chemical plant, where he was exposed to the vapors of benzol and of other volatile chemical substances. You will remember that we have had some severe cases of anemia in this hospital due to benzol poisoning. Dr. Selling reported them some years ago. The anemia in the present case, however, does not seem to have developed immediately after the exposure to benzol. It has come on gradually during the past four years and is more likely due to the condition that has caused the pain and distention in the abdomen. What were the findings on physical examination when he was admitted to the medical ward?

DR. DORSEY: The first physical examination was made by the house officer, Dr. Felting. Since then he has been examined by the assistant resident physician, Dr. H. M. Thomas, Jr., by the resident physician, Dr. Mason, and by Professor Thayer.

Dr. Felting's findings, in summary, were as follows:

Muscular colored man, who has lost much weight, but is still 8 pounds above calculated ideal weight. He lies in bed, complaining of pain of a cramp-like character in the lower abdomen, principally in the middle, but partly in the right lower abdomen. Lips and mucous membranes pale; skin smooth and moist, except for a little branny desquamation of the skin of the abdomen and of the lower extremities; annular skin lesions over the brows suggestive of tinea circinata. Slight enlargement of post-cervical, inguinal, and axillary lymph-glands.

Thyroid isthmus and lateral lobes a trifle enlarged, but no definite struma. Eyes slightly prominent, but no other eye signs of hyperthyroidism. Pupils normal. Eye-grounds normal. Tonsils slightly enlarged and reddened.

Thorax of normal form. Lungs negative throughout. Heart not enlarged; soft blowing systolic murmur at the apex, not well transmitted; pulmonic second sound slightly accentuated. Pulse regular in force and rhythm, 72 to the minute. Blood-pressure, 138 systolic, 75 diastolic. Arteries accessible to palpation definitely thickened.

Abdomen symmetrical at time of examination; on palpation, tenderness was elicited in the right upper half of the abdomen, and the patient then complained of a severe paroxysm of pain, beginning locally, but soon becoming generalized, though maximal in the hypogastric region and the right side of the abdomen. About three finger-breadths below the costal margin in the right mammillary line a mass

was palpable. It seemed to lie rather deep, descended with inspiration, and had an irregular shaped lower edge. The liver edge was palpable just below the costal margin; the liver dulness began above at the fifth rib. Neither the spleen nor the kidneys could be palpated. The abdomen was everywhere tympanitic on percussion.

The physical examination was otherwise negative, except for slight phimosis. The deep and superficial reflexes were all normal. On rectal examination by palpation the prostate was small, soft, and not tender. No hemorrhoids were found.

Dr. Felty's impression was that the man was suffering (1) from a secondary anemia, the etiology of which had to be discovered, and (2) from an obscure abdominal condition, associated with the presence of a mass, the nature of which could not be determined without further study.

He had the intestine thoroughly cleaned out, but this caused no alteration in the findings in the right side of the abdomen.

DR. BARKER: You state that the anemia was striking on admission. What did the examination of the blood reveal?

DR. DORSEY: The blood examination was reported as follows: R. B. C., 2,824,000; W. B. C., 8250; hemoglobin, 21 per cent. Color-index 0.38. Differential count of the white cells: Polymorphonuclear neutrophils, 69 per cent.; no eosinophils or basophils; lymphocytes, 24 per cent.; large mononuclears and transitionals, 7 per cent.

There was marked central pallor of the red cells, with moderate anisocytosis and poikilocytosis. The platelets seemed to be increased, though they were not counted.

DR. BARKER: The blood-picture is characteristic of a severe secondary anemia, the hemoglobin being reduced out of proportion to the decrease in the red cells.

DR. DORSEY: The stools were carefully examined. On one occasion a little blood was seen on the surface of a formed stool, though no hemorrhoids could be detected. Tests made for occult blood in the feces were positive. No parasites could be found in the feces, though it was stated that before he was admitted to this hospital *Trichomonas* had been present in the stools.

DR. BARKER: It would seem scarcely likely that a *Trichomonas* infection alone could be responsible for a history like this. You state that no amebæ were discovered?

DR. DORSEY: Amebæ were absent in all specimens examined.

Indeed, no parasites of any kind were found other than intestinal bacteria. This was in accord with the absence of any eosinophilia in the blood.

DR. BARKER: What further observations were made during his stay in the Medical Ward?

DR. DORSEY: The temperature ranged between 97° and 101.6° F., averaging between 99.5° and 100.5° F. His pulse-rate has been accelerated, varying between 72 and 130.

The stomach contents were examined and showed a total absence of free hydrochloric acid and a total acidity of 10 acidity per cent.; lactic acid was not present, nor were there any Oppler-Boas bacilli. Tests for occult blood in the stomach contents were negative.

DR. BARKER: Was a Wassermann test made?

DR. DORSEY: The Wassermann reaction in the blood-serum was negative.

Dr. H. M. Thomas, Jr., described the mass as definitely localizable in the ascending colon, the cecum being dilated below it. This fact, together with the painful distention in the right lower quadrant, suggested obstruction of the lumen of the ascending colon. The very small amount of blood in the stools did not seem enough to account for the high grade of secondary anemia that existed.

On several occasions, following palpation of the mass in the ascending colon, the large bowel below the mass became clearly outlined against the anterior wall of the abdomen, and Dr. Mason has observed peristaltic waves running up from the cecal region toward the site of the mass.

DR. BARKER: Has the condition of the lower bowel been examined by means of the proctoscope?

DR. DORSEY: Yes; Dr. Harvey Stone made a proctoscopic examination on December 29th and found the anorectal region entirely negative. The proctoscope was passed in for 25 cm. and a very good view was obtained. There were no signs of ulceration, growth, or stricture in the part of the bowel accessible to proctoscopic inspection.

DR. BARKER: Did the urine contain anything abnormal?

DR. DORSEY: The urine was entirely normal.

DR. BARKER: What *x*-ray examinations have been made?

DR. DORSEY: A roentgenogram of the chest was made, as well as a gastro-intestinal series after a contrast meal. An *x*-ray photograph

of the colon was also made after the administration of a contrast enema.

In the roentgenogram of the chest the lungs were entirely negative. There was no evidence whatever of tuberculosis or of tumor metastases. The cardiovascular stripe presented nothing abnormal.

In the gastro-intestinal series, made after a contrast meal, the stomach and small intestine were found to be negative. The barium, however, accumulated in the cecum and ascending colon, stopping abruptly near the upper end of the ascending colon just proximal to the hepatic flexure.

DR. BARKER: Let us look at these x -ray plates as they stand on the illuminating screen. You see that the outlines of the stomach and of the duodenum seem perfectly normal. The passage of the barium through the small intestine presents nothing particularly abnormal. The great dilatation of the cecum and ascending colon, however, in the five-hour plate and in the fifteen-hour plate is striking. You notice that just above the accumulated barium there is a narrow strip showing that a little barium is going through a constricted portion of the intestine. At the flexura coli dextra the air-containing, dilated, transverse colon begins, and a little barium can be seen in this, in the rest of the colon, and in the rectum. You notice that the character of the diminution of caliber of the ascending colon indicates a concentric constriction. If this obstruction were due to some mass causing direct pressure from the outside we should expect a less symmetrical constriction. Moreover, the obstruction can scarcely be due to anything within the lumen of the intestine. It looks as though the constriction were an annular, elongated constriction dependent upon something within the wall of the intestine itself at the upper end of the colon ascendens. Were these plates examined by Dr. F. H. Baetjer?

DR. DORSEY: Yes; he thought the constriction at the junction of the ascending colon with the hepatic flexure was suggestive of tumor, and advised making an additional plate after a barium enema.

DR. BARKER: Here is the plate made after the administration of the barium enema. You see that the barium introduced from below does not pass the obstruction. It stops abruptly at the hepatic flexure of the colon and does not enter the colon ascendens at all.

You state that Dr. Thayer examined the patient. Did he confirm the findings on physical examination?

DR. DORSEY: In Dr. Thayer's note it is stated that a prominence could be seen on inspection in the right lateral abdominal region, and that this prominence descended with inspiration. He could feel a slightly irregular mass in the region of the obstruction, and on one occasion made out distinct gurgling in this region and visible peristalsis leading up to it. The mass was, he believed, in the ascending colon or at the hepatic flexure. Dr. Thayer felt that there was undoubtedly stricture of the intestine, which should be relieved surgically because of the chronic obstruction.

The patient on December 29th received a blood transfusion of 400 c.c. of citrated blood without reaction, and was transferred on the same day to the surgical service. He will be operated upon tomorrow.

DR. BARKER: Let us examine the patient's abdomen now. There is no marked distention at present, though the right side of the abdomen is, perhaps, a little more prominent than the left. When you suspect chronic intestinal obstruction you should look not only for localized distention but also for visible patterns and for a peristaltic wave. The history of colicky pains in the hypogastric region and in the right abdomen suggests recurring spasm of the small intestine, and perhaps of the proximal portion of the large intestine. It is interesting that this patient states that it has always been the right side of the abdomen that has been distended. In chronic intestinal obstruction a localized distention often gives a clue to the site of the obstruction and this would appear to be the case in the present instance. Patients often become so emaciated in chronic intestinal obstruction that an abdominal pattern becomes pronounced. If you are not acquainted with the paper by Wyllie on "Abdominal Patterns," published in the Edinburgh Hospital Reports for 1894, I should advise you to look it up in the library after the clinic. Just at this moment I can see no definite pattern and no peristalsis. Perhaps we can elicit them. On tapping the right side of the abdomen a marked change takes place as you see. A pattern appears in the right lower quadrant evidently corresponding to the outline of the cecum. Now a definite peristaltic wave is passing over this pattern, and passing from below upward toward the site of obstruction in the right upper quadrant. This visible peristalsis does not go beyond the level of the palpable mass. This is an important point, and I hope you will not forget that in stenosis of the intestine marked visible

peristalsis that always becomes arrested at a definite spot is of importance in localizing the site of the obstruction.

Next let us palpate the abdomen. On superficial palpation the abdomen is everywhere soft and there seems to be no spasm of the muscles of the abdominal wall. On deeper palpation there is marked tenderness in this right upper quadrant. The patient winces and complains of the pain. He is so tender that I should think that there must be at least a little peritoneal irritation here. Palpation of the left side of the abdomen is entirely negative, as is palpation of the epigastrium. In the right abdomen the cecum is evidently dilated, and here in the right flank, lateral from the lateral edge of the rectus muscle, is a definite mass which does not seem very hard, but is somewhat irregular in shape, and which descends with inspiration. I do not like to press upon it too firmly, as the patient, you observe, feels considerable pain. There is certainly no marked accumulation of feces in the ascending colon, for I do not get any putty-like depression on palpation with the single finger. I am impressed with the mobility of this mass; not only does it descend on inspiration, but on careful palpation it can be moved a little from side to side. The mass seems to be entirely independent of the liver and it is situated below the gall-bladder. It could not, I think, be connected with the right kidney. It does seem to be a mass in the intestine itself, namely, in the terminal portion of the colon ascends. The wall of the colon below this mass as well as that of the cecum must, of course, be hypertrophied; but I can feel no nodules in the wall lower down, nor is there any mass in the ileocecal region that can be palpated. There is a little gurgling on deep palpation just proximal to the mass.

On percussion the abdomen is everywhere tympanitic, even over the mass.

Were any pus-cells found on examination of the feces?

DR. DORSEY: No pus cells were seen; only a little manifest blood once, and occult blood another time.

DR. BARKER: Were the feces examined carefully for tubercle bacilli?

DR. DORSEY: I do not know.

DR. H. M. THOMAS, JR.: Yes; several tests were made for tubercle bacilli in the feces, but none could be found.

DR. BARKER: I should like to examine the apices of the lungs again carefully. On inspection there seems to be no depression and

no lag at either apex. On percussion the note is quite clear at both apices. On auscultation, even after cough at the end of expiration, I hear no adventitious sounds in either upper lobe. This is in accord with the examinations that have been made in the ward and with the negative x -ray plate of the chest. It seems scarcely possible that there is any active tuberculous process in these lungs. This would seem an important point, since intestinal tuberculosis is, as a rule, associated with pulmonary tuberculosis.

We can summarize the data thus far accumulated in this case in a few brief sentences: Here we have a colored man, thirty-one years old, whose illness began nearly five years ago with colicky pains in the hypogastrium, which have continued, off and on, ever since, becoming maximal last August. About a year after onset he began to have diarrhea, which has also persisted since. He gradually grew weaker and paler, and two years ago had to stop work. His weakness and anemia have caused dyspnea on exertion, ringing in the ears, slight headache, and recently a fainting spell. He has a mass in the right upper quadrant, and the clinical signs (localized distention, visible peristalsis, palpable mass), and the x -ray findings together indicate that there is obstruction due to marked concentric constriction of the lumen of the ascending colon near its junction with the right flexure of the colon. The patient obviously suffers from chronic intestinal obstruction, with severe secondary anemia and asthenia. He has lost 60 pounds in weight, but does not look cachectic. He has an achylia gastrica, but no other symptoms or signs referable to the stomach. There has been a little blood in the feces not due to hemorrhoids. He now has marked local tenderness at the site of the mass in the abdomen and remittent fever, indicating local infection. He has had a soft chancre, but denies lues, and the Wassermann reaction is negative.

We have next to consider the nature of this obstruction in the ascending colon. What are some of the possibilities that have been discussed in the ward?

DR. DORSEY: Some believe the obstruction to be due to a tuberculous lesion. Others incline to think it due to a malignant growth. Syphilitic lesions and benign inflammatory processes have also been mentioned as possibilities.

DR. BARKER: Those are all interesting suggestions. Let us see whether we can arrive at a diagnosis with certainty, or whether we

have to be content for the present with merely a probable diagnosis as to the nature of the obstruction.

As I have said, everything points here to the view that the cause of the obstruction lies in the wall of the ascending colon itself, rather than outside it or within its lumen. It is difficult to think of any cause of obstruction within the wall itself that could be other than inflammatory or neoplastic in nature. If the obstruction were acute, we should have other things to think of, of course; but here the obstruction is chronic.

Let us first consider the local inflammatory enteropathies that might account for this obstruction. We might have to deal with a simple (non-specific) inflammatory process, such as a cicatrizing ulcer of the colon following a dysenteric, a typhoidal, or some other form of colitis causing ulceration. I remember one bad mistake we made at one time in this hospital, in which we had made the diagnosis of sarcoma of the large bowel. There was obstruction in the rectosigmoid region and a hard mass could be felt on palpation there and it could be seen on proctoscopic examination. Members of both the medical and surgical staff felt sure it was a neoplasm. A small piece was excised through the proctoscope and subjected to microscopic examination in one of the laboratories, where a histological diagnosis of sarcoma was made. The case was believed to be inoperable, and the patient was sent back to Georgia. A few months later I had a letter from the patient, who said that one of our own graduates had examined him after he had left this hospital, had found amebæ in the stool, and had administered emetin, after which the mass had disappeared and he had recovered entirely!

The patient before us has had recurrent diarrhea for several years, but he has not observed mucus in the stools and only a little blood has been present in the feces since he has been under observation here. A careful search for amebæ and for cysts has revealed none. The patient gives no history of typhoid.

Of the specific inflammatory enteropathies we should consider: (1) tuberculosis, (2) lues, (3) actinomycosis, and (4) certain rarer forms of mycosis (*e. g.*, blastomycosis, sporotrichosis, etc.).

There are several points that favor the view that a tuberculous lesion may be the cause of the obstruction in this case. Thus, the patient is a colored man, and tuberculosis, as you know, is very common in the colored race. He is a young man, only thirty-one years of age,

a point in favor perhaps of tuberculous lesion; tuberculosis of the large bowel is commonest between the twentieth and the fortieth years. The process, furthermore, is a very chronic one, the history dating back between four and five years. Moreover, the mass is somewhat elongated and is palpable. And finally, the patient has fever without leukocytosis, but with marked anemia. Has the urine been tested for the diazo reaction?

DR. DORSEY: I think not.

DR. BARKER: It might be worth while to make a test for Ehrlich's diazo reaction in the urine. It is usually positive in cecal tuberculosis, and is said to be usually negative in carcinoma of the large bowel.

Though all the above points are suggestive of a tuberculous lesion, there are a number of points that are against the diagnosis of tuberculosis. Thus: (1) There are no signs of pulmonary tuberculosis in this patient, and it is exceedingly uncommon to find tuberculosis of the large intestine without an associated pulmonary tuberculosis; (2) it has not been possible to demonstrate tubercle bacilli in the feces, and they are often demonstrable there in tuberculosis of the large intestine; (3) the mass seems to me rather mobile for a tuberculous mass, the latter being usually fixed, and finally, (4) the site of this mass is not the common site for a tuberculous lesion of the large intestine. The most common site for the latter process is the ileocecal region. Here the ileocecal region is free. It is conceivable, of course, that a tuberculous process could attack the upper extremity of the colon ascendens, but it is certainly a rare site for a tuberculous process.

Next let us consider the possibility of an obstruction of the colon ascendens due to a luetic enteropathy. This patient had what he called a "soft chancre" in 1906. He denies having had syphilis. Syphilis, you must know, sometimes causes obstruction to the large intestine. The obstruction may be due either to a stricture or to a gummatous mass. If lues be the cause of the obstruction in this patient, it must have been through stricture rather than through gumma, for the constriction is concentric and not asymmetrical. Luetic stricture is, however, rare in this particular situation; it is most common, as you know, in the rectum. Moreover, this patient's Wassermann reaction is negative, and that is strongly against the diagnosis of lues, though it does not absolutely rule it out.

Turning next to the possibility of an actinomycotic enteropathy, I would say that there is very little in favor of that diagnosis, for the mass is mobile, the abdominal wall is not invaded, and there has been no fistula formation.

Other mycoses, like blastomycosis and sporotrichosis, are exceedingly rare diseases, and if they were the cause of this enteropathy we might very well expect to find lesions due to the same organisms in other parts of the body (skin, etc.).

Could this obstruction of the colon ascendens be due to a neoplasm? This is a possibility that I think we dare not, as yet, rule out. The data in favor of malignancy would seem to me to be as follows: (1) The site of the lesion in the ascending colon near the hepatic flexure is a common site for neoplasm; (2) the blood in the feces in the absence of tubercle bacilli is suggestive of an ulcerative process; (3) the absence of demonstrable tuberculosis of the lungs is against the inflammatory form of enteropathy most likely to simulate a neoplastic enteropathy, and (4) the x-ray findings show concentric constriction of the lumen of the colon such as is often seen in annular carcinoma.

But there are several points that militate against the diagnosis of malignancy, especially against the diagnosis of carcinoma or sarcoma: (1) The duration is much longer than we would expect with a malignant growth, for this patient has been ill four or five years. If he had a sarcoma he could scarcely have lived that long. Carcinoma of the large intestine is usually adenocarcinoma arising from the cylindrical epithelium of Lieberkühn's crypts, and the duration of even annular carcinoma is usually much shorter than in the present case. There are on record a few instances, however, where carcinoma of the intestine has been in existence for a good deal longer than a year. (2) The age of the patient is against carcinoma, for the latter is rare before the fortieth year. It must be borne in mind, however, that one-sixth of carcinomata of the large intestine occur before the fortieth year, and one-seventh of them before the thirtieth year of life. Carcinoma of the intestine may even occur in infancy. (3) Again, fever is exceptional in carcinoma, at least before ulceration and secondary infection have taken place. (4) And finally, the cachexia is not so marked in this patient as we would expect it to be if a carcinoma of the colon had existed a long time. True it is that he has lost 60 pounds in weight and has a very high grade of anemia,

but one would expect him to be far worse off than he seems to be if he had had a carcinoma for over four years.

Benign neoplasms, like lipoma, fibroma, and leiomyoma, sometimes cause intestinal obstruction; but one would scarcely expect such a concentric constriction of the lumen as the x-ray shows to exist in this patient. The mobility of the mass, however, favors neoplasm, either benign or malignant, rather than an inflammatory process.

After this discussion of the implications of the several diagnostic suggestions made, you will agree with me, I think, that absolute certainty of diagnosis as to the nature of this obstruction cannot be arrived at with the data at our disposal. There are many points that favor the diagnosis of tuberculous colitis and many points that favor the diagnosis of neoplasm; but, as you have seen, there are also several points that can be urged against either of these two diagnoses, and there are certain other possibilities that have to be considered. It is never wise to go farther than the facts permit you to go. It would be easy here for one with cock-sure tendencies to make a flat-footed diagnosis of one or another of the possible lesions I have named, and one might be lucky enough to have that flat-footed diagnosis verified tomorrow at the operation. I cannot impress upon you too strongly, however, the desirability of distinguishing among certainty, probability, and possibility, when trying to arrive at a diagnostic conclusion. One must not, of course, be too cautious, and again, one must not be too bold. Let us push our diagnoses just as far as the facts justify us in doing, but no farther. We must try to avoid self-deception.

It is possible that by waiting longer and making more tests we could secure additional data that would permit of a positive and certain diagnosis in this case, but the indications for surgical interference are definite. This man has gone already too long without attempts at surgical relief of his obstruction. No matter what the cause of the obstruction, it is now wise to try to relieve it at the earliest date possible. He will be operated upon tomorrow morning, and I hope that conditions may be found that the surgeons may not only temporarily but also permanently relieve. I shall make it a point to report to you later the findings at operation, and, if anything be removed, also the reports of examination of the excised tissues to be made in the pathological laboratory.

[*Subsequent History of the Case.*—The patient was transferred to the surgical service on December 30th.

Operation was performed by Dr. M. Reid on January 5, 1921. On opening the peritoneum there was found a fairly extensive mass, involving the ascending colon, just before reaching the hepatic flexure. It was hard, infiltrating a large part of the bowel, and annular. It was necessary to excise practically all of the ascending colon. Two cigarette drains were placed down to the area where the carcinoma had been removed in the posterior wall. Gauze and dry dressing applied.



Fig. 17.—Photograph of adenocarcinoma of ascending colon removed at operation. Note crater-like ulceration. In the upper right-hand corner a polyp is seen.

The specimen removed was carefully examined in the Surgical-Pathological Laboratory by Dr. J. C. Bloodgood. It included the terminal 8 inches of the ileum and a part of the omentum. Directly above the ileocecal valve was a large ulcerating growth, with a necrotic, crater-like ulceration measuring about 5 cm. across (Fig. 17). It was markedly indurated; near it was a polypoid growth, about the size of a walnut, attached by a very small pedicle. Dr. Bloodgood stated that it was the first time that he had observed one of these pedunculated adenomata near a cancer.

All the glands examined were enlarged, hard, and involved in the

new growth. On section, the tissue of the indurated portions resembled that of carcinoma. The polypoid mass, on section, was seen to be made up of looser, softer tissue, was covered by mucosa, and in it could be seen dilated glands. Excellent photographs have been made by Mr. Herman Schapiro.

Report on Microscopic Section (Dr. J. C. Bloodgood).—“This showed that the growth was an adenocarcinoma (Fig. 18), with a few attempts

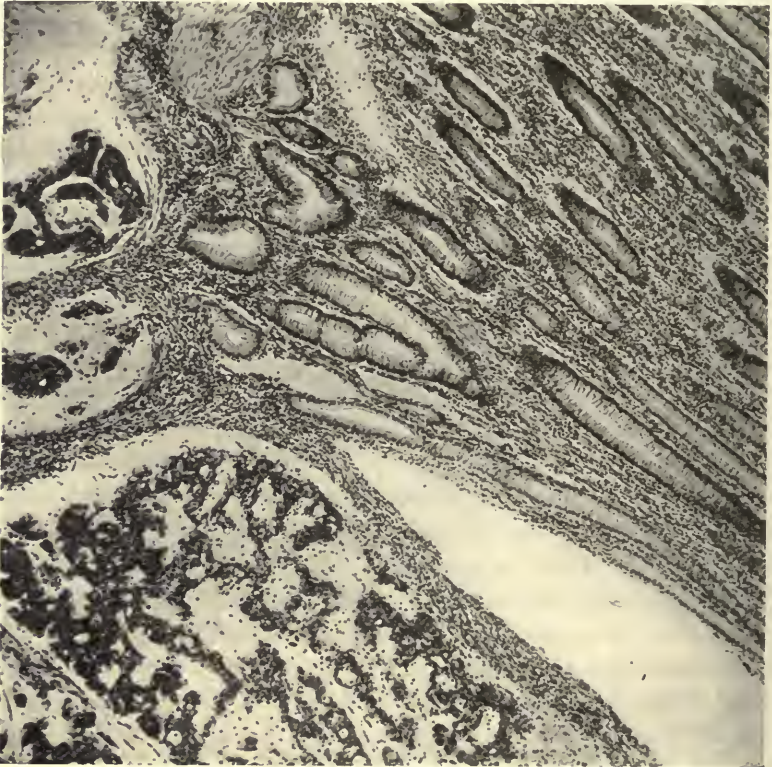


Fig. 18.—Microscopic section showing the adenocarcinomatous tissue.

at acinus formation. It was a fully developed colloid cancer. The infiltration did not extend through the wall of the gut. The pedunculated growth is a benign cystic adenoma (Fig. 19), the stroma consisting of vascular lymphoid tissue. The cells lining the cysts are of the columnar type, secreting mucin.”

The patient recovered rapidly and was discharged on January 23d as “well.” On leaving he said he felt better than for three years.

He was advised to do light work and to build himself up by means of a nourishing diet. Hemoglobin, 45 per cent.

He was still in good condition about five months later (June, 1921). A letter from his physician, Dr. George B. Davis, of Curtis Bay, Md., states that "the present condition of the patient is exceptionally

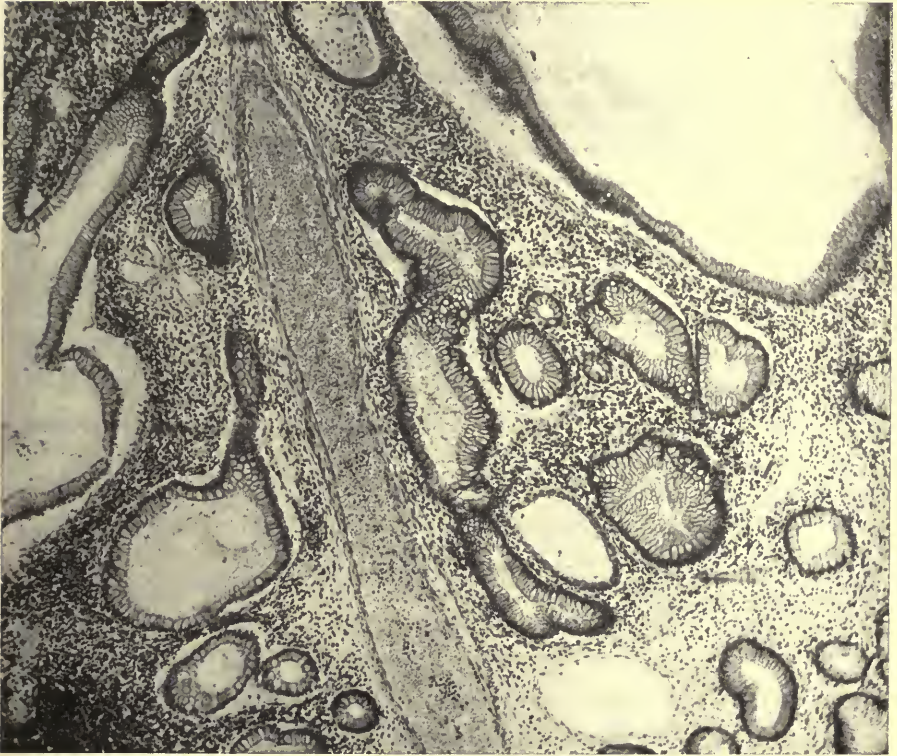


Fig. 19.—Microscopic section of the benign polyp situated near the adenocarcinoma.

gratifying. He claims to be feeling in perfect health and has gained amazingly in weight. He is at present at regular work."]

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XII. DUODENAL ULCER

REPEATED HEMATEMESIS AND MELENA GIVING RISE TO SEVERE POSTHEMORRHAGIC ANEMIA IN A WHISKY DRINKER WHO HAS HAD RECURRING ATTACKS OF HUNGER-PAIN AND OTHER DIGESTIVE DISTURBANCES FOR ABOUT FIVE YEARS. FILLING DEFECT IN DUODENAL CAP. DISCUSSION OF THE CAUSES OF HEMATEMESIS AND COMMENTS UPON ITS TREATMENT

The consideration of the condition of the patient before you today will require us to make another excursion in the domain of the digestive apparatus. This man is one of the hospital orderlies who was brought into the ward on a stretcher some sixteen days ago—

pale, weak, and faint, as the result of vomiting blood and of passing tarry stools. I shall ask Mr. Hinton, the clinical clerk, to give you an epitome of the earlier history of this man and of his state upon admission to the hospital.

STUDENT: The patient, Philip G., a single white man, aged forty-six, one of the orderlies of this hospital, was admitted, as a stretcher case, on January 16, 1921, complaining of faintness and weakness after vomiting of blood and passing tarry stools.

His own past history contains some points of interest. He lived in a family in which there were cases of tuberculosis until he was eighteen years of age. He did office work until two years ago, when he became an orderly. His general health in early life was good. In 1918 he had an attack of pneumonia, and in 1920 all his teeth were extracted on account of severe pyorrhea. He states that he suffered frequently from colds in the head until about three years ago, since when he has been less often affected in this way. In 1885 he had a sore on the penis, which became an ulcer and discharged pus. It healed under local treatment after about six months. Some two years later, he states, he had a skin eruption and some sores in his mouth. Whether or not these were secondary lesions of syphilis, and whether the lesion on the penis was a hard chancre or a soft chancre have not been determined. He never had any antisiphilitic treatment as far as he knows. Aside from the attack of pneumonia in 1918 he has had no symptoms referable to his chest or to his circulation. He had good digestion until about five years ago, when he began to suffer from what he calls "regular attacks of discomfort in the stomach," associated with some pain and a sense of fulness, which he refers to the epigastrium. These attacks occurred every week or ten days with some regularity. The discomfort and pain usually began about three hours after each meal and continued until food was taken. A little food of any sort, even a cracker, would relieve the pain. He soon found that one or two drinks of whisky gave him complete relief, and he states that he gradually found himself taking whisky at least twice a day to gain relief.

DR. BARKER (to patient): Did you have any pain in the night with these attacks? Would the pain wake you after you went to sleep?

PATIENT: No, I do not remember being waked at night by the pain. It came about three hours after each meal.

DR. BARKER: Was the pain severe?

PATIENT: Yes, it hurt a good deal. I could hardly stand it sometimes.

DR. BARKER (to student): When a patient tells you that he has had symptoms of the sort complained of here for as long as five years, what organic disease of the stomach would you think of as probable and what organic disease as improbable?

STUDENT: Such a history sounds as though the patient might have had an ulcer of the stomach or of the duodenum.

DR. BARKER: Yes, his symptoms are strongly suggestive of an ulcer. The chronicity, the hunger-pain, the immediate relief of the distress by eating a little food or taking a little whisky, and the periodicity of the attacks are points that make one consider at least the possibility of duodenal ulcer. Sir B. G. A. Moynihan long ago emphasized the importance of this train of symptoms for the diagnosis of duodenal ulcer. Indeed, he has maintained that the history alone is sufficient for the making of the diagnosis.

Such a long history of digestive disturbances is strongly against the diagnosis of another organic disease of the stomach. What is it?

STUDENT: It is against the diagnosis of carcinoma of the stomach.

DR. BARKER: Yes, it is rare for carcinoma of the stomach to be present in a patient with this history. A carcinoma is, of course, not ruled out by the history, for now and then a carcinoma, as you know, is superimposed upon an old ulcer. The majority of patients with cancer of the stomach, however, give a history of symptoms dating back only a few months. It is rather striking that cancer patients have usually enjoyed good digestion before.

Patients suffering from a psychoneurotic state often give a long history of digestive disturbances also. We must not trouble too much about the nature of the disturbance in this man, however, until we hear more about it. You say he got into the habit of taking whisky to relieve the pain. Did he gradually come to enjoy the whisky for its own sake aside from the relief that it gave him from the pain?

STUDENT: Yes, he gradually increased the amount of whisky taken, and during the past two years he drank a good deal.

DR. BARKER (to patient): Is it true that you have taken more whisky during the past two years than before?

PATIENT: Yes, I have taken a good deal more than before. In

fact, I have taken all I could get. It has been so expensive that I could not get as much as I wanted.

DR. BARKER: I am told that a good many people have been drinking more since prohibition went into effect; but I have understood that this held chiefly for people who had a private stock.

(To patient): Why did you take more during the past two years?

PATIENT: Well, I took it first to relieve the pain in the stomach, but I soon got to like the effects of it. I was never a social drinker. I took to whisky because it made me feel like a different person. Gradually, I wanted more of it.

DR. BARKER: What kind of whisky did you drink?

PATIENT: I used to drink Canadian Club whisky, but for the last two years I have taken what I could get. I am a good judge of whisky, and I can tell good whisky when I get it, but I would rather take bad whisky than get none.

DR. BARKER: Do you mean that you would drink bootleg whisky?

PATIENT: Yes, I have taken a good deal of it. During the past two years the most of the whisky I could get was white corn whisky.

DR. BARKER: The student tells me that you began by taking the whisky in the afternoon. Have you taken any in the forenoons also?

PATIENT: Yes, of late I have taken it in the forenoons too.

DR. BARKER: Have you taken any before breakfast?

PATIENT: Yes, for some time I have had to have some before breakfast nearly every day.

DR. BARKER: Dr. Osler used to lay great stress upon this drinking in the early morning upon an empty stomach. For, in the first place, a man who drinks before breakfast takes, as a rule, several more drinks before night, and in the second place, drinking upon a fasting stomach permits the alcohol to reach the liver in concentrated state. Whisky is much more likely to injure the liver taken fasting than when it is taken with meals or immediately after meals.

(To patient): Have you taken enough to cause intoxication?

PATIENT: Yes, formerly only occasionally, say about once a month, but lately I have been drunk at least twice a week.

DR. BARKER: Evidently the patient has been drinking a good deal of alcohol. His intake has been far beyond Anstie's limit. You

may remember that in the old days it was believed that Anstie's limit (1½ ounces of absolute alcohol or 3 ounces of whisky in the twenty-four hours) was the limit of moderation in drinking. Of the beverages permissible under the Volstead Act one would have to drink about 10 quarts before reaching Anstie's limit of alcoholic intake for the twenty-four hours.

(To student): In addition to this chronic potatorium has the patient any other habits that could have injured his health?

STUDENT: He smokes about twelve pipefuls of tobacco each day.

DR. BARKER: Would you regard that as excessive?

STUDENT: It seems to me to be a good deal of tobacco.

DR. BARKER: To about how many cigars would this correspond?

STUDENT: I should think twelve or fifteen.

DR. BARKER: Scarcely so many, though much would depend upon the pipe and upon the tobacco used. I should think that it would require two or three pipefuls to correspond to an ordinary cigar and perhaps more to correspond to a strong Havana cigar like a Corona-Corona or a large Manuel Garcia. To accustomed pipe smokers a dozen pipes a day would not seem particularly excessive. His tabagism has probably been less harmful to him than his potatorium. Has he taken any habit-forming drugs?

STUDENT: Apparently none, and there has been no marked excess in the use of tea or coffee.

PATIENT: I never had any drug habit, and I did not use any of the substitutes for alcohol, like Jamaica ginger or hair tonic. I was always careful to take whisky, and I tried to make sure that the whisky was good.

DR. BARKER: Did you get so that you felt that you had to have the whisky in order to get along?

PATIENT: Yes; during the past two years I had to have whisky. I just felt I couldn't get along without it. I would make any sacrifice to get it.

DR. BARKER (to student): Why did the patient come into the hospital?

STUDENT: The patient dates his present illness to last October (1920), when he noticed that he was getting pale and the stools were of a very dark color, resembling tar. These tarry stools continued right along and he noticed that his pallor gradually increased.

He continued to have attacks of gastric discomfort, a sense of fulness in the abdomen, and gaseous eructations. He also had pain in the epigastric region about three hours after meals.

About two weeks before admission to the hospital he noticed that he began to tire much more easily than formerly. On January 10, 1921, about 3 o'clock in the afternoon, a very severe pain developed in the epigastrium, and at 7.30 that evening he vomited a quart of dark bloody fluid, which was mixed with some food. He gave himself an enema and passed a good deal of black material, though he did not see any fresh blood. Despite this attack, he returned to work the next morning, but on January 14th he was forced to quit work on account of weakness. His stools continued to look black. On the night of January 14th he vomited about a pint of blood, and on the next day he applied to the Out-patient Department of the hospital for treatment. Unfortunately, no bed was available in the stationary clinic on that day and he had to return to his home. On January 16th he again vomited a pint of bloody fluid and on that day he fainted twice. He was then brought to the hospital on a stretcher and was placed in a bed in Ward F.

DR. BARKER: What was the physical condition of the patient upon his admission to the hospital?

STUDENT: The first physical examination was made and dictated by the house officer, Dr. Telinde. The patient was very pale and weak and was somewhat undernourished. His calculated ideal weight is about 154 pounds stripped, and he weighed some 16 pounds less than this. There was no jaundice. The tongue was somewhat coated, but there was no papillary atrophy of the tongue. All the teeth had been extracted. The thyroid was not enlarged. The lungs were negative. The heart was negative except for a soft systolic murmur over the base. The pulse was regular; pulse-rate 100. The radial arteries were palpable. The blood-pressure was 125 systolic and 70 diastolic. The aorta was not dilated. The abdomen was retracted. There were no dilated veins in the abdominal wall, although the external circumflex iliac veins were slightly overfull. The edge of the liver was just palpable and was firm. The spleen was not palpable and the splenic dulness was not increased. No abnormal masses could be felt in the abdomen, nor were there any areas of marked tenderness. There was no muscle spasm; no ascites. The extremities were negative except for slight varicose veins in the

legs. The deep and superficial reflexes and the pupils were normal. There was no disturbance of sensation.

DR. BARKER: Was the man bleeding when he entered the hospital?

STUDENT: There was still blood in the stools, but he was no longer vomiting blood. The house officer thought that he must have a bleeding ulcer, with an anemia secondary to the hemorrhage.

DR. BARKER: What precautions were taken against further hemorrhage?

STUDENT: The patient was kept at rest in bed and was given a hypodermic of morphin, grain $\frac{1}{4}$. No food or drink was permitted at first, though he was allowed a little cracked ice to suck.

DR. BARKER: How soon was the ingestion of food permitted?

STUDENT: He was starved for three days and was then placed upon a Lenhartz diet.

DR. BARKER: That is a very good régime indeed if ulcer be suspected. You will find it described in detail and adapted to our American conditions in Friedenwald and Ruhräh's *Diet in Health and Disease*. Lenhartz permitted this diet to be begun even when hemorrhage was still going on, though the food, as you will see, according to his scheme, is given in very small amounts and at frequent intervals during the first day. It does no harm, however, to starve the patient completely for a day or two.

It is well to have in mind the management of hematemesis of unknown origin, for one may meet it any time as an emergency. Undoubtedly, complete rest, both bodily and mental, are the most important measures to be instituted. The patient should be kept absolutely quiet in bed in the recumbent position. To relieve his mental excitement and apprehension and to lessen peristalsis, morphin, given hypodermically, is excellent. Morphin prolongs the emptying time of the stomach and, moreover, causes contraction of the antrum pylori. If there be an ulcer in the stomach it is more likely to be in the pyloric antrum than anywhere else. The patient should be protected from any excitement in his environment. Apprehensive friends, especially, should be kept away from him until the dangers of hemorrhage are over. A light ice-bag may be placed upon the abdomen, but it should be changed before the ice has melted. A small ice suppository placed in the rectum may also be helpful, for it is believed to cause reflex vasoconstriction in the upper abdomen.

There should be absolute abstinence from food and drink for a time. The patient does not, as a rule, mind the starvation, but he does object to the thirst. This can often be relieved by letting him suck small pieces of ice, or by permitting him to wash out his mouth occasionally with hot tea. The melted ice and the tea should not, however, be swallowed. If the hemorrhage be prolonged, fluid may be given per rectum, either in the form of salt solution by enema, or of salt and sugar solution by the Murphy drop method.

If the hemorrhage should continue still longer, what other measures could be used?

STUDENT: One might give a blood transfusion.

DR. BARKER: Yes, but before giving a blood transfusion one likes to test out the blood to see what group the patient belongs to. Then it is desirable to find a donor of the same group. This all takes time. What could you do before giving a transfusion?

STUDENT: One could inject some normal horse-serum or some diphtheria antitoxin.

DR. BARKER: Yes, serum is sometimes efficacious in arresting hemorrhage. There are a whole series of hemostatic remedies now available. Vandervelden has recommended the intravenous injection of 10 c.c. of a 7 per cent. solution of sodium chlorid which he asserts shortens the coagulation time. One of the older methods of hemostatic therapy was to give gelatin. If a solution of gelatin be injected one should be sure that it is sterile. Gelatin, as you know, often contains tetanus bacilli; hence the necessity of being sure that the gelatin is sterile.

Some clinicians inject 1 c.c. of undiluted adrenalin solution (1 : 1000) subcutaneously hourly until the hemorrhage ceases. This is rather a stiff dosage of adrenalin. One wants to be sure that the circulatory organs are intact before he uses adrenalin. I have, in at least two instances, seen atrial fibrillation follow a $\frac{1}{2}$ c.c. injection.

Cotarnin salts have been recommended to stop hemorrhage. The hydrochlorate (stypticin) can be given in centigram doses in aqueous solution subcutaneously. Other salts of cotarnin have also been used. These cotarnin preparations, which are very much like hydrastin, seem to have some effect upon hemorrhage from the uterus, but are reported to be less efficacious in hemorrhages elsewhere. I have never made use of them myself in therapy.

Calcium chlorid solutions have been given by enema and also

intravenously in the hope of increasing the coagulation power of the blood.

Since the newer studies on blood coagulation have become familiar various preparations of thromboplastin and of cephalin have been used to stop hemorrhage. Some of these are made from ox brain, some of them from blood-platelets, some of them from blood-serum. Hess' solution of thromboplastin and Squibb's thromboplastin (in 20 c.c. vials) are prepared from ox brain. Coagulin-Ciba is made from blood-platelets and mixed with lactose; 1 gram of the powder corresponds to 20 c.c. of dried blood; a 5 per cent. solution made fresh in salt solution and boiled for three minutes may be injected subcutaneously or intravenously.

In this country Parke, Davis & Company have put upon the market a powder precipitated from normal horse-serum and known as coagulose. Each tube contains 650 mg. of the precipitate ready for solution in warm water. After mixing with the warm water it is allowed to stand for one or two minutes to clear; then the supernatant fluid is drawn off with a syringe. This amount can be injected three or four times daily.

Hematemesis usually ceases after a time on application of one or more of the measures mentioned above, but there are still other means that may be resorted to in case of necessity. In protracted hematemesis Ewald used to wash out the stomach with ice-water, but this is a heroic measure and a big strain upon the patient. Surgeons are very loath to do a laparotomy while hemorrhage is going on. You will find a full discussion of the surgical treatment of acute hemorrhages from the stomach and duodenum in this article by H. Finsterer in the *Deutsche Zeitschrift für Chirurgie*, which I shall pass around the class. This patient's chances are probably better with medical measures than with surgical intervention. If the hemorrhage continue for a long time the four extremities may be ligatured (not too tightly) so as to lock up a good deal of blood within the extremities. In some cases hypodermoclysis may be necessary in order to supply fluid to the body.

Fortunately, in the present instance, the hemorrhage did not continue after the patient entered the hospital. There were tarry stools for a day or two and there are still traces of blood in the feces, as shown by the guaiac test, but the bleeding is now occult; it is no longer manifest.

Prolonged hemorrhage may be very worrying to the physician in charge. During the past month we have had in the hospital a young woman who bled persistently for several days after removal of tonsils and adenoids. Her sister had, earlier, also bled after an operation. The bleeding in our patient continued despite the application of several of the measures mentioned above. Plugging of the anterior nares and of the nasopharynx temporarily held up the hemorrhage, but as soon as the plugs were removed the hemorrhage would begin again. Her hemoglobin percentage fell to 21. Several transfusions were given, but the bleeding continued, nevertheless, for several days before it finally stopped. Dr. Curtis Burnam had told me that in the European clinics which he visited recently, stimulation of the spleen by x -rays has been used as a means of increasing certain coagulation factors and stopping protracted hemorrhage. About one-quarter of an erythema dose of x -rays was applied over the spleen in the young woman mentioned. No further hemorrhage occurred after the application of the x -rays, but it is quite possible that the hemorrhage had just ceased anyway. We are not at all sure that the application of the x -rays had anything to do with the cessation of the hemorrhage. Such stimulation of the spleen, however, might be kept in mind as another measure to be used in protracted hemorrhage that does not yield to ordinary measures.

We formerly used x -rays and radium therapeutically only to kill cells, but the stimulating effect of radiotherapy is coming into vogue. Thus, it is asserted that stimulation of the pancreas increases carbohydrate tolerance in diabetes mellitus, that stimulation of the thymus will cure certain forms of psoriasis, and that stimulation of the pituitary gland can be of some use in hypohypophysism. These are all new measures under trial, and it is too soon to be sure that they are really valuable. I call your attention to them, however, for they seem to me to be of interest.

(To student): How severe was the anemia after the hemorrhage in this patient?

STUDENT: On January 16, 1921 the report on the blood was as follows: Red blood-corpuscles, 1,592,000; hemoglobin, 25 per cent.; white blood-corpuscles, 9000. Differential count showed polymorphonuclear neutrophils, 85 per cent.; polymorphonuclear eosinophils, 1 per cent.; polymorphonuclear basophils, 1 per cent.; small mononuclear elements, 7 per cent.; large mononuclear elements and transi-

tionals, 6 per cent. There was some anisocytosis, slight poikilocytosis, and a little diffuse basophilia. The platelets were not diminished.

Blood examinations have been made daily since. The lowest blood count recorded was 1,480,000 red cells; the lowest hemoglobin percentage was 22; the white cell count fell to 4320, but later rose again.

Yesterday, January 31, 1921, the blood report was as follows: Red blood-corpuscles, 2,768,000; hemoglobin, 40 per cent.; white blood-corpuscles, 6240. Differential count: Polymorphonuclear neutrophils, 77.6 per cent.; polymorphonuclear eosinophils, 1.6 per cent.; polymorphonuclear basophils, 6 per cent.; small mononuclears, 13 per cent.; large mononuclears and transitionals, 2.6 per cent.; no nucleated red blood-corpuscles.

DR. BARKER: How do you account for such rapid improvement in the blood?

STUDENT: On January 23, 1921, that is, nine days ago, the patient was given a transfusion of 500 c.c. of citrated blood from a suitable donor (Group IV). That afternoon his temperature went up to 101.2° F., and the next day his maximal temperature was 102.6° F. He had, however, a very slight reaction otherwise, and the condition of his blood improved markedly after the transfusion. The red blood-count and the hemoglobin percentage have been rising steadily since.

DR. BARKER: Were any other laboratory tests made?

STUDENT: The *urine* was examined and found to be quite normal. The *stool* contained much blood on admission, but this soon disappeared, though occult blood has been present as shown by the guaiac test and is still present. The *Wassermann reaction* in the blood is negative.

DR. BARKER: Have the stomach contents been analyzed after a test-meal?

STUDENT: No, we were afraid to pass a tube.

DR. BARKER: I think you were right not to try. After a hema-temesis of unknown origin it is certainly wise to wait, at least for a time, before subjecting the esophageal or the gastric mucous membrane to the insult of a tube.

Now that the patient has been observed for a period, what is your feeling about the origin of hemorrhage?

STUDENT: I think he must have been bleeding from an ulcer either of the stomach or of the duodenum.

DR. BARKER: Did you think of any other possibility?

STUDENT: On account of his alcoholic history and the firm edge of the palpable liver, bleeding from an esophageal varix had to be kept in mind.

DR. BARKER: Yes, the conditions you have mentioned would seem to be the most probable causes to be considered in this case. Of course, hematemesis can arise from a whole series of different causes. If you will look at the chapter on "Hematemesis" in Herbert French's *Index of Differential Diagnosis*, which I am passing around, you will find the various known causes tabulated. By the way, if you do not make use of French's *Index* let me recommend it to you. It is often valuable for quick orientation in connection with important presenting symptoms. These volumes of Richard Cabot's *Differential Diagnosis* are also valuable for the same purpose. These books are helpful books of reference and deserve a place in your library.

In a man of forty-six, with such a pronounced alcoholic history as this man has given, with a history of digestive disturbances extending over the last five years, and with a palpable liver the edge of which is firm, the hematemesis might very well be accounted for by rupture of an esophageal varix. This would account also for the melena. There are, however, certain objections to the view that the hematemesis in the present instance was due to alcoholic cirrhosis hepatis and ruptured esophageal varix, for, though this man probably has cirrhosis hepatis, it does not seem to be of high grade as yet. There is no ascites; the patient has had no trouble with hemorrhoids, or only very slight trouble; the spleen is not palpable, and there is no evidence of a collateral circulation in the abdominal wall. Of course, hematemesis from esophageal varix can occur in the absence of the signs mentioned, but let us consider the other possible causes of hematemesis and see if we can find evidence for the existence of one of them.

Let us turn to ulcer, both of the stomach and of the duodenum. From the history and the physical examination of the patient, would you consider the presence of ulcer of the stomach or of ulcer of the duodenum the more probable?

STUDENT: I should think ulcer of the stomach more probable than ulcer of the duodenum.

DR. BARKER: Why?

STUDENT: Well, the patient has not been waked up by pain during the night as he would have been if he had a duodenal ulcer. The time of his pain points to gastric ulcer.

DR. BARKER: It is true that this man has had no pain that waked him in the night, and that is rather strange if he has a duodenal ulcer. Your other statement, however, that the time of the pain points to gastric ulcer, I cannot agree with. The pain in gastric ulcer usually follows very quickly after the ingestion of food. In this man the pain did not come until about three hours after the ingestion of food and continued until food or liquid was taken. This "hunger-pain" is, in my opinion, much more suggestive of duodenal ulcer than of gastric ulcer.

There is, however, one sign here that might make one think of gastric ulcer rather than of duodenal ulcer. What is it?

STUDENT: Perhaps the vomiting of blood.

DR. BARKER: Yes. Vomiting of blood is much more common in gastric ulcer than in duodenal ulcer. Indeed, in duodenal ulcer, hematemesis is rather rare. It does sometimes occur, especially if there be any stenosis of the duodenum.

Has it been possible to make *x*-rays of the stomach and duodenum in this patient?

STUDENT: Yes. They were made yesterday afternoon and we have them here.

DR. BARKER: Let us examine them. This first plate was taken immediately after the ingestion of the barium, the second plate ten minutes later, and the third plate at the end of twenty minutes.

The outline of the stomach is everywhere perfectly clear. There are no filling defects in it and no incisuræ. The pylorus is clean cut and the space between the pylorus and the duodenal cap looks normal. When we look at this duodenum, however, we see a very definite filling defect, and if you will notice, it persists in all three plates. Moreover, the duodenum is distorted, as though there might have been a periduodenitis with adhesions to the surrounding parts. These three plates are certainly strongly suggestive of duodenal ulcer and of periduodenal adhesions. (Two of the plates are reproduced in Figs. 20, 21.) Have the plates been reported upon by the hospital roentgenologist?

STUDENT: They have not yet been seen by Dr. Baetjer, but

his associate, Dr. Pierson, looked at them this morning and said he felt sure that there was a duodenal ulcer with adhesions.

DR. BARKER: With the stomach as normal as it appears in these plates and with the filling defect in the duodenum so obvious as it



Fig. 20.—Roentgenogram revealing a filling defect in the duodenum due to ulcer.

is here, we can feel sure that this man has a duodenal ulcer. It would be interesting if the periduodenal adhesions had caused enough obstruction to the duodenum to account for the hematemesis in this case.

Of course, a man might have a duodenal ulcer and periduodenal adhesions and have, in addition, bleeding from an esophageal varix



Fig. 21.—A second roentgenogram made a few minutes later. Persistent filling defect in the duodenum due to ulcer.

due to cirrhosis hepatis. We must not be too positive in our conclusions. The weight of evidence, however, would seem to me to be in favor of bleeding from an old duodenal ulcer.

How would you proceed with the further treatment in this case?

STUDENT: I think he should continue with the Lenhartz diet or with a Sippy diet for a time, and later remain on a protective diet. The blood should be restored to normal if necessary with the aid of additional transfusions. He should gain 10 pounds or more in weight, and he should become a total abstainer.

DR. BARKER: Yes. Those are all good points, and this form of treatment will doubtless be followed in the ward. Let us suppose, however, that despite this form of treatment hemorrhage returns, or attacks of pain and digestive disturbance recur so frequently that the patient's life is a burden. What would you recommend then?

STUDENT: Then he should have a surgical operation.

DR. BARKER: Yes. If he does well enough on medical therapy, well and good; but if hemorrhage recurs, or if his life be made a burden from the disturbances of digestion and the pain, then I would advise an exploratory laparotomy, asking the surgeon to do whatever seems best when he gets in. In most cases a posterior gastro-enterostomy is the best solution. Sometimes it is wise, also, to occlude the pylorus.

The danger of death from massive hemorrhage from duodenal or gastric ulcer has been somewhat exaggerated. The mortality rate in these cases is far lower than seems to be generally supposed. There is more danger, perhaps, from frequently recurring small hemorrhages and the severe anemias to which they often give rise. Ulcers of the duodenum and of the stomach belong in the borderland of medicine and surgery, and in their treatment physicians and surgeons should co-operate with one another in the closest way.

Every care should be taken by this patient to do no further injury to his liver. The treatment he is receiving at present ought to give him a start in his fight against alcoholism. In addition to encouraging total abstinence we should try to re-establish this man's general health and vigor and to fortify his nervous system. Psychotherapy should be combined with physical therapy if we hope to make the man victorious in the hard struggle against chronic alcoholism.

[*Subsequent History of the Case.*—The patient improved steadily and was discharged on March 5, 1921, looking and feeling well. For three weeks before his discharge he had been on ordinary ward diet. He was instructed to lay off work for at least three weeks longer. In June, 1921, between three and four months later, he was still in good condition.]

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XIII. CARCINOMA OF THE PANCREAS

A MAN OF SIXTY-FOUR WITH DISTENDED GALL-BLADDER, INTENSE JAUNDICE, ACHOLIC FECES, RAPID EMACIATION, AND ASTHENIA. EXPLORATORY LAPAROTOMY; CHOLECYSTENTEROSTOMY; DEATH; AUTOPSY

THE patient to be studied this morning is a man sixty-four years old, a carpenter by trade, who entered the hospital on February 17th, complaining of "jaundice and hemorrhoids."

The anamnesis, except as regards the present illness, is rather barren. The only point of interest in his family history is that his mother died of cancer at seventy years of age. The patient himself had the usual diseases of childhood, and when twelve years old had an attack of typhoid fever that lasted two months. When sixteen he had diphtheria and could not speak for two years afterward. (To patient): Why could you not speak?

PATIENT: On account of my throat. I could whisper, but could not talk out loud.

DR. BARKER: For most of life (from the time he was seventeen until he was fifty-nine) he was subject to severe headaches, but he says he never had any dizziness. Ever since he was twenty years old he has had a "chronic cough," which is worse at night when he is lying down. He says he has one bad cold every winter. He has never had any hemoptysis or night-sweats. When he was forty-one he had pneumonia and was ill for six months. About twenty-five years ago he had a sudden attack of severe cramp-like pain in the epigastric region, which began in the evening and lasted all night. It seems to have been distinctly localized in the epigastrium and did not radiate to either side nor to the arms. There was no nausea or vomiting following it. He has had no similar attacks since. He has had at no time in his life any symptoms referable to the neuromuscular system or to the genito-urinary system.

On inquiry into his habits, he stated that from the time he was nineteen until he was twenty-two he did not "draw a sober breath," but he has used no alcohol since then. He smokes a pipe, but not to excess. He has been married twenty-five years and has no children. His wife has had no miscarriages.

Thus, aside from a long series of infections (including typhoid,

pneumonia, diphtheria, and perhaps pulmonary tuberculosis), a temporary period of alcoholic excess, habitual headaches, and one attack of severe epigastralgia, his past history is negative.

His present illness began four months ago, when he felt weak and tired and noticed that his feet were swollen at night. Three months ago he began to lose weight, and since then has lost 40 pounds. Notice that we have here a record of weakness beginning four months ago, and of rapid loss of weight beginning three months ago. Two months ago he noticed that his eyes and face were jaundiced, and this jaundice has increased in extent and severity, his whole body having become deeply bile stained. Was there no retrocession of the jaundice at any time since it first appeared?

STUDENT: No; none.

DR. BARKER: This is an important point. When jaundice is due to obstruction of the biliary tract from gall-stones it usually decreases at times and returns again. When it is caused by compression of the common bile-duct from cicatrix or neoplasm it almost never recedes, but steadily increases in severity to a maximum, which persists.

About six weeks ago his skin, as in almost all cases of continued jaundice, began to itch severely, but there has been no sweating and he has had no chills. At this time he noticed that his stools were gray in color. He has had no diarrhea. During this illness his appetite has been good. There has been no pain in the stomach or abdomen; no nausea or vomiting; nor has there been any pain or discomfort after eating. In short, his digestion, as far as he could subjectively make out, has been good, an interesting point, because it is scarcely what we should have expected. His only complaints are jaundice, piles, and a general feeling of malaise and of weakness. (To patient): How old are you?

PATIENT: Sixty-four.

DR. BARKER: Physical examination of this patient on entrance to the hospital showed a poorly nourished man who had the appearance of having recently lost much weight. The scleræ and the skin of the whole body were deeply jaundiced, the color having increased in intensity, he asserts, ever since it first appeared two months ago. Examination of the head, except for the mouth conditions and the jaundice, was practically negative. The pupils reacted normally to light and on accommodation. The pharynx was somewhat in-

jected. The teeth and gums are reported as being in bad condition. What is the trouble with them?

STUDENT: There is some pyorrhea; the teeth are all discolored and many of them are carious.

DR. BARKER (to patient): Let me see your mouth. His teeth and gums are in a dreadful condition. There is very extensive pyorrhea alveolaris, and he has evidently many dead teeth. We have recently learned the frequent connection between dead teeth and a number of morbid conditions and realized the importance of investigating the teeth in every case of chronic disease. About a year ago we had a man here with a big tender liver, a temperature of 102° F., and a leukocytosis. The liver dulness extended down to the umbilicus. We thought we had to do with a general septic infection secondary to oral sepsis; we tried to treat the severe pyorrhea by means of local measures, but we had no success. As local treatment failed and the suppuration was intense the patient was advised to get rid of the bad teeth. On thorough examination in the dental department it was reported that no teeth ought to be saved—a rare order, for our dental surgeons consider it a tragedy to lose a tooth unless it be definitely and irremediably infected. The patient consented to have them all extracted. Within a week his temperature was normal and his liver was down to one-half its former size. Later the liver edge receded to the costal margin, and he was soon a relatively well man, being freed from a severe toxic-infectious process. Let me advise you always to be on the lookout for pyorrhea alveolaris; if you find it, see that it is carefully treated. If there are any dead teeth they should be x-rayed, and if there is a marked absorption area around the roots of a tooth, indicating a definite granuloma, that tooth should be extracted and the socket cured. In the case of a tooth with a single root it may be possible to cut off the apex and save the rest of the tooth, but when a very large area is present it may be better to extract the tooth and to curet the socket; otherwise metastatic infection may occur. Studies here and elsewhere indicate that in arthritis, anemias, and in beginning arterial disease absorption from the gums or from periapical granulomata may be an important etiological factor. In this patient we have serious gingival and periodontal disease, but in this particular case I do not think it at all probable that the main symptoms, that is, the jaundice and the emaciation, are due to the oral sepsis. More-

over, we are to find conditions in this patient that make attention to focal infections superfluous.

The examination further showed that the cervical and the epitrochlear lymph-glands were palpable. There were also some inguinal glands the size of a pea. The epigastric angle was rather narrow and the ribs prominent. In the front of the chest there was impairment of the percussion note as far as the second intercostal space on the right and above the clavicle on the left. In the back there was impairment down to the third thoracic spinous process on both sides. Vocal fremitus was impaired over both apices. To what did you consider this impairment due?

STUDENT: To old apical lesions with thickened pleura perhaps. No râles have been heard.

DR. BARKER: Has a roentgenogram of the lungs been taken?

STUDENT: Not yet.

DR. BARKER: It is probable from the history of chronic cough in earlier life and from the physical findings that this man at one time had tuberculosis of both apices.

In a case of this kind an x -ray picture is not specially helpful in making the diagnosis of the pre-existence of a tubercular process, but it would help to determine its extent and distribution.

The size and position of the heart were approximately normal and there were no heart murmurs. An occasional premature beat occurred. Were these extrasystoles of ventricular, atrial, or nodal origin?

STUDENT: Of ventricular origin.

DR. BARKER: How do you know that?

STUDENT: By the compensatory pauses following them.

DR. BARKER: Did the extrasystole arise in the right or in the left ventricle?

STUDENT: I don't know.

DR. BARKER: How can you find out whether ventricular premature beats originate in the right or in the left ventricle?

STUDENT: By means of an electrocardiogram.

DR. BARKER: Yes; most easily by the electrocardiogram. How often does the patient have these extrasystoles?

STUDENT: Every two or three beats for an hour or two at a time.

DR. BARKER: On account of the much greater gravity of the abdominal condition in this patient I think we may safely ignore

these premature ventricular beats. It is not likely that they are of any serious import.

Examination of the abdomen on admission showed that there were numerous dilated veins over the surface, and owing probably to the emaciation, peristaltic waves could be made out on the left just above the umbilicus. There was no sign of fluid in the flanks. The liver edge was palpable near the umbilicus. The gall-bladder was distended and could be easily seen and felt. The spleen was not palpable. The reflexes in the extremities were normal.

A glance at the patient this morning shows that the jaundice is outspoken. I am sure you can see the yellow color even from a distance. (To patient): Look up, please. Look down. The scleræ, as you see, are intensely yellow. (To student): Now how can we show the jaundice in the lips?

STUDENT: By driving the blood out by pressure with a glass slide or some similar object.

DR. BARKER: Yes; as you are close to the patient you can see the yellow color through the glass slide. About 2 inches to the right of the umbilicus I can see and feel a lump the size of a hen's egg. Was this lump visible or palpable on entrance?

STUDENT: It was both.

DR. BARKER (to patient): Lie quite flat on your back, please. The emaciation is striking. The costal angle and the tip of the xiphoid process are very easily visible. You notice that the patient has a well-defined waist. There is nothing strikingly asymmetrical about the abdomen except that the margin of the rectus on the right side is a little fuller than on the left. The liver edge is at the level of the umbilicus; palpation shows it to be smooth and firm, but it is not tender on pressure. The spleen is not enlarged. On the right side the abnormal mass can be felt below the edge of the liver. There are three ways of palpating the edge of the liver and the gall-bladder region: (1) Devoto's, (2) Rheinstein's, and (3) Glénard's. In this particular case you can palpate without much difficulty by any method, but in obscure cases one may wish to employ all three of the methods I have mentioned.

First, let me illustrate Devoto's method of palpation of the right upper quadrant: The patient must be standing or sitting upright. The examiner stands behind him, puts his arm around the patient so as to encircle him, and while the patient takes a deep breath

palpates the edge of the liver and anything that can be felt underneath the liver. In this case the liver is very large and smooth; on the right side I can feel a firm, elastic mass underneath it. If there are gall-stones you can sometimes elicit soreness with the fingers hooked under the right hypochondrium. (To patient): Is there any soreness there?

PATIENT: No.

DR. BARKER: While the patient is standing up I may as well speak of Rheinstein's method, because in this, also, the patient should be standing, but it is not as much used as the other two. The examiner places the thumb of his right hand on the anterior surface of the abdomen at the margin of the liver, the other fingers being held upright. He then exerts counterpressure with the thumb of the left hand placed behind the patient's right flank, with the thumb in front of the right hypochondrium.

The best method of all for palpating the anterior margin and the lower surface of the liver including the gall-bladder is Glénard's thumb method (*procédé de pouce*). The patient lies on his back, and the examiner sits on the edge of the bed to his right. Both hands are used, the intention being to press the mass of intestines upward and thus to direct the anterior margin of the liver toward the abdominal wall. The examiner's left hand is placed behind the patient's right flank with the left thumb in front in the right hypochondrium. The right hand is placed on the front of the abdomen in the position in which you see mine now, the base of the hand below the umbilicus, and the fingers directed obliquely lateralward and downward toward the groin. Now, using the wrist as a center, this right hand is rotated so as to bring the fingers from the oblique downward position into a transverse position and then into a position in which they are directed obliquely upward and lateralward. I now press deeply with the ball of my left thumb below the anterior margin of the liver.

(To the patient): Now please take a deep breath. I palpate the anterior margin and the lower surface of the liver with the thumb as they descend during inspiration. In this case it is necessary to place the left thumb very low since the patient's liver edge is in a low position, below the umbilicus. The thumb catches also this mass below the liver very easily. (To patient): Take a deep breath, please. Now take another.

We have here a somewhat elongated mass, very smooth, quite tense, and firm. The mass is somewhat pyriform, the shape described by the French as of the shape of the clapper of a bell (*embaton de cloche*). The big end of the pear corresponds to the fundus of the gall-bladder, and feeling over in the median line, one tries to get the umbilical incisure of the liver. Above this pyriform mass I do not find it easy to outline a definite vesicular notch.

In palpating in a case like this it is well to keep in mind the position of the head of the pancreas and of the ductus communis choledochus. A good rule for mentally locating them is to draw a transverse line through the umbilicus and then a vertical line also through the umbilicus. You have then outlined the four quadrants of the abdomen, namely, the right upper and the right lower, and the left upper and the left lower: $\begin{array}{c} \text{A} \quad \text{B} \\ \text{C} \quad \text{D} \end{array}$. Bisect the angle A and you have the normal position of the head of the pancreas, and the ductus communis choledochus is in the area between the vertical and the oblique line.

In this particular patient, however, the liver is so much enlarged that the abdominal conditions are somewhat changed. When you have reason to suspect enlargement of the head of the pancreas, feel in this region, however, and try to ascertain whether there is any increased resistance there. (To student): What do you take this mass to be?

STUDENT: An enlarged gall-bladder.

DR. BARKER: Yes; it could hardly be anything else. It is too far to the right to be a cyst of the pancreas. Its form is against a mesenteric cyst. Its pyriform shape; its position in relation to the liver edge; its consistency; its smooth surface—all are evidence that it can hardly be anything other than a distended gall-bladder.

What does such a gall-bladder contain?

STUDENT: Probably mucus and bile.

DR. BARKER: Bile retention is certainly the commonest cause of a distended gall-bladder.

Where would the obstruction be that causes the retention?

STUDENT: I should think in the common bile-duct.

DR. BARKER: Yes, since there is jaundice. If there were no jaundice, the distention could be due to obstruction of the cystic duct. The size of the gall-bladder depends upon the completeness

of the obstruction and upon the distensibility of the gall-bladder itself. It is greatest in neoplastic obstruction, whereas in occlusion from gall-stones it is slight or, more often, it is absent altogether. In gall-stones the walls of the gall-bladder are often rigid owing to thickening from chronic inflammation. When there is obstruction to the cystic duct, mucus and secretions from the wall of the gall-bladder accumulate and distend the gall-bladder, with formation of a cholecystocele. If acute inflammation of the gall-bladder ensue consequent to this, we may have suppuration; how would you designate a gall-bladder filled with pus?

STUDENT: Empyema of the gall-bladder.

DR. BARKER: Yes; empyema. Do you think in this case we have to do with empyema, with cystocele, or with bile retention.

STUDENT: With bile retention.

DR. BARKER: I think you are right; the distention here is probably due to the retention of the bile; not to an empyema. If we had an empyema of the gall-bladder we should, in all probability, have chills and fever and a leukocytosis. What is this man's white blood-count?

STUDENT: 7200.

DR. BARKER: You see there is no leukocytosis. He has no fever. Moreover, in empyema we should have marked tenderness, and there is none here, so I think we may rule out empyema. Now let us consider whether we can rule out cystocele. The patient has jaundice, but that would not in itself be sufficient evidence without something more. The presence of jaundice shows that there is an obstruction to the passage of bile through the biliary passages; it is being reabsorbed into the blood and it is being dammed back through the cystic duct into the gall-bladder. Of course, one might have a combination of hydrocele (due to obstruction of the cystic duct) along with jaundice (due to obstruction of the common bile-duct), but it is always a good plan to be parsimonious in your hypotheses, that is, to try to explain a condition upon the grounds of a single lesion rather than to assume multiple lesions, though you must not forget the possibilities of the latter. What might cause such bile retention in the gall-bladder?

STUDENT: It is often due to gall-stones.

DR. BARKER: Occasionally, but not often; and in this case I do not think it is due to gall-stones. What law has been formulated

as describing the relation between jaundice, on the one hand, and contraction or dilatation of the gall-bladder on the other?

STUDENT: Courvoisier's law.

DR. BARKER: Yes. A contracted gall-bladder associated with jaundice suggests gall-stones, because the inflammatory thickening of the gall-bladder wall resulting from the recurrent infections accompanying gall-stones leads to gradual contraction, whereas a dilated gall-bladder with chronic jaundice points to biliary obstruction, due to causes other than gall-stones and especially to carcinoma of the head of the pancreas or of the ampulla of Vater. A recent novel by Paul Bourget, *Le Sentiment du Mort*, contains a most interesting description of the illness of a great French surgeon, who makes a diagnosis of his own case and, in doing so, mentions Courvoisier's law. Novelists do not usually go so deeply into differential diagnosis.

Almost every patient who has cholelithiasis has also chronic recurrent cholecystitis. If a chronic cholecystitis exist over a long period of time there is almost always a thickened, contracted gall-bladder. In order to have distention of the gall-bladder there must first be an obstruction to the flow of bile, and, second, the gall-bladder wall must be capable of distention. If there is an old chronic calculous cholecystitis, in which the wall of the gall-bladder has become thickened to three or four times its normal thickness, and a stone gets into the common duct, it will cause obstruction, but it cannot cause dilatation of the gall-bladder. When, especially in elderly people, there is marked distention of the gall-bladder, with persistent jaundice that does not recede, and *not* associated with epigastric pain, the obstruction is nearly always due to neoplasm rather than to calculi. So Courvoisier's law should always be kept in mind when studying cases in which jaundice is present.

Here we have a thin-walled gall-bladder, markedly distended; we have jaundice, coming on, not suddenly, but slowly and insidiously, showing no recession since it first appeared. The patient has no pain. Now then, since everything points to an obstruction not by gall-stones, let us consider the sites at which such an obstruction could occur. What would they be?

STUDENT: The head of the pancreas is the commonest site.

DR. BARKER: That is certainly one of the most common, but what others are there?

STUDENT: The bile-duct itself and the duodenum.

DR. BARKER: Yes; the bile-duct could be obstructed either by a growth within it or by something compressing it from without. In metastatic cancer of the lymph-glands in this region the metastatic growth may compress the bile-duct.

Crohn, in his recent analysis of biliary obstruction, mentions six different sites at which neoplasms can cause obstruction of the gall-bladder: I, the common bile-duct; II and III, the ampulla of Vater and the duct of Wirsung; IV, the duodenal surface of the papilla of Vater; V, the duodenal mucosa; and VI, the head of the pancreas. He asserts that the site of the neoplasm can generally be determined by careful examination of the duodenal contents and furnishes clinical evidence of it, confirmed by autopsy in all but II and III. In a certain proportion of cases diagnosed as carcinoma of the head of the pancreas a careful examination proves that the disease did not begin in the pancreas, but in the ampulla of Vater, the papilla of Vater, or in the ductus communis choledochus itself. Does the ductus communis choledochus run through the head of the pancreas?

STUDENT: I think it always does.

DR. BARKER: How many of you think that it always runs through the head of the pancreas?

ANOTHER STUDENT: I think it never does so.

DR. BARKER: One of you thinks it always runs through and another thinks it never does. As a matter of fact, the common bile-duct runs posterior to the pancreas in 25 to 30 per cent. of all cases and in about 75 per cent. it runs through it. In surgical work it is very important to know this, but it is important in medical work as well, for there are certain abnormal conditions in the head of the pancreas that may lead to compression of the bile-duct. An indurated head of the pancreas in chronic indurative pancreatitis, for example, can press upon the common bile-duct and cause jaundice even when no neoplasm is present. How can we tell whether the pancreas is involved in this case or only the bile-duct?

STUDENT: We might get important information by examining the stools.

DR. BARKER: How could a stool examination throw light upon the problem of deciding whether the pancreas is or is not involved?

STUDENT: If the pancreas is involved, we would have undigested protein and fat in the stools.

DR. BARKER: Yes. If the external secretion of the pancreas were

disturbed we might find muscle-fibers and free fat in the stools. because the assimilation of proteins and fats would be interfered with. But the pancreas has two secretions: an external and an internal, or endocrine, secretion. When the endocrine secretion is affected what symptoms would we have?

STUDENT: Those of diabetes mellitus.

DR. BARKER: Yes; one form of diabetes is due to the loss of the internal secretory function of the pancreas. Now, in this case we want to know, first, whether the ductus communis choledochus is involved; second, whether the external secretion of the pancreas is involved; third, whether the internal secretion of the pancreas is involved? How can we find out?

STUDENT: By examination of the stools and the urine.

DR. BARKER: A whole stool or part of one?

STUDENT: I don't know.

DR. BARKER: I have one of the patient's stools here, and it is very interesting. (*Stool passed round for examination.*) The color is striking or, rather, the absence of color is, for, as you see, it is distinctly gray or clay-colored, showing an absence of bile pigments. You will also perceive at once that the odor of the stool is unusually offensive. It is not, however, a very "buttery stool," nor is it a very bulky stool. In lack of the external secretion of the pancreas the stools are usually much larger than normal. (To patient): Are your stools always like this?

PATIENT: No. They vary in size, but the color is like that.

DR. BARKER: In extensive pancreatic disease or in obstruction to the pancreatic ducts the stools are, as I have said, commonly very large. It is surprising how bulky the so-called pancreatic stool can be. It is sometimes really enormous. I have known a patient to pass so large a stool that it would nearly fill a 4-quart pail.

This patient has passed typical acholic or hypocholic stools and everyone should know what such stools look like. But the grayish color of a stool may be due either to the absence of bile pigments in the intestine or to insufficiency of pancreatic secretion there. Walker has furnished some evidence to show that the normal brown color of the feces is dependent upon the mutual reaction of the bile and the pancreatic juice in the intestinal tract, and that, in diseased conditions, a deficiency of pancreatic secretion may be responsible for colorless or clay-colored stools as much as a deficiency of bile. In

support of this view he points out that if the normal feces were colored only by the bile they would appear yellow, like other things colored by the bile, instead of being brown, as they are. This view of Walker's should be tested further before we give it full credence.

We have just said that if the external secretion of the pancreas is diminished the stools may contain undigested fats (steatorrhea) and undigested meat fibers (azotorrhea). What diet has the patient had?

PATIENT (suddenly): Ain't had a mouthful of meat for four weeks.

DR. BARKER: Under these circumstances you could scarcely expect to find any meat fibers in this stool. It would be interesting to put this patient upon the so-called standard intestinal diet, also known as the Schmidt-Strasburger diet, for a little while. This diet is so arranged that you standardize the feces and you know exactly what to expect in a normal person on macroscopic and microscopic examination. Deviations from the standard can then be easily recognized in pathological cases. There are two forms of the intestinal test diet, first, the "general test diet," and second, the "detailed test diet." In the detailed variety we give the following food:

DETAILED TEST DIET

Breakfast: 500 c.c. milk (or, if milk be badly borne, 500 c.c. of cocoa, made of 400 grams water, 20 grams cocoa, 10 grams sugar, and 100 grams milk); in addition, 50 grams of zwieback.

Forenoon: Half a liter oatmeal gruel, made of 40 grams oatmeal, 10 grams butter, 200 grams milk, 300 grams water, 1 egg, and a little salt, the whole to be passed through a sieve.

Midday: 125 grams hashed beef (weighed raw), broiled with 20 grams butter, as rare Hamburg steak; 250 grams purée of potato (made of 190 grams mashed potato, 100 grams of milk, 10 grams butter, and a little salt).

Afternoon: Same as breakfast.

Evening: Same as forenoon.

This diet corresponds to 102 grams of protein, 111 grams of fat, and 191 grams of carbohydrates; the whole corresponding to 2234 calories. We mark the diet at its beginning and at its end by giving 0.3 gram of finely powdered carmin enclosed in a con seal. This diet is given for three days or longer, and the stool passed on the third day is examined. We mix the whole stool thoroughly until a homogeneous mass is formed. Then a bit of this is rubbed in a porcelain mortar with a little distilled water; a little of this mixture is then

examined microscopically. The advantage of such a standard diet for the clinical examination of feces lies, as I have said, in the fact that only in some such way is it possible to establish a normal standard feces, slight deviations from which can be easily recognized.

The "general test diet" of Schmidt and Strasburger is less rigid than the above, but it is satisfactory enough for ordinary diagnostic work; it is especially useful when testing out-patients. It is as follows:

GENERAL TEST DIET

Morning: Half a liter of milk, or of tea, or cocoa made with milk or with water; 1 roll with butter; 1 soft egg.

Forenoon: 1 portion strained oatmeal, boiled with milk, with salt or sugar added, if desired.

Noon: One-quarter pound chopped lean beef, broiled on the outside, with a little butter (raw inside); 1 portion purée of potato (passed through a fine sieve).

Afternoon: As in the morning, but no egg.

Evening: One-half liter of milk or 1 portion of soup; 1 roll with butter, and 1 or 2 soft-boiled eggs (or scrambled eggs).

It would be interesting to determine whether this patient, after eating meat, passes any meat fibers in the feces. When making this test we could also employ the Schmidt "meat-bag nucleus test." This test is based on the fact that the nuclei of muscle-fibers are digested in the intestine by the pancreatic secretion and not by the stomach juice, the presence of muscle nuclei expelled in the feces indicating, therefore, a defective pancreatic secretion. For this test fresh lean beef is cut into centimeter cubes and hardened in absolute alcohol. These cubes are enclosed in tiny bags of silk gauze and kept in alcohol, to be washed in water for a few hours before they are used. The patient, on a Schmidt-Strasburger standard intestinal diet, swallows these bags daily for two or three days. The bags are then recovered by diluting the feces with water and straining. The muscle-fibers removed from the bags can be hardened, sectioned, and stained, or they can be teased in acetic acid or dilute methylene-blue, and examined microscopically. Complete preservation of the nuclei indicates absence of pancreatic secretion. There are, however, three sources of error in connection with this test: (1) in diarrhea the bags may be passed through the intestine too quickly to permit of the digestion of the nuclei; (2) when the bags remain too long in the intestine the nuclei may be destroyed by bacterial action; and (3) though trypsin, pepsin, and erepsin cannot

dissolve the nuclei, it sometimes happens that in active gastric digestion the muscle-fibers are so completely digested that the nuclei are lost.

The Sahli glutoid capsules are also a very good test of pancreatic function. To obtain direct evidence regarding the chemical activity of digestion within the intestine Sahli has used these capsules made from gelatin hardened in formaldehyd. Such capsules are not soluble in the gastric juice, but dissolve quickly in mixtures containing pancreatic juice. The capsules are filled with substances such as iodoform, salicylic acid, and potassium iodid, which, after absorption, may be recognized in from fifteen to seventy-five minutes in the saliva or in the urine. Glutoid capsules ready for use can be bought in the market. It is best to give the capsules with a test-meal and to collect the saliva or the urine three hours afterward and at regular intervals thereafter in numbered beakers. It is essential in performing this test to know whether or not the gastric motility is normal, for motor sufficiency of the stomach might retard the entrance of a capsule into the intestines. When the gastric motility is normal the glutoid capsule gives the resultant of the power of pancreatic digestion and the absorptive power of the intestine.

In testing for pancreatic insufficiency, besides the microscopic examination of the feces for undigested meat and fat, the examination for neutral fats and fatty acids by chemical methods is also very helpful. If you are in doubt, you can try the "butter test." This rests upon the fact that in deficiency of the external pancreatic secretion so much fat may sometimes be present in the stools after ingestion of butter that, on cooling, the stools look like butter. In normal digestion, 250 to 300 grams of butter *per diem* can be assimilated. Now if a patient in whom imperfect digestion and assimilation of fat is suspected be fed 250 grams of butter a day, mixed with some cereal, say oatmeal, the absence of "buttery stools" will indicate good pancreatic digestion. If, on the other hand, the external pancreatic secretion is deficient, a typical "buttery stool," containing yellow masses that look like butter, will be passed. How about the microscopical examination of this patient's stools?

STUDENT: There is a large amount of neutral fat present.

DR. BARKER: That is very suspicious. You must remember, however, that fatty stools occur in biliary obstruction when there is no pancreatic disease, but the fat in such acholic stools is usually

split and not present as neutral fat. With a large amount of neutral fats you should always suspect some disturbance of the external pancreatic secretion.

There is still another way to test for sufficiency of the external secretion of the pancreas which is better than any of these. Do you know what it is?

STUDENT: Cammidge's test can be tried, but that is not believed now to be of value.

DR. BARKER: I am glad to hear you say so, for I myself feel very sure that no reliance can be placed on Cammidge's test. It was introduced less, however, as a test for the external than for the internal secretion of the pancreas.

The best way of all, however, to test for sufficiency of external pancreatic secretion is to make examinations of the duodenal contents, obtained directly from the duodenum by means of Einhorn's duodenal pump or Gross's duodenal tube. Or you may, if you prefer, secure duodenal contents for examination by giving the Volhard oil-breakfast or the fat-and-fatty-acid breakfast of Boldireff. These cause regurgitation of the duodenal contents into the stomach, whence the fluid may be removed by stomach-tube, say a half-hour after the ingestion of the breakfast. Some 20 or 30 c.c. of the duodenal contents can usually be thus obtained for examination.

The pancreas supplies at least three digestive ferments to the intestinal contents, you recall. What are they?

STUDENT: A proteolytic ferment (trypsin), an amyolytic or diastatic ferment (amylase), and a lipolytic ferment (steapsin or lipase).

DR. BARKER: Yes; these are supplied by the pancreatic juice and you can apply the casein test for measuring the trypsin content, Wohlgemuth's test for diastase, and the monobutyryn test for lipase. Have the duodenal contents been drawn off in this case?

STUDENT: We made one trial, but were not able to get anything.

DR. BARKER: Perhaps you will be more successful later. Now, suppose that we do find a deficiency of the external pancreatic secretion, along with obstruction of the ductus communis choledochus, what do you think would explain both?

STUDENT: Something causing obstruction to both the bile-duct and the pancreatic ducts.

DR. BARKER: Have you a specimen of the urine? (*Specimen shown.*) You see it is of a deep brown color, the color of dark mo-

lasses, though not of the same consistence. This urine is characteristic of deep jaundice. Notice, when I shake the urine, how yellow the froth is. Was albumin found in it?

STUDENT: There was a trace of albumin and also a few casts.

DR. BARKER: In a patient as deeply jaundiced as this man it would be strange not to find albuminuria and cylindruria, for the biliary constituents in the blood cause irritation of the kidneys and set up a slight toxic-degenerative nephropathy.

(To student): What do you think the most probable cause of the biliary obstruction in this patient?

STUDENT: A carcinoma of the head of the pancreas or a chronic indurative pancreatitis.

DR. BARKER: Yes, I agree with you. Chronic indurative pancreatitis is, in turn, often associated with pancreatic calculi or with gall-stones. In every case in which pancreatic stone is suspected an x -ray should be taken of the pancreatic region, as pancreatic stones are usually lime stones, which cast a shadow on the x -ray plate. Pancreatic calculi must be very rare, however, as Dr. Opie, analyzing our statistics here at the Johns Hopkins Hospital, could find only two instances recorded in the reports of 1500 autopsies. As regards malignant disease, carcinoma of the ampulla of Vater is possible, as well as carcinoma of the ductus communis choledochus, of the duodenum, or of the head of the pancreas. Primary carcinoma of the pancreas itself is almost always adenocarcinoma, originating in the pancreatic ducts. Jaundice is present in 75 per cent. of the cases of primary pancreatic cancer and is due to compression of the common bile-duct. Palpable tumor, aside from the distended gall-bladder, is present in only about 25 per cent. of the cases of primary cancer of the pancreas.

Another form of disease which must not be overlooked is lues—luetetic inflammation of the pancreas or a gumma of the liver compressing the ductus choledochus and causing obstruction. Has a Wassermann test been made in this case?

STUDENT: The Wassermann test is negative.

DR. BARKER: It occasionally happens that the Wassermann test is positive in jaundice, as in scarlet fever, when there is actually no lues. To return to the question of carcinoma. How much weight has this patient lost?

STUDENT: About 40 pounds in two months.

DR. BARKER: As a rule a chronic indurative pancreatitis may be clinically differentiated from a carcinoma of the pancreas by the lower degree of emaciation, of weakness, and of cachexia. Pronounced emaciation, cachexia, and asthenia speak in favor of carcinoma. If jaundice be present, with a big gall-bladder and without much emaciation or the development of cachexia, then the possibility of chronic indurative pancreatitis must be kept in mind. When there is any doubt, the patient ought to be given the benefit and surgical exploration undertaken. If, at operation, we find a chronic indurative interlobular pancreatitis, the gall-bladder may be removed or drained, and the patient may recover symptomatically. Even if, at operation, carcinoma be found, it may be advantageous to do a cholecystenterostomy to relieve the jaundice, though if primary carcinoma of the pancreas exist there can be no hope of permanent relief, even if resection of the pancreas, an operation in which the mortality is very great, be undertaken. A circumpapillary cancer of the duodenum causing jaundice might conceivably be successfully removed if operation were done early.

I saw a patient in Washington last year who had deep and progressive jaundice with a palpable gall-bladder, in whom I made a probability diagnosis of carcinoma of the head of the pancreas. Dr. Finney saw the patient and concurred in the diagnosis, as did several other consultants. The patient had had lues early in life, but the Wassermann reaction at the time of our examination was negative. We advised against operation. Finally, the patient died, and the autopsy revealed a large gumma of the liver. The Wassermann reaction was negative, but there was luetic infiltration of the head of the pancreas, though it was not very marked, and, most important of all, an extensive carcinoma of the liver, which, together with the gumma of the liver, had pressed upon the common bile-duct, causing the jaundice and the distention of the gall-bladder.

The patient before you has, I believe, carcinoma of the head of the pancreas, which has compressed the ductus choledochus, causing biliary obstruction as shown by the jaundiced skin and mucous membranes, the bilirubinuria, the acholic stools, and the distended gall-bladder. Deep jaundice lasting over six weeks in a man of sixty-four is nearly always due to cholelithiasis, to chronic pancreatitis, or to carcinoma; and when the jaundice is of the intensity we see here, never showing recession, it is rarely due to gall-stones. The

rapid loss of weight and the cachexia in this patient make the more benign lesion of the pancreas improbable; we are driven inevitably to the conclusion therefore that we must be dealing with a neoplasm.

[*Subsequent History of the Case.*—The *x*-ray report, made on the day the clinic was held, showed a fish-hook stomach, prolapsed, but with good contractions and good expulsive power. The transverse colon was prolapsed, pulled in, and adherent to the cecum, and there were signs of cecal stasis. There was evidence also of adhesions in the right lower quadrant.

A test breakfast was removed and 180 c.c. of stomach contents obtained; the fluid was thin and contained a little mucus. On titration of the acidity, free HCl 30 acidity per cent. and combined HCl 15 acidity per cent. were found. No raisin 'skins, no Oppler-Boas bacilli, and no sarcinæ were present.

The patient, against the advice of Professor Janeway and of the resident physician, Dr. Bloomfield, who explained the improbability of any benefit to be derived from surgical interference, insisted upon operation, and was transferred to the surgical service on February 24th, four days after the clinic was held. The pre-operative impression in the surgical department was that he had a carcinoma in the head of the pancreas.

Operation was performed by Dr. Reid on February 24th. No free fluid was found in the peritoneal cavity. A greatly distended gall-bladder presented in the right rectus wound. A mass could be felt also in the head of the pancreas, said to have been of about the size of a small orange. It was quite firm and hard, and seemed to the operator to be undoubtedly carcinoma. The common bile-duct, the cystic duct, and the hepatic duct were all dilated, the common bile-duct being about 2 cm. in diameter. The operator decided that a cholecystenterostomy would be the best palliative measure at command and, accordingly, performed the operation. On its conclusion the anastomosis was apparently satisfactory. There was no leakage anywhere and the bile could be seen to pass from the gall-bladder into the duodenum.

The patient's condition at the end of the operation was fairly good, considering that he was "a bad risk." On return to the ward he did well at first, but on the next day his condition grew worse. He had constant vomiting of dark, thin fluid, that resembled old blood, though tests for blood (chemical and microscopical) were

negative. On the third day after the operation he became rapidly worse. Stimulation with caffeine and salt infusion was resorted to. An intravenous injection of 300 c.c. of glucose (10 per cent.) was given at 8 P. M. and another of 200 c.c. at 12.30 A. M., with no reaction. On the fourth day after the operation the patient died. The pulse had kept up well to the end. Just before death there was a definite left-sided convulsion, the head being drawn to the left, with jerky movements of the arm and leg on the left side.

Report of Autopsy (Made by Dr. Finney).—Carcinoma of the head of the pancreas, compression of common bile- and pancreatic ducts, fibrous pancreatitis, jaundice, cholelithiasis, emaciation. (*Operation:* cholecystenterostomy.) Pseudolobar pneumonia; right central necrosis of the liver; cloudy swelling of the viscera; fibrinous pleurisy.]

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XIV. ALVEOLAR ECHINOCOCCUS(?) OF LIVER

RUPTURE OF CYST INTO PERITONEAL CAVITY. EXPLORATORY
LAPAROTOMY

BEFORE the patient is brought in I shall ask Dr. Dorsey, the resident physician in charge of the private wards, to give you an account of his history.

Every now and then there is a patient in the private wards of such special interest as to merit presentation to the class. It says much for the understanding of the laity that even when under treatment in the private wards they are willing, on request, to be presented before the class of medical students. You will recall that a number of such cases have appeared before you, and I may say that I have as yet never had private patients decline to come when I have asked them to do so.

The malady from which our patient of today suffers is of unusual interest, as you will soon see.

DR. DORSEY: The patient, a white man, aged thirty-eight, is a tea planter, a native of Paraguay. Indeed, he has made the trip from that country to Baltimore in the hope that light may be thrown upon the malady from which he suffers.

He complains of "an enormous swelling of the abdomen, of weakness, and of recurrent attacks of slight fever."

In his earlier life he suffered from neisserian and treponemal venereal infections, for which he was carefully treated. He used tobacco to excess, but there was no excess in the use of alcohol. His life was an active one, out of doors, involving horseback riding for long distances.

During the past sixteen years he has suffered from various infections. Thus, in 1904, he had a severe attack of tertian malaria. During the years between 1909 and 1916 he had frequent attacks of irregular fever, which lasted for ten to fifteen days at a time. As he was living in a malarial district it is supposed that these were, also, attacks of malarial fever. In 1915 he suffered from an acute dysenteric attack for some three weeks, having daily from twenty to fifty stools containing blood and mucus. The attack was accompanied by high fever. It is said that there is much amebic dysentery in Paraguay, but that the bacillary form of dysentery is almost unknown there.

In 1916 he suffered an accident in which a blow was struck over his right side in the region of the liver. He fainted from the pain and was prostrated for several days, but recovered without any apparent residue. In 1917 he was seen by the surgeon who has accompanied him to this country. His liver then reached the level of the umbilicus and the spleen was also enlarged. At this time he had an intermittent fever, which disappeared under the administration of quinin. It is said that the liver and spleen were also somewhat reduced in size by the use of quinin.

In the next year, 1918, the patient suffered, at periods, from malaise, headache, and chilliness, but had no fever. At these times quinin failed to benefit him. On account of his earlier lues he was given some twenty injections of mercury intravenously, and by the mouth potassium iodid, after which his condition improved.

In 1920, after a long trip on horseback, he suddenly "felt something happen" in his upper abdomen. The abdomen quickly became much enlarged, and signs of fluid in the abdomen were detected by his physician. He had a little fever and the parasites of tertian malaria were found in his blood. He was given more quinin and also some more antiluetic therapy. The fluid, however, did not go away, and in August, 1920, a needle was introduced into the peritoneal cavity on two occasions, but only about 10 c.c. of an opalescent, viscous fluid could be withdrawn. From August on, his condition remained very much the same. He continued to be weak and occasionally had a little fever, but there was no pain. He states that since 1917 he has lost about 35 pounds in weight.

At the first physical examination, made outside the hospital by Dr. Maurice Pincoffs, the essential points were the following: "A tall, sallow man, moderately emaciated, with striking enlargement of the whole abdomen and a little pitting on pressure at the ankles; no skin eruption; right pupil larger than the left; both pupils reacted, however, well to light and on accommodation; black line at the gum margin suggestive of lead line; marked pyorrhea alveolaris; no glandular enlargement; scars of incision in the right groin (earlier buboes); lower aperture of thorax markedly widened, with flaring costal margin and great widening of the epigastric angle; a little dulness at both apices, with harsh breath sounds there; fine moist crackles at both bases. Heart negative except for a systolic murmur at the base. Pulse 80, regular; vessel wall not thickened. Blood-pressure,

120 systolic, 84 diastolic. Enormous distention of the abdomen, with bulging flanks; slight dilatation of lateral abdominal veins and of the superior epigastric veins; very marked fluctuation wave elicitable; abdominal walls flaccid. A large tumor mass was palpable in the midline, above the umbilicus, with small hard nodules palpable on its surface. In the lower abdomen, there were many irregular nodular masses, palpable through the fluid. The relation of these masses to one another not determinable, owing to the abdominal distention. Liver and spleen probably markedly enlarged, though palpation of these organs was unsatisfactory on account of the fluid in the peritoneal cavity under pressure. Deep and superficial reflexes normal. On rectal examination, prostate negative, but a nodule about the size of a hickory nut palpable through the wall of the rectum.

On roentgenoscopic examination of the chest the heart was found to occupy a transverse position doubtless owing to the distended abdomen pressing up the diaphragm. There was moderate diffuse dilatation of the aorta. Some spotty infiltration was apparent in the lungs, more marked in the lower lobes than in the upper. The diaphragm descended moderately, and apparently equally, on the two sides. An attempt at roentgenoscopic examination of the gastrointestinal tract was unsatisfactory owing to the distention of the abdomen with fluid. *x*-Rays of the paranasal sinuses and of the skull were negative.

Several laboratory tests were also made before the patient entered the hospital.

Blood examination: Red blood-corpuscles, 4,616,000; white blood-corpuscles, 7680; hemoglobin, 72 per cent. Differential count: Polymorphonuclear neutrophils, 72 per cent.; polymorphonuclear eosinophils, 1 per cent.; small mononuclear elements, 14 per cent. The red blood-corpuscles looked pale in the smear; no basophilic stippling, so that lead-poisoning can probably be ruled out, the black line of the gum margin having some other origin.

The *Wassermann reaction* in the blood was entirely negative with three different antigens.

Stomach contents: Free HCl, 25 acidity per cent.; total acid, 40 acidity per cent.; otherwise negative.

Stool: Bile was present. No parasites were found in the feces.

Urine: Specific gravity, 1026; reaction acid; faint trace of albumin; occasional hyaline cast, and a few white blood-cells.

The patient was also seen at this time by Dr. Barker, whose first impression was that he suffered either from multiple neoplasms or from echinococcus cysts. He was also examined by three members of the surgical staff, who verified the above findings and arrived at similar impressions, but could not be sure of the nature of the masses without further investigation.

At Dr. Pincoffs' suggestion the patient consented to an exploratory laparotomy. This operation was done on October 26, 1920 by Dr. Richard Follis. Since then the patient has been under observation in the private ward of this hospital.

At the operation Dr. Follis made a McBurney incision, and as soon as the peritoneal cavity was opened there was a gush of yellow, gelatinous fluid, containing many hundreds of whitish-yellow bodies, which varied in size from that of a pea to that of a hen's egg, some 4 or 5 liters of material being evacuated through the opening. The enormously enlarged liver presented in the wound and Dr. Follis could make out many cyst-like masses extending to the surface of the organ. These cysts seemed to be about the size of a lemon, and many of them were soft in consistency. No attached masses were seen upon the parts of the peritoneum that could be inspected. The peritoneum itself looked a little reddened from vascular injection. The yellowish-white capsules which were so numerous in the fluid have thin, translucent, membranous walls with contents of a creamy white material.

Cultures were made from the fluid obtained from the peritoneal cavity, but they have remained sterile.

The patient felt very much relieved by the removal of the fluid, and the wound has healed satisfactorily without fistula formation.

DR. BARKER: You have heard this remarkable history. We shall now have the patient brought in in order that you may see his present condition.

The patient speaks no English, but a member of his family has acted as interpreter so that we have been able to secure a very full history of the case. It is quite possible, from the account given, that the patient might have contracted a parasitic invasion through the dog as intermediary.

You will observe that, though the patient is a little thin (aside from his abdomen), yet there is no high grade of undernutrition.

He does not look cachectic. There is not the slightest trace of jaundice. Bile has been present in the feces, and there is no bilirubinuria.



Fig. 22.—Anterior view of patient with multiple echinococcal cysts and ascites. The widening of the lower aperture of the thorax and the distention of the abdomen are well shown.

We can now palpate the abdomen much more satisfactorily than before the fluid was drawn off. You will be struck at once by the enormous widening of the lower aperture of the thorax (Fig. 22); by the marked prominence of the epigastric region extending well down

toward the umbilicus, and by another large prominence in the left hypogastric region (Fig. 23). I can now make out, on palpation, that this mass in the epigastrium and in the right upper abdomen is certainly the enlarged, cystic liver.



Fig. 23.—Lateral view of patient with multiple echinococcal cysts and ascites.

Boss-like eminences are easily palpable on its surface; some of them are soft, others very hard and nodular.

The mass in the left hypochondrium seems to be continuous with the rest of the liver mass. Still further to the left a large spleen can

be felt. On the left side of the abdomen below the liver and spleen I can, by ballottement, reach another large mass. On bimanual palpation I can press this mass forward from the lumbar region against the anterior hand, and when I press down upon it with the anterior hand I can feel the impulse with the hand in the back. This is probably a large left kidney. In the lower abdomen on both sides, by ballottement, I can feel large masses which are very firm, though the hand has to go through considerable fluid to reach these. There seem to be cysts or masses widely distributed through the abdomen. The veins of the abdomen are still a little distended, but less so than before laparotomy. There is now no edema of the ankles.

The patient may now return to his room in the Marburg building. (*Patient removed.*) We shall now proceed with the further discussion of the case.

Many of the causes of enlargement of the liver may be immediately ruled out here; thus, fatty liver, stasis liver, amyloid liver, abscess of the liver, and hypertrophic cirrhosis of the liver can be immediately dismissed. Even lues can, I think, be ruled out as a cause of this abdominal condition. Gummatous processes, so extensive and so widely distributed, are improbable in view of the fact that the man has a negative Wassermann reaction in the blood-serum now, and, moreover, has had intensive antiluetic therapy over a long period (mercury, iodids, neosalvarsan).

Neoplasm, which seemed quite probable before the laparotomy, seems most improbable now. We are evidently dealing with a cystic disease of some sort.

There is a remarkable form of cystic disease of the liver that occurs in association with congenital cystic kidney and congenital cysts in the pancreas, but such cysts are, as a rule, filled with clear yellowish fluid. The occurrence here of an enormous number of smaller and larger free cysts in the peritoneal cavity is strongly suggestive of the rupture of some cyst, perhaps originally of the liver, with setting free of daughter-cysts from the inside. This makes us think of echinococcus cyst as the only satisfactory explanation of the findings in this patient.

You will remember, from your reading, that echinococcus disease of the liver may develop either as *echinococcus cysticus* (sometimes called *echinococcus unilocularis*) or as *echinococcus alveolaris* (sometimes known as *echinococcus multilocularis*).

If this patient has echinococcus disease of his liver and other organs, we must try to determine which form we are dealing with—echinococcus cysticus or echinococcus alveolaris.

When only a single cyst is present it is most often due to echinococcus cysticus. The fluid in such instances is often under such tension that the mass feels like a solid tumor. Occasionally a peculiar thrill, known as the hydatid thrill, is demonstrable on palpation, owing, it is supposed, to the rubbing of daughter-cysts upon one another within the mother-cyst. In this case no hydatid thrill could be made out either on palpation or percussion. In echinococcus cysticus it is common to find either scolices or hooklets in the fluid. Dr. Clyde Guthrie has searched very carefully for these in the fluid removed at laparotomy, but has been unable to find any; moreover, all the members of the third-year class in clinical microscopy were put at work in a search for such hooklets and scolices, and no one succeeded in finding any.

In echinococcus alveolaris multiple masses are common, and many of them are firm and nodular. Hydatid thrill is never made out, and it is often impossible to demonstrate the presence of either hooklets or scolices, probably owing to their degeneration. Moreover, when a large number of very small cysts are found the findings speak for echinococcus alveolaris rather than for echinococcus cysticus. Against echinococcus alveolaris is the absence of jaundice, for at least four-fifths of the alveolar cases are markedly jaundiced. The absence of jaundice does not, however, rule out echinococcus alveolaris, for in about one-fifth of the cases jaundice is absent throughout the entire course of the disease.

The fluid obtained from the abdomen has been carefully studied, chemically and physically, by Dr. Guthrie. Its specific gravity was 1027; its total nitrogen content is 15.54 mg. per cubic centimeter; the content of non-coagulable nitrogen is 0.38 mg. per cubic centimeter. A reducing substance (nature as yet undetermined) is present in the fluid.

Some of the cysts have been hardened for microscopical examination and we shall have, later, a report from Dr. Rich in the pathological laboratory upon the histological findings. Animal inoculation experiments are being made also in the pathological laboratory. Thus, some of the material has been fed to dogs, and some of it has been injected intraperitoneally in other animals. We did not possess,

unfortunately, any echinococcus antigen for making complement-fixation tests and doing precipitin reactions. I have telegraphed Dr. J. Homer Wright, of Boston, and Dr. J. A. Kolmer, of Philadelphia, for antigens, and as soon as they arrive the tests will be made.

The *precipitin reaction* is positive in only about one-third of the cases that are examined, so a negative reaction does not rule out echinococcus. Echinococcus fluids obtained from human beings are used as antigens. One or 2 cm. of such fluid are mixed with from $\frac{1}{2}$ to 1 c.c. of the blood-serum of the patient to be tested. The mixtures are kept for from two to four hours in a thermostat and then allowed to stand until the following day at the room temperature. If a precipitate occurs, one must make sure that it is really due to precipitins and not to bacterial growth.

The *complement-fixation test* for the demonstration of the presence of echinococcus antibodies was first resorted to by Ghedini (1906), and afterward by Weinberg and his co-workers in Paris, and by Apphatic and Lorentz of Argentina. Positive reactions are obtained in about 80 per cent. of the echinococcus cases. A negative result, therefore, does not rule out echinococcus disease. Most of the complement-fixation tests have been performed upon patients with echinococcus cysticus, not upon patients with echinococcus alveolaris. There are on record, however, instances of positive reaction with the latter, notably by Dobrotine (1910) in Russia.

The technic of the complement-fixation reaction is somewhat complex. You will find this fully described in the article by Weinberg in the second edition of Kolle and Wassermann's *Handbuch der pathogenen Mikroorganismen*.

Some interesting studies have also been made upon the presence of *anaphylactic antibodies* in the serum of echinococcus cases. How far such allergic methods will prove valuable for diagnosis it is as yet too early to say, though there is already quite a bibliography on the subject.

Three biological types of human reaction to echinococcus invasion have been distinguished by Chauffard and Vincent: (1) The complete form in which there is eosinophilia and positive complement-fixation reaction; (2) the dissociated form in which the complement fixation is positive, but there is no eosinophilia; and (3) the latent form in which there is neither eosinophilia nor a positive complement

reaction. Of all the biological tests, the complement-fixation test seems to be the most important for diagnostic purposes.

Attempts have been made to draw conclusions from the relative sizes of the spleen and liver in the differential diagnosis between echinococcus alveolaris and other enlargements, such as primary carcinoma of the liver and biliary hypertrophic cirrhosis. The spleen-liver index, S/L, in echinococcus disease is $\frac{1}{8}$ to $\frac{1}{11}$; in carcinoma $\frac{1}{15}$ to $\frac{1}{20}$, and in hypertrophic cirrhosis $\frac{1}{2}$ to $\frac{1}{3}$. In other words, the spleen is relatively large in hypertrophic cirrhosis, small in carcinoma, and of medium size in echinococcic disease. I would not, however, say much stress upon this S/L index as a diagnostic criterion, though considerable attention is paid to it in this excellent article by Posselt on the symptomatology and clinical diagnosis, which I am passing around.

Another point, upon which Posselt lays some stress, is the relatively good state of nutrition that is maintained, at least for a long time, by patients suffering from invasion by echinococcus alveolaris. The patients have a good appetite and may even gain in weight. In many of the Russian cases, however, observed by Posselt a terminal cachexia developed.

I shall pass around, too, this large monograph by Melnikow-Raswedenkow, which contains an exhaustive histological study of the tissues and cyst walls in echinococcus alveolaris. If you can find time to look this over, and to examine the beautiful illustrations accompanying it, you will, I am sure, be deeply interested.

Though alveolar echinococcus is most often primary in the liver of man and of animals affected, it may occasionally be met with as a primary lesion in the brain, in the spleen, or in the suprarenals.

This form of echinococcus is a much more dangerous variety than echinococcus cysticus, for the primary nodule or cyst in echinococcus alveolaris can give rise to metastases by way of the lymph-vessels or the blood-vessels to other organs, especially to the lymph-glands of the lungs and of the brain.

The descriptions and illustrations of the histological make-up of the tumor in the liver are exceedingly interesting. The many chambered mass contains multiple embryos. The neighboring granulomatous tissue resembles very closely that met with in infectious granulomata of bacterial origin. Some of the embryos are

inclosed tightly within the alveoli; some of them are visible between liver cells; others can be seen migrating.

There has been a lively discussion between those who believe in the unity of echinococcus cysticus and echinococcus alveolaris and those who believe in a duality. The latter look upon echinococcus cysticus as the larval form of *Tænia echinococcus* and upon echinococcus alveolaris as the larval form of another worm, *Tænia alveolaris* (Posselt). The dualistic theory seems to be favored by the different geographical distribution of the two disease forms. On the other hand, the unitarians maintain that stages intermediate between echinococcus cysticus and echinococcus alveolaris have been observed, especially in the multilocular echinococcus cysts of bone. Dévé (1912) thought that he could bring the proof that multilocular echinococcal cysts of bone are due to echinococcus cysticus, and have nothing to do with echinococcus alveolaris proper. According to Weinberg, there are at present only two marks that serve to distinguish the two forms of echinococcosis, namely, (1) the malignant activity of germinative plasmodium, and (2) the irregularity of the vesicular formations that are characteristic of echinococcus alveolaris. It is to be hoped that experimental investigation will ultimately settle this dispute between the unitarians and the dualists. At present it seems to me that the weight of evidence favors an origin of the two forms from two different worms, although these two varieties of *Tænia* may belong to a single species.

From the standpoint of the biologist and the morphologist the study of tapeworms is a fascinating subject. In structure these parasites would seem to be the apotheosis of brainless sex. The adult worm possesses nervous, muscular, excretory, and generative organs embedded in the mesenchyma, but the nervous system is extremely rudimentary. There is no definitely demonstrable brain, though there is some nervous thickening in the scolex. The differentiation at this end of the parasite is so slight, as far as the nervous system is concerned, that there are reputable zoölogists who think that the scolex marks the tail-end and not the head-end of the worm! The contrast of this rudimentary nervous system with the elaborate development of the reproductive organs is a remarkable feature. The reproductive organs are usually repeated in each proglottis of the worm, and in some families each segment contains both male and female sex organs (external and internal). The body of a tape-

worm is, therefore, regarded as a single organism within which the genital organs have become segmented.

The tapeworms possess no trace of a digestive tract at any stage of their development. The worms are nourished entirely by the chyle of the host. The worm by means of the appendages of its scolex attaches itself to the mucous membrane of the small intestine of the host, and is capable of resisting the peristaltic action of the digestive tube in which it lives. The food enters its body entirely by osmosis through the striated cuticle. The *Trematodes*, or flukes, on the contrary, as you will remember, take blood from the host, but these *Cestodes*, or tapeworms, do not draw blood; they live on the chyle which they absorb.

Dr. Guthrie and Dr. Evans have placed under the microscopes, on the adjoining table, some typical echinococcic hooklets derived from other cases that have been observed in this hospital. On this table, too, are examples of several kinds of tapeworms and of hydatid cysts loaned to us from the Pathological Museum by Professor MacCallum for demonstration at the clinic. You may, if you will, examine these at your leisure at the end of the clinic.

If during the coming week you could find time to look up the article by F. W. Gamble, entitled "Tapeworm," in the twenty-sixth volume of the eleventh edition of the Encyclopedia Britannica, you will find in it a very interesting account of the general morphology and biology of the different forms of tapeworm. For accurate classifications and description of the exact form of the different types you cannot do better than consult the excellent articles by C. W. Stiles and his associates published by the Marine Hospital Service.

In the *treatment of alveolar echinococcosis* prevention is, of course, exceedingly important. The ordinary *Tænia echinococcus*, a small tapeworm about $\frac{1}{4}$ inch long, spends its adult life in the intestine of the dog, sometimes in that of the cat. That prophylactic measures should be adopted by persons who have much to do with dogs or cats is obvious. Aside from strictly personal cleanliness on the part of the human being concerned, the greatest care should be exercised to avoid contamination in any way from the fecal excretions of dogs. An occasional vermifuge should be administered to animals kept as pets.

When echinococcosis is met with in a human being radical treatment should be resorted to in the early stages if possible. A single

mass in the liver can be successfully excised and the patient permanently cured (Nordmann and others). Unfortunately, once alveolar echinococcus has metastasized, the hope of complete eradication by surgical methods is very slight. Such a metastasizing echinococcosis is as serious a disease as a metastasizing malignant neoplasm. The cases all end fatally sooner or later, though the disease may last for several years.

Attempts have been made to destroy the growths by incision after the injection of formalin and curetage, the so-called *formolage* of the French.

An Italian investigator, de Renzi, believes that echinococcosis can be successfully treated by administering ethereal oil of male fern, a well-known remedy for tapeworm in the intestine. He states that given consistently over a certain period even the larval form of tapeworm (hydatid disease, alveolar echinococcus) will be killed by the male fern. This seems to me, however, very improbable. When one thinks of the large number of scolices that are so thoroughly protected within the interior of the tumor mass, it is scarcely conceivable that sufficient of the male fern should reach the embryos to kill them off. Since de Renzi has reported favorable results, however, and we are devoid of other means of treatment that are satisfactory, the method should, I think, be given a trial. It may be well to experiment also with other parasitocidal agents (diarsenol, copper salts, etc.) in the hope of finding one that will kill these parasites without injuring the host. Even if the parasites could be killed there might be some danger from absorption of the dead parasites. In such a desperate disease, however, we are justified in taking somewhat desperate risks. Langenbuch, well known for his work on the surgery of the liver, commenting upon this disease, said, "This horrible and terrible form of echinococcus of the liver excites in us ever again the wish that we could discover some specific substance that could be given internally that would kill these parasites."

There is one method of investigation that has not been applied in this case that might be helpful in the localization of the exact distribution of the several cysts, namely, pneumoroentgenography of the peritoneal cavity. Perhaps we can get the patient's consent to make this examination. There is very little risk in applying the method and it would be interesting to see how much it would aid us in a diagnostic way.

[*Further History of the Case.*—Microscopic examination of the cyst by Dr. Rich showed a definite fibrous-appearing wall in which were seen many large cells, with honey-comb reticular protoplasm and irregular nuclei, small in proportion to the size of the cell. The cyst contents appeared to be homogeneous, granular, or reticular coagulated masses. Here and there embedded in this eosin-staining material were stellar “aggregates” of darkly staining bodies, irregular in shape. A culture made from the cyst found in the abdomen was negative.

An echinococcus antigen was obtained from the University of Pennsylvania and another from Dr. Mallory in Boston. A complement-fixation test was attempted by the Phipps Laboratory with this material against the patient's serum, but the serum was found to be anticomplementary in dilution of 1 : 2500, so that the test was not satisfactory.

The patient was discharged on November 9th, about six weeks after admission, and after remaining in Baltimore for a week or ten days, as advised, returned to Paraguay. Nothing further is known regarding the case.]

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XV. HOOKWORM INVASION WITH SEVERE ANEMIA

SEVERE HEMOLYTIC ANEMIA WITH ACHYLIA GASTRICA, ORAL SEPSIS, AND LEMON-YELLOW TINT TO THE SKIN, UNDER TREATMENT FOR TWO YEARS BEFORE RECOGNITION OF THE EXISTENCE OF A SEVERE UNCINARIASIS. DISCUSSION OF THE NATURE OF THE ANEMIA AND OF THE POSSIBLE COEXISTENCE OF ANEMIA OF UNCINARIASIS WITH A CHRONIC HEMOLYTIC ANEMIA OF THE ADDISON-BIERMER TYPE.

You will notice the striking lemon-yellow tint of the skin and the marked pallor exhibited by this patient. What diagnostic idea do you think would first enter the mind of a physician or a medical student glancing at this patient?

STUDENT: Every one who has seen the patient has been struck by the resemblance of his condition to that seen in patients suffering from pernicious anemia.

DR. BARKER: I understand that the patient has been under treatment for some two years for anemia, and that up to the time of admission into the hospital one of the principal causes of his anemia has gone entirely undiscovered.

Mr. A., will you give the class a brief history of the patient?

STUDENT: The patient, J. T., a white married farmer, aged thirty-seven years, a resident of North Carolina, was admitted to Ward F

of the Johns Hopkins Hospital on December 15, 1920, complaining of "weakness."

When asked regarding the history of his present illness, he stated that it began about two years ago, when he had an attack of influenza, and had to remain in bed for some three weeks. Since that time he has not been able to do a full day's work, though there were a couple of periods when he improved somewhat and was able to do a little work. He feels sure that he has never been "up to par" since the influenzal attack. A few months after the attack he noticed that his skin became of a light yellow color, and this change in color has persisted ever since. He has had some headache, some ringing in the ears, and a little breathlessness on exertion. He has been weak all the time, but has not noticed any progression in the loss of strength. He states that he is somewhat more sensitive to cold than formerly. His digestion has, on the whole, been good, though he has occasionally suffered from brief attacks of diarrhea after some dietary indiscretion such as the eating of raw apples. He has noticed at times a little swelling of the ankles, and occasionally, when tired, a feeling of burning in the stomach. During these two years he has consulted several physicians—at least four; all of them told him that "his blood was thin." The cause of the thin blood, however, was not ascertained, and he himself believes that it was due to the attack of influenza.

When admitted here his chief complaint, as I have said, was that of weakness. In addition, there has been some headache, tinnitus, and dyspnea, though his subjective symptoms are very slight considering the degree of anemia that has been found to be present. Moreover, the patient is a rugged type of farmer who tends to minimize his symptoms. He has now no pain, dizziness or digestive disturbances, and no profuse sweating. There has been no marked change in body weight. He had on admission a little cough, which he ascribed to a cold caught on the way up.

DR. BARKER: Before telling us of the physical examination on admission to the hospital would you mention any points of importance in the previous history of the patient and in his family history?

STUDENT: In childhood the patient was not robust. He had a number of the ordinary diseases of childhood, including measles, mumps, whooping-cough, and diphtheria. He states that he also had Saint Vitus' dance, though he gives no history of tonsillitis or of

arthritis. He states that while a boy he had "ground-itch" every few years, and that it was very common in his neighborhood. Since early youth he has worked on a farm. His habits have been good. He denies venereal infection. He has not suffered from traumata, nor has he undergone any surgical operation.

His family history seems unimportant. He married at twenty-five, and his wife, after having one miscarriage, gave birth to two children that are living and well.

DR. BARKER: Please give us, in brief summary, the positive findings on physical examination at the time of his admission here six days ago.

STUDENT: The first physical examination was made and dictated by the house officer, Dr. Telinde. Since then he has been examined by Dr. Mason, the resident physician, and by other members of the medical staff.

The principal positive findings were the following: Marked pallor, marked yellowish discoloration of the skin of the whole body, most marked on the exposed parts and on the palms of the hands and the soles of the feet; well nourished; pulsating carotids; temperature 98.6° F.; two palpable lymph-glands in the left axilla, and slight enlargement of the retrocervical lymph-glands; pulse-rate, 68; respiration rate, 16; blood-pressure, 155/50 (which soon fell after admission to 130/50); scleræ of a pearl-grayish-white color (no icterus); clean, smooth tongue, with moderate atrophy of the lingual papillæ; marked malocclusion of the teeth; pyorrhea alveolaris; much dental caries and several crowned dead teeth; lungs negative, except for a few sticky râles in the left lower lobe, probably due to the cold recently contracted; heart much enlarged to the left; apex-beat in the left anterior axillary line forcible; slight systolic thrill at the apex; cardiac dulness, 4 cm. to the right, 13½ cm. to the left; no marked retrosternal dulness; loud blowing systolic murmur at the apex well transmitted to the axilla, and audible also at the base of the heart and over the body of the heart; slight diastolic murmur at the base and down the left margin of the sternum on admission, though this soon disappeared after rest in bed, the systolic murmur persisting. Abdomen negative, except for a palpable liver edge just beneath the costal margin; extremities negative; genitalia and rectum negative; reflexes normal.

DR. BARKER: What was the first impression formed from this history and physical examination?

STUDENT: Before any laboratory tests were made it was thought that the patient suffered from "pernicious anemia" on account of the marked pallor, the lemon-yellow tint to the skin, the smooth tongue with atrophy of the lingual papillæ, and the history of headache, tinnitus, dyspnea on exertion, and asthenia. It was thought also that he suffered from both aortic and mitral insufficiency.

DR. BARKER: You doubtless made an examination of the blood at once. What were the findings?

STUDENT: Yes; the blood was examined on the day of admission, with the following results: R. B. C., 850,000; W. B. C., 5100; hemoglobin, 17 per cent.; color-index, 1. Differential count: P. M. N., 71.6 per cent.; P. M. E., 1.3 per cent.; P. M. B., 0.4 per cent.; S. M., 19 per cent.; L. M. and Tr., 6.3 per cent., and a few unclassified cells.

There was considerable anisocytosis and a little poikilocytosis. The red cells looked pale and the platelets, I thought, were diminished in numbers.

The blood-picture resembled very much that of an Addison-Biermer type of anemia, though it differed from it in that there was a relative increase of the polymorphonuclears and a relative diminution of the small mononuclears; moreover, the red cells were rather pale, the anisocytosis and poikilocytosis were not very marked, and no megaloblasts were seen; indeed, no nucleated reds at all were seen.

DR. BARKER: The smooth tongue with atrophy of the lingual papillæ is a little suggestive. To what does it point?

STUDENT: That made me think also of pernicious anemia, though there was no inflammation of the tongue.

DR. BARKER: A tongue of this sort makes one think of an achylia gastrica. Was the stomach juice examined?

STUDENT: Yes; on the third day after admission. There was no free hydrochloric acid present, and the total acidity was only 9 acidity per cent.

DR. BARKER: Was the Wassermann test made in the blood-serum?

STUDENT: Yes; the Wassermann reaction was negative.

As the patient's anemia was so profound, it was thought best to give him a transfusion at once, before proceeding farther with the studies. He was found to belong to Group II, and on the day after admission he was given 500 c.c. of citrated blood by transfusion. This was followed by a marked urticarial eruption over the whole

body which lasted for about two hours. There was no other reaction to the transfusion.

DR. BARKER: Did he seem to benefit by the transfusion?

STUDENT: Yes; on the day following, blood examination showed a distinct improvement: R. B. C., 1,600,000; W. B. C., 4250; hemoglobin, 27 per cent.; color-index, 0.85. In the differential count we found: P. M. N., 81 per cent.; P. M. E., 4 per cent., and lymphocytes, 9 per cent.

DR. BARKER: Was the blood studied by either Dr. Guthrie or Dr. Evans of the clinical laboratory?

STUDENT: Yes; the counts and smears were gone over carefully by Dr. Frank Evans, who concluded that the anemia resembled that of a secondary type rather than that of a primary type. He came to this conclusion because the color-index was as low as 0.85 and because the anisocytosis and poikilocytosis were so little marked; moreover, he thought the platelets were not diminished and commented upon the absence of nucleated red corpuscles. He stated that the red cells were paler than normal, though there was a little diffuse basophilia; another point in favor of secondary anemia, he thought, was the relative increase in the polymorphonuclear neutrophils, although the total white count was somewhat diminished.

DR. BARKER: The blood-picture is certainly an interesting one and is somewhat confusing. An anemia of this grade with a color-index that, though lower than 1 is fairly high, with a leukopenia, with some anisocytosis and poikilocytosis, with a lemon-yellow tint to the skin, with a smooth, atrophic-looking tongue, with oral sepsis, and with achylia gastrica, would make one think twice before ruling out an Addison-Biermer type of anemia. On the other hand, Dr. Evan's comments are pertinent. The anisocytosis and poikilocytosis are but little marked in this blood-smear when you consider the high grade of anemia that exists. The differential formula is against the Addison-Biermer type, for in it we would expect besides the leukopenia a relative lymphocytosis, whereas here we have a relative lymphopenia and a relative increase of the polymorphonuclear neutrophils. In an Addison-Biermer type of anemia of this grade we should certainly expect to find some nucleated red corpuscles, normoblasts, and particularly megaloblasts. None of these cells is present. The only signs of regenerative activity reported lie in the diffuse basophilia. Moreover, the platelets are not diminished in numbers,

or if so, only slightly, whereas in the Addison-Biermer type of anemia we expect to find a definite reduction in the platelets.

Has he had any paresthesias in his hands or feet? You will recall how common it is to have numbness and tingling in the hands and feet, the signs of a beginning funicular myelitis in the Addison-Biermer type of anemia. These symptoms may, it is true, occur in a secondary anemia, but they are far less common than in the chronic hemolytic anemias.

STUDENT: He has not complained at all of paresthesias in hands or feet.

DR. BARKER: Has anything been found thus far in the patient that could account for a secondary anemia of this high grade?

STUDENT: On the third day after admission a stool was obtained for microscopic examination. It was found to contain occult blood and, on microscopic examination, a very large number of eggs of *Necator americanus* or the American form of hookworm was observed.

DR. BARKER: That is, indeed, an interesting finding. Could hookworm invasion give rise to an anemia of this high grade?

STUDENT: Yes, I think it could, though most of the cases of hookworm do not have so profound a degree of anemia. A number of cases have been observed, however, in which the red cell count was below 1,000,000.

DR. BARKER: Where does this patient live?

STUDENT: He lives in North Carolina, and, as it happens, in a county of that state in which I personally had the opportunity of studying hookworm invasions last summer.

DR. BARKER: Was hookworm prevalent in that county?

STUDENT: Yes; very prevalent. Of a large series of children examined at random in the county, no less than 30 per cent. were invaded by hookworm.

DR. BARKER: Had this patient's feces been examined before?

STUDENT: No examination of the feces had been made, and apparently the possibility of hookworm invasion had not been thought of, though the patient had been anemic for two years. Probably the yellowish discoloration of the skin misled the physicians whom he chanced to consult.

DR. BARKER: Is it common to have this definite yellow tint of the skin in the anemia caused by hookworm?

STUDENT: I am not sure. I think it is not common.

DR. BARKER: Certainly in our experience here it is not common to see this lemon-yellow tint in the secondary anemia due to hookworm. I am told, however, by those who have worked in the hookworm regions in the South that certain of the patients have shown it.

Well, one of the advantages of these clinics is that we study concrete cases of disease and have the opportunity of seeing how they deviate from the typical text-book pictures. We shall have to consider, in this case, whether or not the whole picture could be due to the hookworm invasion, or whether the disease-picture has been contributed to by other factors. I am especially interested to know whether or not this anemia entirely depends upon the hookworm invasion or whether other etiological factors have been concerned. The lemon-yellow tint to the skin in the Addison-Biermer type of anemia is supposed to depend upon a slight icterus, and it, in turn, when associated with urobilinuria, is usually a sign of a chronic hemolytic anemia. Was there any urobilin in the urine of this patient?

STUDENT: There is a trace of urobilin in the urine, but the reaction was not marked. We are making further studies of the urine with this point in view. Aside from this abnormal finding the urine was negative.

DR. BARKER: Has the fragility of the red blood-corpuscles been tested, and has the blood been examined by the method of vital staining?

STUDENT: Those tests have not yet been made.

DR. BARKER: On palpating in the region of the spleen there is some fulness, but I cannot definitely get the edge of the spleen.

STUDENT: We were unable to palpate the edge of the spleen in the ward.

DR. BARKER: It is not always possible to feel the edge of the spleen, even in chronic hemolytic anemia, but very often the spleen is somewhat enlarged and even so much as to be palpable. Has the patient had malaria?

STUDENT: There is no history of malaria, and there are no malarial parasites in the blood at present.

DR. BARKER: Do you think of anything that has been discovered in this patient besides the hookworm invasion that could account for an anemia of high grade?

STUDENT: The oral sepsis and the achylia gastrica, perhaps, ought to be considered.

DR. BARKER: Yes; I think so too. We do often see a high grade of anemia in association with marked oral sepsis; and, moreover, achylia gastrica is a constant concomitant of chronic hemolytic anemia of the Addison-Biermer type. When I see a patient who presents the picture of the Addison-Biermer type of anemia, and who has free hydrochloric acid in the stomach juice, I begin to doubt the diagnosis and to look for a form of anemia other than the so-called "pernicious." In my experience, let me emphasize again, achylia gastrica is practically a constant finding in the Addison-Biermer type of anemia.

STUDENT: We have made only one examination of the stomach contents.

DR. BARKER: It will be desirable to have further examinations of the stomach juice, and perhaps, an examination by the fractional method. The results of a single examination might be misleading. At the same time the appearance of the tongue is strongly suggestive of the existence of achylia gastrica.

Did Dr. Evans test this patient's blood-serum with reference to its power to protect red cells from hemolysis by sodium oleate?

STUDENT: Unfortunately, Dr. Evans did not see the patient until after the transfusion of blood had been made and the introduction of normal blood into the patient would vitiate the test.

DR. BARKER: It certainly would have been interesting to have made this test before the transfusion was given. You will remember how helpful in this hospital that test has of late seemed to be in differentiating the chronic hemolytic anemias of the Addison-Biermer type from other forms of anemia. It might be interesting, too, to study the duodenal contents of this patient with reference to their contents in the biliary pigments.

There can be no doubt, I think, that the hookworm invasion is responsible for a large part of the anemia exhibited by the patient, but whether it is responsible for the whole of it I do not think we can yet be sure. It is quite conceivable that we have a hookworm invasion and a hookworm anemia in a patient who also suffers from a chronic hemolytic anemia. With hookworms in the intestine it is surprising that the blood does not show a more marked eosinophilia. Have you any idea how many hookworms this man harbors?

STUDENT: He must have a good many considering the degree of anemia and the large number of eggs found in the feces.

DR. BARKER: Has he been given a vermifuge yet?

STUDENT: No, not yet. And we have found no adult worms in the feces as yet.

DR. BARKER: Those who have been working on the hookworm anemias have a rough-and-ready rule for estimating the number of hookworms present from the degree of anemia. If you will look over this article by Dr. S. P. Darling in the London *Lancet* for July 10, 1920, you will find some interesting comments on this point. Dr. Darling was a member of the Malayan Board, which studied hookworm in the Far East, in Malay, Java, and the Fiji Islands, under the auspices of the British Colonial Office and the Netherland Indies Health Department. This work was supported by the Rockefeller Foundation of New York. The observers found that a given number of hookworms produce a corresponding amount in loss of blood. They estimated that about 12 hookworms are required to cause a loss of 1 per cent. hemoglobin. If we were to apply this measure to the anemia in the present case it would indicate, assuming that the whole anemia was due to the hookworm invasion, that there were between 900 and 1000 worms in this patient's intestines. Are as many worms as this ever found in a hookworm patient?

STUDENT: Yes; more than a thousand worms have been discovered in a given patient in more than one instance.

DR. BARKER: How could we find out how many worms this patient harbors?

STUDENT: By expelling the worms with a vermifuge, recovering them from the feces, and counting them.

DR. BARKER: Yes, that can be very easily done. Dr. Darling and his associates found that two treatments with oil of chenopodium, with 1.5 cm. at a dose, removed 99 per cent. of the hookworms present; and this dosage causes no unpleasant symptoms. It would be very interesting, indeed, to expel the worms from this patient, count the number found, and check up the relationship of the number of worms to the hemoglobin reduction.

The use of oil of chenopodium has now become very general in the treatment of hookworm invasion. Dr. Levy in this clinic in 1913 called attention to the work of European investigators with oil of chenopodium and was the first to use the oil here in the treatment of hookworm invasion. Formerly we had depended upon thymol, but the chenopodium treatment seems to be really more

efficacious than the thymol treatment. Moreover, it is less expensive. The oil of chenopodium necessary costs about 3 cents per patient, whereas the thymol costs about 15 cents per patient. The difference in cost would not be a serious matter if the thymol were more efficacious, but, as a matter of fact, the oil of chenopodium is definitely more efficacious. And when one comes to the "mass treatment" of hookworm, the matter of cost becomes exceedingly important. If you will recall that of the population of 300,000,000 people in India, probably two-thirds are infected with hookworm, and will then count the difference in cost of treating 200,000,000 people with a 3-cent preparation, on the one hand, and a 15-cent preparation on the other, you will see that the item of cost becomes very important. The International Health Board has to deal with battles on a large scale against the hookworm, and with them the item of cost, as a result, looms large.

Do you know of any other treatment for hookworm besides the thymol treatment and the treatment with oil of chenopodium?

STUDENT: I understand that betanaphthol has been used.

DR. BARKER: Yes; many have been treated, and successfully, with betanaphthol. In the doses in which it was first employed, namely, 0.2 to 0.5 gram, it was only slightly toxic, but recently it has been customary to use larger doses. Thus Bayma and Alves (1918) gave 6 grams in divided doses and reported 85 per cent. of cures; and Gonzaga and Lima (1918) gave 6 grams per day for three successive days and reported 73.5 per cent. of cures without severe toxic symptoms. Smillie, in Brazil, however, has shown that betanaphthol is capable of causing marked destruction of the red blood-corpuses, producing a change in them very much like that produced by benzol. In this paper of his in the *Journal of the American Medical Association* for last May (1920) he reports 4 cases of betanaphthol poisoning, and warns us of its dangers. I think we cannot do better than adhere to the oil of chenopodium treatment of hookworm, at least for the present. It is possible that the substance known as "carvacrol," an isomer of thymol, prepared from spruce turpentine, may prove to be a reliable and inexpensive drug for combating hookworms. Members of the Hygienic Laboratory of the U. S. Public Health Service are now experimenting with this drug.

How do you suppose this patient became the subject of hookworm invasion?

STUDENT: He lives in an area in North Carolina in which there is much pollution of the soil and in which the population has not yet been fully educated as to the precautions necessary to prevent hookworm invasion. He had "ground itch" several times as a boy, and he has been a farmer all his life, working the land.

DR. BARKER: Yes, certain portions of North Carolina are still in a very bad state as regards hookworm, though, thanks to the local health authorities, the U. S. Public Health Service, and the Rockefeller Foundation agencies, the people are rapidly becoming educated, hookworm patients are being treated *en masse*, and prophylactic measures are rapidly being introduced. The North Carolina of today is a wholly different state from that of a few years ago.

When the soil is polluted by human excreta containing hookworm eggs, or hookworm larvæ, a person can infect himself in either one of two ways. Let me refresh your memory regarding the mode of infection.

The hookworms in the human intestine give off oviposited eggs which escape with the feces. After they leave the body they begin to develop, and in about twenty-four hours the so-called rhabditi-form embryos are formed. The latter shed their skin (*ecdysis*) in two or three days. The second shedding of the skin occurs in from five to nine days when the larvæ have reached the so-called encysted stage and are ready to infect man. After this stage has been reached the larva takes no more food until it again enters a human being or other host.

One of the commonest ways in which human beings are infected is through the skin, especially the skin of the bare feet.

In the skin the larva causes a form of dermatitis, known as "ground itch." This "ground itch" occurs between the toes or on the surface of the feet, though it may involve the buttocks or even other parts of the body. Many names have been applied to this "ground itch." In some places it is known as "toe itch" or "foot itch," in other places as "wet weather" or "dew itch." Among the Cornish miners in England it is known as "New-Sump bunches," whereas in Porto Rico the natives speak of it as "mazamorro."

The larvæ, besides setting up the local irritation in the skin, may pass through the skin and enter the blood-stream. They thus reach the right side of the heart and pass to the lungs. There they may leave the blood-vessels to enter the air passages, and, passing up to

the larynx, are swallowed through the esophagus into the stomach, and thence reach the small intestine.

Another method of human infection is by direct ingestion, through the mouth, of food or water contaminated by the larvæ.

It is interesting that animals other than man may suffer from hookworm invasion. Thus, some years ago, there was great economic loss due to the invasion of the herds of seals in Alaskan waters by hookworms.

What means are used to prevent the soil pollution in infected districts?

STUDENT: By controlling the disposal of feces.

DR. BARKER: Yes; the sanitary scientists who attempt to control the spread of hookworm infection have, as a rule, adopted the latrine system, and have provided for thorough systems of inspection to make sure that the latrines are erected in sufficient numbers and are properly used. They have to depend largely upon an intensive educational campaign among the people, and it has been found especially important to secure the co-operation of the local authorities and of the business interests in the prosecution of this work.

Let me pass around this Sixth Annual Report of the International Health Board of the Rockefeller Foundation. You will see in it, illustrated, some of the latrines that have been recommended. You should secure, if possible, a copy of this report, for you will find in it all that is important regarding the modern campaign for the control of hookworm. Our time will not permit us to go further into the subject at the clinic this morning, but this report is in the hospital library and you may consult it at your leisure. I can highly recommend its careful perusal.

Before concluding the clinic I wish to say a word about the cardiopathy from which this patient suffers. We have seen, on physical examination, how large the heart of this patient is. We saw also that on admission there was a mitral systolic and an aortic diastolic murmur present. Now the aortic murmur is no longer present, but the mitral systolic murmur is loud and rough and is well transmitted to the axilla. There is a slight thrill at the apex. The first sound is also rather abrupt, though there is no definite presystolic rumble or murmur. The pulmonic second sound is accentuated. Remember, too, that this patient had Saint Vitus' dance, that is, chorea minor, in childhood, though he gives no history of rheumatism

or of tonsillitis. I think it very probable that this patient had an endocarditis at about the time he suffered from chorea, and that this endocarditis attacked the mitral valve, leaving a mitral insufficiency and, possibly, a slight mitral stenosis. The left ventricle is so very large too that one wonders whether or not the myocardium was involved at this time in the inflammation. Here is a tele-roentgenogram made of this man's heart. You will notice that the two curves on the right side are but little changed, although the lower curve is perhaps a little more prominent than normal, but the three curves on the left have undergone marked change. In the first place, the upper aortic curve is wide; in the second place, the second curve, due to the pulmonary artery and the left atrium, is more pronounced than normal, and, in the third place, the lower large curve or third curve is very much displaced to the left, indicating marked enlargement of the left ventricle. In other words, here we have a typical so-called "mitral configuration of the heart," such as we see in association with old mitral lesions. Now, of course, in a patient with this high grade of anemia it is common to have relaxation of the mitral ring and occasionally relaxation of the aortic ring. I have no doubt that the muscular rings in both the mitral orifice and the aortic orifice have been somewhat relaxed owing to the anemia. The fact that the aortic diastolic murmur has disappeared would indicate that, in all probability, the slight aortic insufficiency that was present on admission was a functional insufficiency due to relaxation of the muscular ring. With rest in bed and with the transfusion of blood the patient's cardiac condition is somewhat better, and the relaxation of the rings probably less than on admission. But in addition to this functional insufficiency I believe that this man has an organic mitral lesion due in all probability to an earlier endocarditis.

The patient's systolic blood-pressure was 150 on admission, but since rest in bed it has fallen to 130. The radial vessels are palpable and his brachials are thickened and tortuous. We may conclude, therefore, that a beginning atherosclerosis exists also in this patient.

But by far the most interesting condition we have discovered is the severe anemia with slight eosinophilia, associated with uncinariasis, on the one hand, and with oral sepsis and achylia gastrica and a lemon-yellow tint to the skin on the other. A chronic hemolytic anemia of the Addison-Biermer type is a much more serious disease

than a secondary anemia (no matter how severe) due to uncinariasis. The former disease is ultimately fatal, the latter curable. Let us hope for the patient's sake that the anemia is here really due to the uncinariasis; I very much fear, however, that we have to deal with a chronic hemolytic anemia, and that the uncinariasis is an accidental association. We shall see how he gets on with HCl after meals, blood transfusion, and vermifuges. You will be interested I know in hearing later on of the further progress of this interesting case.

[*Subsequent History of the Case.*—The patient was discharged on January 5, 1921, as "improved." The R. B. C. count fell to 2,070,000; Hb., 38 per cent. The fragility of the red blood-corpuses was tested by Dr. Ostro on the day after the clinic was held. Hemolysis began with 0.50 per cent. NaCl solution; it became complete with 0.35 per cent. NaCl solution. The last stool examined, after the administration of a vermifuge, showed some hookworm eggs, but no worms. Examination of the heart just before discharge showed a palpable thrill at the apex. There was no shock felt. A systolic murmur at the apex could be heard all over the precordium and was transmitted to the axilla. The impression at the time of discharge was that the patient had a primary anemia, an organic heart lesion, and uncinariasis.]

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DISEASES OF THE UROGENITAL SYSTEM

XVI. CHRONIC DIFFUSE GLOMERULOTUBULAR NEPHRITIS

A SURVEYOR OF TWENTY-TWO WITH ALBUMIN, CASTS, AND BLOOD IN THE URINE, A TENDENCY TO FIXATION OF THE SPECIFIC GRAVITY, RETENTION OF WATER, CHLORIDS, AND NITROGEN, GENERAL ANASARCA, PALLOR, AND SLIGHT ARTERIAL HYPERTENSION.

TODAY I have the opportunity of presenting to the class an interesting case of renal disease which will permit us to discuss briefly the methods of arriving at a diagnosis when we have to differentiate among abnormal conditions of the kidneys.

The patient is twenty-two years old and his occupation is that of a surveyor. He was admitted to Ward F of this hospital nearly three weeks ago complaining of "swelling of the entire body and of pain in the left hip, knee, and ankle." His family history is irrelevant. According to his own past history, he has always had good health until his present illness. When he was between ten and twelve, however, he had measles, and at fourteen he had chicken-pox. Did he ever have scarlet fever?

STUDENT: No. There is no history of it.

DR. BARKER: When he was eighteen he had a Neisser infection which lasted two months; during this time he was treated three times a week in the Johns Hopkins Dispensary, with complete relief. There has been no recurrence. He has now been married three years and has two children living and well. He works hard, and his work is of a kind that exposes him to wet, wind, and weather. Last autumn he was occupied in one of the training camps where he stayed until January 1st. During this time he was much exposed and caught a cold that developed into pneumonia, causing an illness that lasted altogether about four weeks. The first week that he was ill with pneumonia he spent in his own home. Then he was taken to the Mercy Hospital, where the crisis occurred on the eighth day, twenty-four hours after his admission. No complications occurred and he left the hospital at the end of three weeks.

The patient's habits are good. He uses neither alcohol nor tobacco. An interesting point in the case is that he says he has always disliked salt in his food. This is lucky for him, because for the present, at any rate, he must take as little salt as possible.

The history of the onset of symptoms connected with the present illness is not very definite. He thinks his trouble began about March 1, 1917, that is, about fourteen months ago. At that time he noticed some swelling of his ankles when he took off his shoes at night; this swelling would be gone by morning. He also noticed that when he drank water freely he voided urine very quickly and in large amounts. (To patient): Are you quite sure your feet were swollen as long ago as a year?

PATIENT: Yes.

DR. BARKER: When you pressed your finger upon the skin, like this, did it leave a dent?

PATIENT: No.

DR. BARKER: How did you know the ankles were swollen?

PATIENT: I knew by my shoes being too tight.

DR. BARKER: Was your face swollen then?

PATIENT: No.

DR. BARKER: How much do you usually weigh?

PATIENT: 180 to 190 pounds.

DR. BARKER: And how tall are you?

PATIENT: I am 6 feet, 1 inch.

DR. BARKER: If he is 6 feet, 1 inch in height, 180 pounds would be about his ideal weight. When he came into the hospital he weighed 212 pounds, but a great deal of that was due to water accumulated in his tissues and much of this has disappeared under appropriate treatment.

This is an interesting history. The patient's condition after March of last year was apparently stationary until last autumn and winter, when he was in the training camp. All that he noticed wrong at that time was the slight swelling of the ankles at the end of the day and the polyuria. When in January he was at the Mercy Hospital, after his pneumonia, the edema disappeared and urination seemed to be normal. He was in the hospital for three weeks, and for a week after he left he thought he was quite well. Then his feet and legs began to swell again at night and the swelling did not subside by morning as it had done previously. At this time not only

were his lower extremities swollen but also his face, thighs, upper extremities, abdomen, and external genitals. He noticed, too, that he passed a great deal of urine on first getting up in the morning, but during the day the amount voided was very small, and had a disagreeable odor. He consulted a physician in regard to this point, who prescribed compound jalap powder to be taken every morning, and told the patient to drink 2 quarts of milk every day. At the end of two weeks the edema began to clear up. The patient then began taking large quantities of salt on his own initiative (though he greatly dislikes it), thinking that it would occasion thirst and that the increased amount of water that he drank to relieve the thirst would assist in removing the fluid from his tissues. This little experiment on the patient's part is quite interesting. His idea was that he could induce an increased output of water by increased ingestion of it, and in order to achieve that end he induced thirst on the same principle that governs the consumption of pretzels in beer saloons by forcing himself to take large amounts of sodium chlorid. After he instituted this practice he became weaker and, to his surprise, though not to ours, the edema, instead of lessening, increased. About this time he began to have pain also in his left lower extremity, especially at the hip, the knee, and the ankle. No other disturbances of any kind were observed. His appetite was good and his bowels were regular.

Physical examination, made three weeks ago on admission here (in the middle of April), showed a tall, well-developed young man lying in bed, free at the moment from pain and discomfort. His skin was pallid and there was outspoken general anasarca. His tonsils were enlarged, especially on the right side, but they were not hyperemic. There was some little tremor of the tongue and it was slightly coated. The lymph-glands at the angle of the jaw were palpable on both sides. Examination of the lungs and pleuræ showed slight dulness over both bases, especially marked on the right side. The breath sounds were a little distant at the bases behind, but the voice sounds were clear over the entire lung areas, and there were no râles to be heard. In this connection we must bear in mind that the patient has general anasarca, and we must not forget that he has recently had double pneumonia. We got the details of his illness this morning from the house physician at the Mercy Hospital. When he left there the consolidation had cleared up and there were

no complications or sequels of the pneumonia as far as could be ascertained.

Examination of the heart on admission showed no murmurs or other abnormalities. How about the blood-pressure?

STUDENT: I should think it was rather high.

DR. BARKER: What would you say was normal for a man twenty-two years old?

STUDENT: About 125 systolic, and 70 diastolic.

DR. BARKER: Yes; 115 to 130 systolic would be normal. We would hardly call 130 high for the systolic pressure at twenty-two, but 140 is distinctly so. The diastolic pressure also is above normal for a young man.

There is still, as you see, considerable general edema. There is a little fluid in both pleural cavities and also some in the peritoneal cavity. The liver is palpable one to two fingerbreadths below the costal margin. No tenderness has been noted. On percussion of the abdomen there is some movable dullness due to the presence of fluid in the flanks. Undoubtedly there is a good deal of fluid, though I do not get a fluctuation wave. The genitalia are very edematous. In general anasarca they usually show considerable swelling. Sometimes it is impossible to retract the prepuce. You can see how markedly the thighs and legs are swollen and how deep the pitting is upon pressure. I can also see the imprint of the bell of the stethoscope upon his chest wall where I applied it. Even the upper extremities pit a little on pressure. The patient says that the edema has been even more marked, however, than it is at present. Notice the pallid, pasty look of the face. It is not as marked as it was a short time ago, but it is still quite striking. In general, the puffy, pale, pasty look of the face that accompanies the condition from which this man suffers is so marked that any physician observing it as he walks down a ward thinks at once of the existence of renal disease of a particular type. How about the patient's reflexes?

STUDENT: They are normal.

DR. BARKER: How about the eye-grounds?

STUDENT: They are normal too.

DR. BARKER: So much for the physical examination in general. In this hospital this patient's temperature has varied between 94° and 100° F., though it has usually been a little subnormal (about 97° F.); the pulse-rate has been between 60 and 90, more often the

former, and the respiratory rate 16 to 26, with a vital capacity of 20 to 30. Now for the laboratory tests.

STUDENT: The urinary output measured only 500 c.c. for the first twenty-four hours that the patient was in the hospital.

DR. BARKER: At that time he passed typical smoky urine, but the urine has become much clearer since. The specimen now being passed around is, as you will see, only slightly smoky. Smoky urine means what?

STUDENT: The presence of casts and albumin.

DR. BARKER: You can have casts and albumin without the urine being smoky. But the smoky appearance is very characteristic of something else; what is it?

STUDENT: The presence of blood in the urine.

DR. BARKER: Yes; hematuria. The patient's urine contains both red and white blood-corpuscles, and the guaiac test is positive. The reaction is acid and the specific gravity 1021. The albumin present is "quadruple plus," and the specimens contain both hyaline and granular casts. This patient, therefore, has oliguria, albuminuria, cylindruria, and hematuria. How about the blood examination?

STUDENT: Examination of the blood, made the day after admission, showed:

Red blood-cells.....	3,060,000
White blood-cells.....	10,000
Hb.....	55 per cent.

The differential count was:

P. M. N.....	56.3	per cent.
P. M. E.....	4.4	"
P. M. B.....	0.3	"
Lymphocytes.....	23	"
L. mononuclears.....	11	"
Trans.....	4.3	"

DR. BARKER: Obviously, there was a marked secondary anemia. Would you expect the color-index to be low or high in such a condition?

STUDENT: Low.

DR. BARKER: Yes; rather low—the opposite of what we observe in the primary or hemolytic anemias. On one count there was a slight leukocytosis, but it has not been observed since. This man's

blood presents a picture of secondary anemia characterized by diminution of hemoglobin and of red blood-corpuscles, and a low color-index. The differential count shows 4 per cent. of eosinophils. That is rather a high, though not a very high, percentage. It might be worth while to hunt for parasites.

STUDENT: It has been done, but none were found.

DR. BARKER: Have the contents of the stomach been examined?

STUDENT: No.

DR. BARKER: How about the sputum?

STUDENT: No examination has been made. He has no cough now, and no sputum has been obtained.

DR. BARKER: How about the Wassermann test?

STUDENT: It was negative.

DR. BARKER: I suppose the patient has been too ill thus far for any x-ray examinations to be made?

STUDENT: Yes.

DR. BARKER: How about his teeth?

STUDENT: They are in excellent condition.

DR. BARKER: Then we cannot ascribe the renal disease to dental infection.

I notice that this man's tonsils are enlarged, though they are not injected. The glands that drain the tonsils are enlarged. Tonsillitis is a common precursor of glomerular nephritis. He had ringing in both ears while he was at the Mercy Hospital; he may have had a slight middle-ear catarrh then, and this history should make us look for infected lymphoid tissue in the nasopharynx. The only other history of infection in his case is the Neisser infection, four years ago, and the recent pneumonia. Is there any prostatitis now?

STUDENT: No; there is nothing abnormal about the genitalia except the edema.

DR. BARKER: The urinary findings point to the kidneys rather than to the bladder or to the urethra. Was the patient put upon a renal test diet?

STUDENT: Yes. He was tested with Dr. Mosenthal's modification of Schlayer's renal test diet. This contains a good deal of protein, and means, if eaten, a considerable intake of nitrogen. Here on the blackboard are the results of the test.

URINE AFTER RENAL TEST DIET

Hours.	C.c.	Specific gravity.	NaCl.		Nitrogen.		Albu- min.
			Per cent.	Grams.	Per cent.	Grams.	
8-10.....	58	16					
10-12.....	51	16					
12- 2.....	51	20					
2- 4.....	70	19					
4- 6.....	82	17					
6- 8.....	104	15					
Total day (8 to 8).....	416	..	.36	1.50	.73	3.04	16.0
Total night (8 to 8).....	330	15	.10	.33	.76	2.51	10.0
Total output (24 hours)...	746	1.83	...	5.55	
Total intake (24 hours)...	1760	2.10	..	13.40	
Balance.....	+1014	+ .27	...	+7.85	

Impression: Moderate oliguria with slight fixation of specific gravity, and retention of chlorids and of nitrogen.

DR. BARKER: The output of salt is definitely diminished in this patient's urine. How much salt does a person take, ordinarily, in twenty-four hours? How much, for example, do you think you take in that space of time?

STUDENT: I should think 4 or 5 grams.

DR. BARKER: That is rather a slender estimate. Most people ingest much more than that. This man, on his test diet, took in only 2.10 grams, and he gave out only 1.73 grams. That means, of course, that despite a very small intake he gave out less than he took in. Why was that?

STUDENT: I don't know.

DR. BARKER: If you took in 2.10 grams do you think you could give out as much?

STUDENT: I think so.

DR. BARKER: I hope so, I am sure, for your own sake. But patients who have general anasarca, together with oliguria, albuminuria, cylindruria, and hematuria, are not able to excrete much sodium chlorid. A condition of reduced chlorid content of the urine is known as *hypochloruria*. This man, then, has a *hypochloruria*. Though he took in only 2.10 grams of sodium chlorid he could give out only

1.73 grams. Normally, when the blood-plasma contains as much as 5.62 grams per liter of sodium chlorid, the kidneys begin to excrete it in the urine, so as to maintain the plasma concentration at about this level. In renal disease with edema the concentration of the blood-plasma in chlorids is higher than normal, even though salt and fluid with it goes out into the subcutaneous tissues. The patient, though hypochloruric, becomes hyperchloremic.

There was also a slight deficiency in the nitrogen output. A man should give out in his excretions as much nitrogen as he takes in. Most of the nitrogen taken in as food is excreted as urea-nitrogen in the urine. On an ordinary mixed diet the amount of total nitrogen excreted in the urine by a normal person varies between 10 and 16 grams a day. But this man, though he took in 13.40 grams of nitrogen, gave out in the urine only 5.55 grams. In other words, he has *hypazoturia*—his kidneys are not eliminating the nitrogenous end-products of metabolism as they ought to do.

In addition, the reports on the urine of this patient indicate that there is a slight *hyposthenuria*—in other words, a tendency for the specific gravity of the urine to be maintained at a fixed level. The patient has then not only an oliguric, albuminuric, cylindruric, and hematuric renal disease but also a hypochloruric, hypazoturic, and hyposthenuric renal disease. The patient, I observe, is beginning to look as if he wondered whether there was any chance at all for a man with an ailment decorated with such long names. But these terms are valuable “shorthand” expressions for the conditions they designate.

When you have elicited all these various pathological-physiological facts about a case of renal disturbance you are in a position to draw some deductions regarding the pathological-histological changes that have been, and still are, taking place in the patient's kidneys. To begin with, we are sure that the patient has a *renal disease*, or to use the technical term for that, a *nephropathy*. Renal disease and nephropathy are terms that mean the same thing. In the word “nephropathy” the prefix means the “kidney” and the suffix means “disease.” This term designates only renal disease; it says nothing of the character, or nature, or cause of the renal disease. In the same way, the terms “cardiopathy,” “gastropathy,” “encephalopathy” (and so on for all the organs or sets of organs in the body) are general terms that signify merely disease of the heart, of the stomach, of the

brain, etc. All you have to do is to use the name of the organ affected for the first part of the term you require and add the suffix meaning disease. Then you can subsequently indicate more precisely the time relations, character, nature, and etiology of the disease by using qualifying adjectives. Thus, as to time relations we may have an "acute," a "subacute," or a "chronic" nephropathy; as to pathological-histological character we may have, on the one hand, a nephropathy of "inflammatory," of "circulatory," or of "degenerative" nature, and, on the other; according to the site or distribution of the lesions, an "interstitial" or a "parenchymatous" nephropathy, a "glomerular," a "tubular," or a "glomerulotubular" nephropathy; or, again, a "focal" or a "diffuse" nephropathy. On the etiological side we may have a "traumatic," a "toxic," a "circulatory," a "neoplastic," or an "infectious" nephropathy.

The term "nephritis" means an inflammation of the kidneys; in other words, it is a brief synonym for "inflammatory nephropathy." The term "nephritis" is often used as though it were synonymous with "nephropathy," *i. e.*, with renal disease in general, and that is a pity, for it should be restricted to inflammation of the kidneys, as the suffix implies. Again, the term "nephrosis" rightly used as a brief synonym for "toxic-degenerative disease of the renal tubules," should not be confounded with "nephritis." The same reasoning leads us to use the term "arteriolar nephropathy" for the renal disease that is associated with sclerosis of the small organ arterioles and arterial hypertension. This is, in large part, a renal atrophy with contraction of the kidney due to the arteriolar disease; it is, in its late stages, the "small red granular kidney" or the "genuine contracted kidney" of the pathological anatomists. It is often erroneously spoken of in the text-books and by clinicians as "chronic nephritis" or "chronic interstitial nephritis," and it is only comparatively recently that it has been sharply differentiated from "true chronic diffuse nephritis" (or contracted kidney due to true chronic inflammation of the organ). I cannot emphasize too strongly to you the importance of cultivating a feeling for the true meaning of the words that you use in describing disease, for inaccuracy in the use of terms means, necessarily, inaccuracy or confusion in thought. Never coin a new word unless the growth of knowledge demands it, but be sure never to use a word that means one thing to designate another different thing!

After this terminological digression let us return to the condition in the patient before us. In the first place, do you think that this nephropathy has been present since birth or that it has been acquired since birth?

STUDENT: He has suffered from marked symptoms referable to the kidneys for about four months and has had slight symptoms for a little more than a year. He was not born with it.

DR. BARKER: Yes; it is an "acquired" nephropathy, not a "congenital" nephropathy. The bilateral polycystic kidney is a congenital disease, but the condition of our patient's kidneys is not congenital.

Next, let me ask you, What structures in this man's kidneys have undergone pathological change?

STUDENT: I think the glomeruli are involved in the pathological process.

DR. BARKER: Why do you think so?

STUDENT: Because of the blood in the urine, giving it its smoky appearance, and the presence also of blood-casts.

DR. BARKER: Yes; those facts, and others that you might adduce, indicate that the blood in the urine of this patient is of renal origin rather than of ureteral, vesical, or urethral origin. But even when the blood is of renal origin, need it necessarily have come from the glomeruli?

STUDENT: In this case I think the blood is of glomerular origin.

DR. BARKER: I think so too; though you must remember that even when hematuria is associated with cylindruria, the blood may not owe its appearance to glomerular disease, for in some instances a disease of the pelvis of the kidney (such as nephrolithiasis or tuberculosis) causing hemorrhage may be associated with a true renal disease causing cylindruria, and in others (*e. g.*, renal infarction) the bleeding may be from renal vessels other than those of the glomeruli.

Do you think that we are dealing here with a pure glomerular disease or are the renal tubules also involved in the pathological process?

STUDENT: The patient cannot eliminate salt properly and salt excretion is a tubular function.

DR. BARKER: Yes; the presence of the general anasarca is partly due to the faulty elimination of chlorids with chlorid retention. Moreover, the studies made with the aid of the renal test diet show

that this man's kidneys are not capable at present of excreting more than small quantities of chlorids in the twenty-four hours.

Has Rowntree and Geraghty's functional renal test with phenol-sulphonephthalein yet been made?

STUDENT: Yes. The output of phthalein was low; he excreted only 12 per cent. during the first hour and only 10 per cent. more during the second hour, making only 22 per cent. in all, instead of the normal 60 to 70 per cent.

DR. BARKER: This faulty elimination of the phthalein points to tubular involvement also. We can be sure, I think, that *this* patient has then a renal disease in which both glomeruli and tubules are diseased; in other words, he suffers from a *glomerulotubular nephropathy*.

Do you think that the process is diffuse or merely focal?

STUDENT: I think it is a diffuse process.

DR. BARKER: Why?

STUDENT: Because of the diminished quantity of urine, the reduced capacity to excrete chlorids, phthalein, and nitrogenous substances, the tendency to fixation of the specific gravity, and the increase in blood-pressure.

DR. BARKER: Yes. You have summarized very well indeed the reasons for believing that we deal with a diffuse rather than a focal process. The oliguria, the hypochloruria, the hypazoturia, the hypostenuria, and the arterial hypertension all point to a degree of renal insufficiency that would be scarcely compatible with merely focal involvement. Indeed, it is surprising to find how well renal functions can be maintained even when an extensive focal nephropathy exists; the uninvolved parts of the kidneys engage in compensatory overwork in such cases. But here there is definite renal insufficiency. So many glomeruli and tubules are involved that chlorids, urea, and other substances cannot be excreted in normal amounts. The process, whatever it is, must be a rather diffuse one. We have to deal with a *diffuse glomerulotubular nephropathy*.

Do you think that we are dealing here with a true inflammation, or merely with a disturbance of the circulation (as in chronic passive congestion), or simply a degenerative process (or nephrosis).

STUDENT: The process must be inflammatory. The glomerular involvement rules out a simple degenerative nephropathy or nephrosis, and there is no marked myocardial insufficiency or other cause of stasis-nephropathy.

DR. BARKER: I agree with you. This man has a *diffuse, inflammatory, glomerulotubular nephropathy*. We may here quite justifiably use a shorter term and say that he has a *true nephritis*, and, if you like, you may say that he has a predominantly *parenchymatous nephritis*, though I do not like the latter term, since some would exclude the glomerular tuft from the parenchyma of the kidney, and the glomerular tuft as well as the uriniferous tubules are certainly diseased in this patient.

Do you think that the nephritis in this patient is an acute or a chronic process?

STUDENT: Acute or subacute, because of the presence of hematuria.

DR. BARKER: The hematuria of itself does not necessarily indicate an acute process, though it is common in acute nephritis and in acute exacerbations in the course of a chronic nephritis. In deciding regarding the acuteness or the chronicity of the renal disease in the patient before us we must be guided not so much, perhaps, by our present findings (though these must be duly considered) as by the history of the onset, and the course of the disease up to the present time. Whatever the condition of things may be, we know that the marked symptoms have developed since the pneumonia period of about four weeks ago. The only question is whether the patient had some renal disease in March, 1917, that is, fourteen months ago, when he first noticed the tightness of his shoes, and if so, what form of renal disease existed then. Our diagnosis of his present condition would differ, according as we understand the renal condition to have developed entirely since the attack of pneumonia or whether we believe that some form of renal disease also antedated the pneumonia. In the former case the condition might be a subacute glomerulotubular nephritis; in the latter case we should have to think of an exacerbation in the course of a chronic glomerulotubular nephritis. The prognosis in the former would be better than in the latter.

We have, therefore, to try to differentiate between these two conditions. The history is somewhat ambiguous. Let us go over carefully the points likely to help us in the differential diagnosis. The attack of pneumonia in 1918 could, of course, be the starting-point either of an acute diffuse glomerulotubular nephritis in healthy kidneys or of an exacerbation of a chronic nephritis. The history of slight edema, first observed nearly a year previous to the attack

of pneumonia and succeeded by polyuria, strongly suggests the insidious onset so often observable in subacute and chronic forms of glomerulotubular nephritis (the so-called Rose-Bradford type of chronic parenchymatous nephritis) in the course of which the attack of pneumonia has been responsible for a sudden exacerbation. We must remember, however, that edema in moderate amount, coming on at night in the case of a heavy man who is on his feet all day, does not necessarily mean the presence of nephritis. He might have had an obesity-cardiopathy with slight myocardial insufficiency. When we telephoned the Mercy Hospital for details of his illness there, we were told that when the patient was admitted there was considerable albuminuria. But he had then had pneumonia for a week, and it is quite possible that an acute nephropathy had developed in that time as a complication of the pneumonia. On the other hand, if we accept our second possibility, we must assume that the pneumonia caused a marked exacerbation of a chronic nephritis already existent.

Another point in favor of our having to do with an exacerbation of an already existing chronic process is that hypertension, with a tendency to fixation of the specific gravity of the urine such as we have here, is more likely to occur in a condition that has existed for some time. The fixation of the specific gravity, however, is not very marked. During a renal test diet carried on for twelve hours the specific gravity of the urine varied from 1015 to 1020. Now that is not so great a variation as we should expect in a person with normal kidneys; on the other hand, the fixation is not so great as we often see in severe cases of renal insufficiency. It is interesting that the patient's blood-pressure has fallen since he has been under treatment in the hospital. It is now 115 systolic and 80 diastolic, almost normal for a man of his age. The persistence of the hypochloruria, of the hypazoturia, and of the hematuria, however, indicate that a diffuse glomerulotubular disease is still existent. The data, as a whole, seem to me to indicate an acute exacerbation of a subacute or a chronic nephritis. The fact that the patient is suffering from secondary anemia is an additional point in favor of it, for anemia is very common in diffuse nephritis of the subacute or chronic variety. The pallor, pastiness, and edema are striking features in this patient. As I said before, a physician can often pick out patients suffering from chronic glomerulotubular nephritis as he walks through a hospital ward.

We can be fairly certain that at the present time the patient has a diffuse, inflammatory nephropathy, with edema, ascites, hydrothorax, oliguria, hypochloruria, slight hypazoturia, albuminuria, cylindruria, slight hematuria, slight hyposthenuria, and slight arterial hypertension. In addition to his nephropathy he has hypertrophied tonsils, secondary anemia, slight obesity, and probably a slight arthritis in the joints of the left lower extremities.

A word as to the *etiology* of the renal disease in this man. Many cases of diffuse glomerulotubular nephritis are due to streptococcus infection. Streptococcal angina, streptococcal pneumonia, streptococcal cellulitis, or streptococcal infection at any site can be the starting point of a diffuse glomerulotubular nephritis. It may be that local infections due to pneumococci and to other pyogenic bacteria may also be the primary cause of subacute or chronic glomerulotubular nephritis. Whether the renal disease develops as the result of actual metastatic infection of the kidneys or is due to the action of absorbed toxins from the primary local infections is a mooted point, though the evidence favors, I think, the view that actual metastatic infection is sometimes responsible.

In therapy, therefore, one of the first things to be done in a case of this kind is to hunt for primary foci of infection, as we do in cases of infectious polyarthritis, and if we find them, to try to get rid of the foci. In young persons, infected adenoids and infected palatine tonsils are the most common sources of metastatic streptococcal infections. Sometimes infected paranasal sinuses, infected teeth, or an infected pleural cavity may be incriminated. In the etiological inquiry we examine all possible portals of entry for streptococci or other bacteria in the hope that we may locate a primary focus of infection, removal of which will stop further metastases or further intoxication.

At the same time we do all that we can to protect the kidneys by diminishing the amount of work that the injured organs have to do. You have learned that this man, owing to the renal insufficiency resulting from his glomerulotubular disease, retains water, salt, and nitrogen (urea) in his blood and tissues. Formerly in such cases we pushed the water in our treatment with the idea of "washing out waste products," and it is an interesting feature of this case that the patient tried to pursue this mode of treatment on his own initiative without benefit. Now we do not push water beyond a

certain point, for he is already "water-logged." Much more important than free water drinking is the reduction of chlorids and of proteins in the patient's diet. His intake of liquids should be limited to $1\frac{1}{2}$ liters or less in the twenty-four hours and his salt intake should be limited, for a time at least, to the smallest possible amount. His intake of protein should be limited to 60 grams in the twenty-four hours. We may be more liberal, however, with the intake of easily digestible carbohydrate. It should be kept in mind, however, that he has been obese and that it will not hurt him to live on a low caloric diet for a time. Among foods that contain very little sodium chlorid I may mention milk, unsalted butter, eggs, cereals, vegetables, and fruits. In constructing salt-poor and protein-poor diets you will be much helped by consulting the excellent book on diet by Friedenwald and Ruhräh, and the convenient article by H. Strauss. To help combat the anemia iron in some form should be administered. I should avoid the use of arsenic, for it might be an additional irritant to the kidneys. (*Patient removed.*)

If this man has, as I fear, chronic diffuse glomerulotubular nephritis the outlook is very grave. Such patients rarely live over a year or two. The most we can hope for is to secure a subsidence of the inflammatory process and the gradual development of secondary contraction of the kidney. Very few patients reach this stage. The majority of them die from uremia, from pulmonary edema, or from some intercurrent terminal infection while the kidneys are still large. The lesson to carry away from the clinic is: Strive to prevent this form of nephropathy by prevention of streptococcal infections, and by prompt and careful treatment of such infections when they occur.

Further History of the Case.—The patient was put for a time upon the Karell milk diet and upon sweat baths, to which treatment he responded very well as far as the edema was concerned. No other improvement took place, however, except a slight loss in weight (8 pounds) until he had been in the hospital about six weeks. After that he improved, though very slowly, and about a month later he was given a good maintenance diet.

The note made by the resident physician, Dr. Bloomfield, on July 12th, when the patient had been in the hospital just three months, is as follows: "The disease has existed for at least four or five months. Some symptoms are improved as evidenced by loss of edema, but

the essential process still continues. The urine still continues to contain large amounts of albumin and many red blood-corpuscles. The diastolic blood-pressure is still a little high. The patient looks pallid and pasty. There has obviously been loss of weight. Slight edema of dependent parts is still present as well as quite a marked collection of fluid in the abdomen.

“Impression.—There is a chronic nephritis, probably of the hemorrhagic type with edema. Prognosis bad.”

The patient was discharged as “improved” on July 25th, three and a half months after admission. There was still slight edema of the ankles, but the face was no longer pasty. There had been, however, no appreciable diminution of the ascites for several weeks before discharge.

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XVII. THE PREGNANCY KIDNEY

CONVALESCENCE FROM A SEVERE PREGNANCY NEPHROPATHY AND PREGNANCY MYOCARDIOPATHY. RAPID IMPROVEMENT UNDER APPROPRIATE THERAPY AFTER THE DELIVERY OF TWINS.

We have the opportunity this morning of studying a patient who suffered during pregnancy (1) from a severe pregnancy nephropathy with renal insufficiency, and (2) from a severe myocardopathy with marked circulatory insufficiency. She had a rather stormy time after the delivery of twins, but is now making an excellent recovery. The case presents certain features of unusual interest which, during the hour, I hope that we shall find time to discuss. The clinical clerk, Miss Putnam, will first give us a summary of the history of the patient and of her condition on admission to the hospital.

STUDENT: This patient, Olivia G., a colored housewife, aged twenty-three, was admitted to the obstetrical service (Prof. J. Whitridge Williams) of the Johns Hopkins Hospital on December 2, 1920, complaining of marked breathlessness and of general dropsy. She was at full term and was delivered of twins on the following day.

The family history presents nothing of interest, except that her father was said to have suffered from kidney trouble, one brother from heart trouble, and one sister from asthma.

Aside from measles and mumps in childhood and an attack of influenza in 1918, the patient stated that her own general health had been good. Some four years ago she married. She has one child eighteen months old, the present pregnancy being her second.

The patient has had from time to time trouble with her teeth

and also with her nose and throat. About six years ago there was some swelling of her ankles, and the physician who attended her at the time stated that she had "kidney trouble." With her first pregnancy, too, there was some edema.

The patient states that she has occasionally suffered from night-sweats, and that during the past three years there has been considerable palpitation of the heart. She has risen two or three times at night to pass urine for many years. The urine has always been abundant until the past illness, and she states that it has looked "natural." She asserts that she has always been nervous and high strung.

Her habits have been good except for the drinking of coffee and tea. She drinks six cups of each of these beverages daily.

When asked about the *onset of her present illness*, she informed us that it began seven and a half months ago when she had been pregnant about one and a half months. The first symptom was that of breathlessness, noticeable especially at night. This shortness of breath increased until she found that she could not lie flat upon her back, but had to sit up in bed. Some two and a half months before admission she noticed that her ankles and feet began to swell and that her face was puffy. This edema seems to have been more marked in the morning and to have passed off largely toward noon. Later, however, the amount of edema increased until the whole body became swollen. Through the pregnancy the patient has suffered, too, from cough, and has occasionally expectorated blood-tinged sputum. The pulse has been rapid and she has suffered from palpitation on exertion. She has had headaches in the frontal region. These headaches, she states, are worse at 2 A. M. She can sometimes relieve them by rising and walking about. At no time has there been any nausea or vomiting.

The *physical examination* on admission may be summarized as follows: Marked orthopnea and tachypnea; marked tachycardia, pulse-rate 150; temperature normal, though followed by fever later (see chart); respiration rate, 40; hacking cough; marked general anasarca.

Eye-grounds normal, except for a slight distention of the veins and slight hyperemia of the optic papillæ; no albuminuric retinitis; no retinal hemorrhages. In the mouth some pyorrhea, many snags of teeth, and obvious dental caries. Tonsils not large. No struma.

Lungs negative except for many moist râles in both backs (edema). Heart markedly enlarged; apex-beat in the sixth left interspace

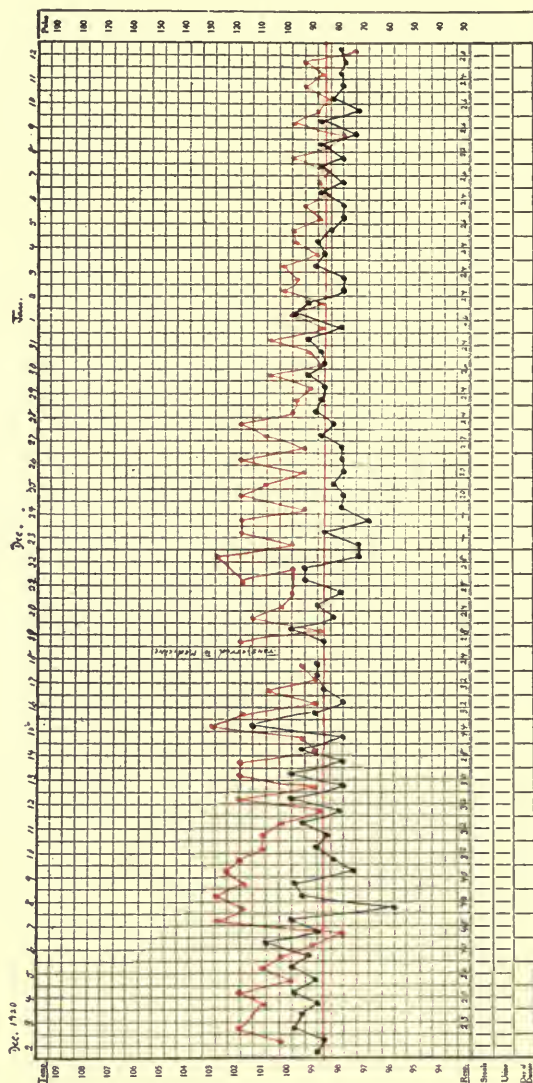


Fig. 24.—Red = pulse. Black = temperature. Temperature chart and pulse curve of patient suffering from pregnancy nephropathy.

about 12 cm. to the left of the middle line. Relative cardiac dulness $3\frac{1}{2}$ cm. to the right and 13 cm. to the left. Heart rate 150 per minute;

no murmurs; marked gallop rhythm (presystolic at first; proto-diastolic later). Blood-pressure, 180 systolic, 110 diastolic. Abdomen distended by pregnant uterus, the fundus reaching to within four fingerbreadths of the xyphoid. Motility, sensation, and reflexes normal.

DR. BARKER: What did the examination of the urine show at this time?

STUDENT: The urine was acid; specific gravity 1030; 6 grams of albumin per liter, and many hyaline and granular casts on microscopic examination. No red blood-corpuscles were present in a catheterized specimen of the urine, however.

DR. BARKER: I understand that some chemical tests of the blood were made immediately after her admission.

STUDENT: Yes. The results were as follows: Blood urea nitrogen, 10.2 mg. per 100 c.c.; blood-carbon dioxide, 43.5; blood-sugar, 0.067; serum chlorid, 6.38 grams per liter.

DR. BARKER: Obviously, this patient suffered from a nephropathy and also from a cardiopathy. It is interesting that the first symptom complained of was breathlessness at the end of the first six weeks of pregnancy. The edema apparently developed later.

STUDENT: The patient was placed upon a restricted diet, and the intake of fluids was limited to 400 c.c. at first. She was given two doses of strophanthin hypodermically, 0.65 mg. at each dose.

On the following day, that is, on December 3d, the patient gave birth to twins, being in labor sixteen and a half hours. Instruments were used for the second child, but no anesthesia was required. The blood-pressure at this time was 200 systolic, 140 diastolic.

DR. BARKER: Will you please tell the class the progress of the case after delivery?

STUDENT: On December 4th, the day after delivery, the patient was in much better condition. The edema had become less and the breathing was easier.

Another examination of the blood was made on December 6th, when the blood urea nitrogen was 17.4 grams per 100 c.c., and the serum chlorid 6.55 grams per liter.

On the following day (December 7th) the patient suffered from two attacks of pain in the precordial region and in the left flank. With these attacks the orthopnea became more marked, the respiration being very rapid and shallow. Physical examination on this

date revealed a small accumulation of fluid in the right pleural cavity, some ascitic fluid in the abdomen, and generalized edema. The blood-pressure was 185 systolic, 140 diastolic.

The patient continued to be very ill. A week later (December 14th) the pulse was still rapid, 120 to the minute, though the heart-beat was regular. The apex-beat could be localized in the anterior axillary line. There was marked gallop rhythm and moist râles could be heard throughout both lungs (pulmonary edema). The patient received more strophanthin. The blood-pressure at this time was 195 systolic, 140 diastolic.

On December 18, 1920 the patient was transferred to the medical service. At this time, on palpation at the wrist, a definite pulsus alternans was observable; on applying the manometer cuff it was found that every other beat came through at 180 mm. mercury pressure, whereas all the beats came through at 168 mm.

An *electrocardiogram* made on this day revealed a normal conduction mechanism, but illustrated the effect of strophanthin administration. Blood-pressure now 175 systolic, 135 diastolic.

The patient looked pale, and the examination of the *blood* gave the following results: Red blood-corpuscles, 3,040,000; white blood-corpuscles, 14,000; hemoglobin, 52 per cent. Differential count showed 84 per cent. polymorphonuclear neutrophils, 14 per cent small mononuclears, and 2 per cent. large mononuclears and transitionals.

The *urine* at this time had a specific gravity of 1014, was alkaline, contained still much albumin and a few hyaline and granular casts, but no red blood-corpuscles. The guaiac test for occult blood in the urine was negative. The patient was given digitalis and was kept on a salt-free cardiac diet, which was also made somewhat protein poor.

A *phthalein test* was done on December 20th. The patient excreted 45 per cent. in one hour.

Another *electrocardiogram* was made at this date. The conduction mechanism was still normal; the curves showed left ventricular preponderance.

A *brachial sphygmogram* was also made at this time. It showed that the pulsus alternans continued. The blood-pressure at this date was 176 systolic, 130 diastolic (Figs. 25, 26).

On December 22d the patient began to show marked polyuria, and the edema very quickly subsided. The behavior of the blood-

pressure and the relation of fluid intake to fluid output are well shown in Fig. 27. By December 25th the blood-pressure had fallen to 138 systolic, 100 diastolic.

The patient continued to improve, and on New Year's Day the gallop rhythm and the evidences of pulsus alternans had entirely disappeared.

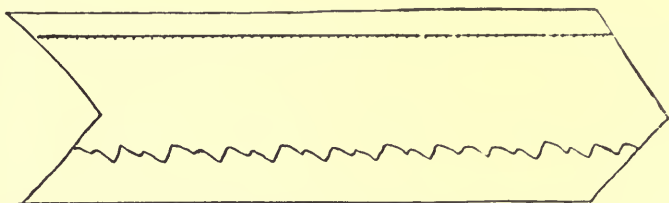


Fig. 25.—Copy of tracing of brachial pulse waves, December 20, 1920. There is apparently a definite pulsus alternans present. The heart rate is approximately 125 per minute, hence the smaller waves are not dicrotic waves. No other arrhythmia.

Another electrocardiogram was made on January 4, 1921 (Fig. 28). It revealed a normal mechanism. The blood-pressure at this time was 122 systolic, 82 diastolic.

The chemical conditions in the blood also steadily improved. On January 5, 1921 the blood urea nitrogen was 15.4 grams per 100 c.c., the blood-carbon dioxid 74.1, the serum chlorid 5.67 grams per liter. The blood-pressure on that day was 120 systolic, 80 diastolic.

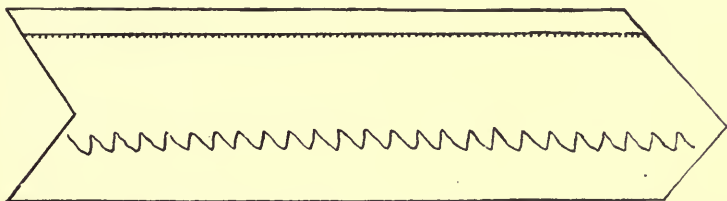


Fig. 26.—Copy of tracing of brachial pulse waves, made in same way as above, January 4, 1921. The pulsus alternans is no longer present. No arrhythmia.

On the next day (January 6th) another phthalein test was done, and it was found that the patient excreted 90 per cent. in two hours, showing a hyperpermeability of the kidney for phthalein.¹ The specific gravity of the urine was 1013. Albumin was present, but in less amount. No casts were seen and no red blood-corpuscles.

¹[See reference to Dr. Walter Baetjer's article on "Hyperpermeability."]

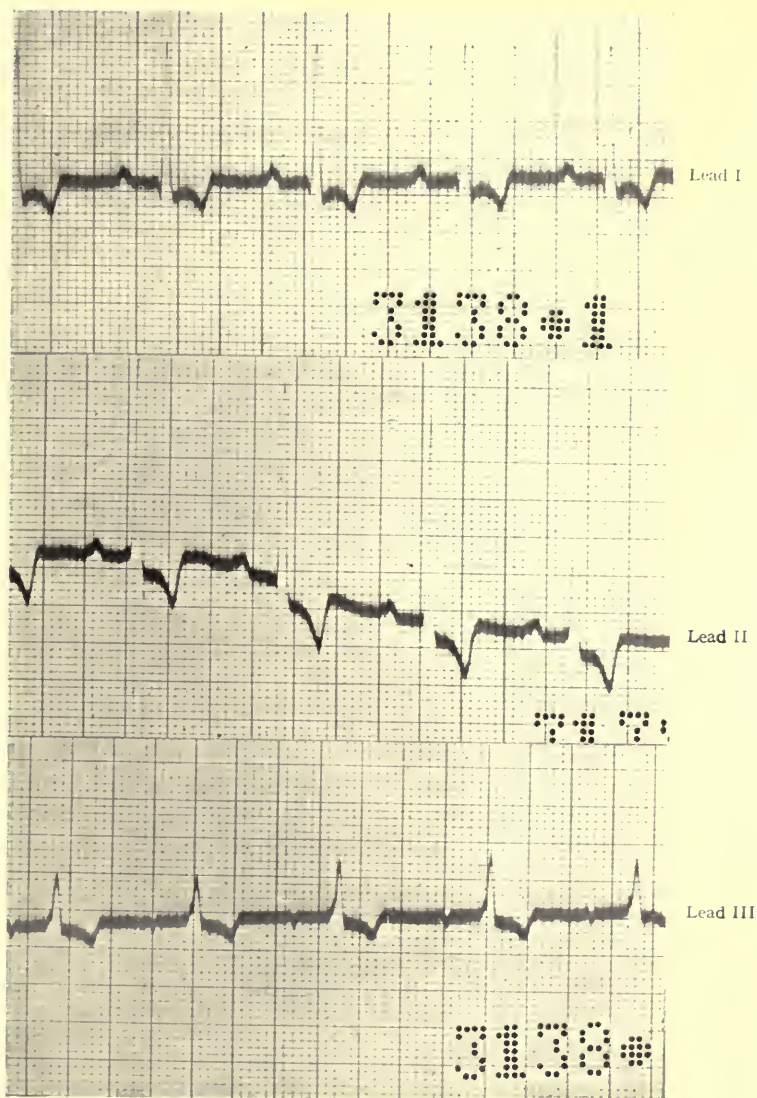


Fig. 28.—Patient with pregnancy nephropathy. Electrocardiographic report, January 4, 1921. Rate 86. Rhythm regular. The P. R. interval measures 0.20 second. Remarks: T_I and T_{II} are negative.

On January 9, 1921 the blood-pressure was 105 systolic, 70 diastolic; in other words, the marked arterial hypertension had entirely disappeared and the patient exhibited a hypotensive state.

On January 11, 1921 still another electrocardiogram was recorded. It showed a normal conduction mechanism, except that the T-wave in all three leads was negative (Fig. 29).

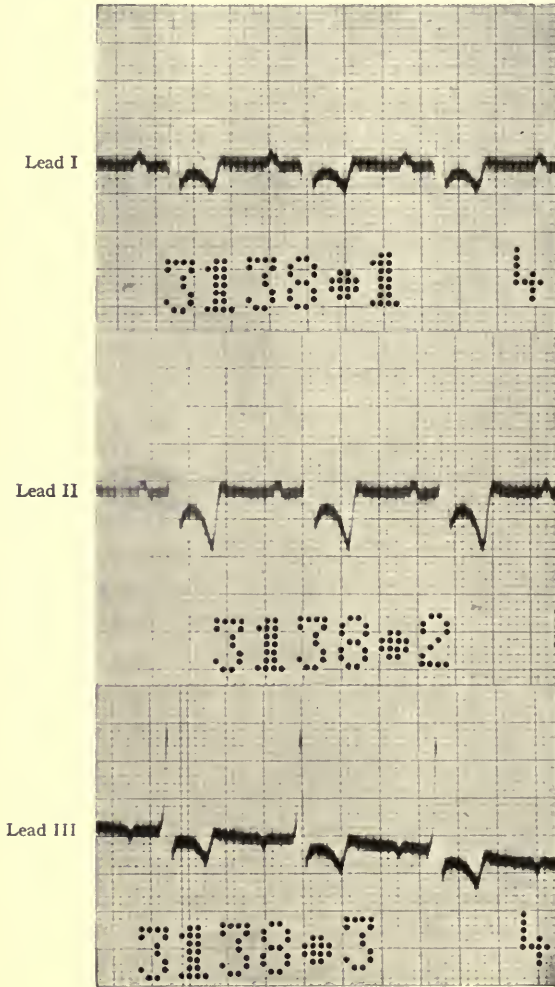


Fig. 29.—Patient with pregnancy nephropathy. Electrocardiographic report, January 11, 1921. Rate 86. Rhythm regular. The P. R. interval measures 0.19 second. Remarks: P_{III} is negative. T_I , T_{II} , and T_{III} are negative.

DR. BARKER: That is a remarkably interesting history. When one considers how seriously ill this patient was a couple of weeks ago,

with renal decompensation and marked myocardial insufficiency, it is really surprising to see how well she is today. You see her sitting here, breathing perfectly quietly, and apparently very well. The kidneys are excreting nearly normally and the myocardial insufficiency has practically disappeared along with the arterial hypertension. There is no edema and the blood chemistry is approaching normal. She is still, of course, quite anemic, but with good care during the next month or so she should become very well indeed and the blood will probably rapidly recuperate.

We may now profitably analyze the conditions that have existed in this patient during her pregnancy and during the early puerperium.

To what organs or systems have her symptoms and signs predominantly pointed?

STUDENT: To the urogenital system and the circulatory system.

DR. BARKER: Yes. We have had evidences of marked disease of the kidneys with renal decompensation and evidences of marked circulatory disturbance with dilatation of the heart, myocardial insufficiency, arterial hypertension, and chronic passive congestion with general anasarca.

Let us analyze the renal disturbances first and try to draw some deductions regarding their nature.

Do you think that we have been dealing with an acute process or a chronic process in the kidney?

STUDENT: Mainly with an acute process. Whether or not a slight chronic process had existed over a long period is not certain. The patient stated that six years ago the doctor said she had "kidney trouble" at a time when there was some edema. In her first pregnancy, also, she had slight edema, and probably some renal trouble. Whether or not these former disturbances of the kidneys were entirely recovered from or whether there was a residual chronic process is not certain.

DR. BARKER: In any event, the main renal disturbance here has been of short duration, having developed during the pregnancy and rapidly subsided during the puerperium. We doubtless have mainly to deal with the "kidneys of pregnancy" or the so-called "pregnancy nephropathy."

Let us review the phenomena observed in this single concrete case of pregnancy nephropathy and compare them with the phenomena that we have observed here in other cases and with those that have

been described in the literature as characteristic of the pregnancy nephropathy.

Was the quantity of urine increased or diminished in this patient?

STUDENT: The patient seems to have passed rather a large quantity of urine before her pregnancy, but after the symptoms developed during the pregnancy the amount of urine passed became diminished.

DR. BARKER: Yes, at times there was marked oliguria. We have had to deal with an oliguric nephropathy rather than a polyuric nephropathy, an interesting point when you recall that the blood-pressure has been high. Do you think that this oliguria could have depended upon the chronic passive congestion due to the myocardial insufficiency, or was it due to changes in the kidney other than those of chronic passive congestion?

STUDENT: I think it would be hard to say.

DR. BARKER: Yes, it is somewhat difficult to judge. I am inclined to think that both factors played a part in the oliguria. In other words, in addition to the pregnancy nephropathy proper we have had to deal with a stasis nephropathy also.

Would you comment upon the specific gravity of the urine in this patient?

STUDENT: On the whole, the specific gravity has been high rather than low during the period of observation. At the first examination the specific gravity was 1030; on December 18th it was 1014; on January 6th it was 1013.

DR. BARKER: Those figures permit us to make certain decisions regarding the nephropathy present. In the first place, we can say with certainty that the kidney still had the ability to concentrate the urine passed, and in the second place, we can say that there was no definite tendency to fixation of the specific gravity, or in other words, the kidney is not compelled to excrete a urine of constant holding in solids. We have not had to deal, then, with a hypostenuric nephropathy. The term "hypostenuria" is used, you will recall, to designate the condition in which there is a tendency to fixation of the specific gravity at some level. In diabetes insipidus, for example, the specific gravity is fixed at a very low level, whereas in some of the vascular nephropathies there is a tendency to fixation of the specific gravity at a relatively high level, say 1010 to 1015.

Have albumin and casts been constantly present in the urine during the course of this renal disturbance?

STUDENT: Yes; there was marked albuminuria and cylindruria. In the early period of observation here in the hospital the urine contained 6 grams of albumin per liter and many hyaline and granular casts.

DR. BARKER: We have had to deal then with an albuminuric and cylindruric nephropathy. The presence of albumin in the urine in a nephropathy always indicates, in my opinion, some disturbance of the glomerular function, but albuminuria does not necessarily point to an inflammation of the glomeruli. Very slight disturbances in the functional activity of the glomeruli, and especially of the capsular epithelium, can lead to albuminuria. We meet with albuminuria not only in the nephritides (or inflammations of the kidney) but also in the nephroses (or toxic degenerative states of the kidney) and in the nephropathies of circulatory origin (such as chronic passive congestion and arteriolar sclerosis). We often find albumin in the urine without finding casts, but it is rare to find casts without at least a trace of albumin. Indeed, the casts of hyaline nature are probably due to solidification of the protein solution in the tubules of the kidney through the absorption of water and an increase of acidity. Sometimes a cast has accretions upon it derived from degenerated epithelial cells of the tubules through which the cast passes.

Was there any blood in the urine of this patient at any time?

STUDENT: There has been no blood present in the urine during the patient's stay in the hospital. On repeated microscopic examinations no red blood-corpuscles could be seen in the sediment, and the guaiac test for occult blood was negative.

DR. BARKER: That is a very important observation, for in acute inflammation of the glomerular tufts of the kidney (acute glomerulonephritis) there is nearly always some blood, either macroscopic or microscopic, in the urine. In other words, a glomerulonephritis is, as a rule, a hematuric nephritis. The total absence of blood from the urine in this patient strongly suggests that we are not dealing with a glomerulonephritis, but with some other form of nephropathy. The large amount of albumin present indicates that the glomeruli are diseased, but the disease of the glomerulus is probably either a toxic-degenerative change, or some circulatory change, rather than an inflammatory proliferative change.

In the so-called "glomerulonephrosis" there may be outspoken

albuminuria and cylindruria without hematuria. There is a good deal of evidence that the pregnancy nephropathy is accompanied by toxic-degenerative changes in the capsular epithelium of the glomeruli. In other words, that a glomerulonephrosis is a part of the pregnancy nephropathy. This is not to say that a glomerulonephritis never occurs during pregnancy. Of course, a glomerulonephritis may sometimes occur in the course of a pregnancy, but in that event the urine usually contains blood, either macroscopic or microscopic. But such a glomerulonephritis is very different from the common form of pregnancy kidney. The pregnancy nephropathy proper does not lead to hematuria. Usually there are no red corpuscles in the urine on microscopic examination, or if there are any, there are only a very few. This is a marked distinction between the common form of pregnancy nephropathy and the rarer forms of renal disease occurring in pregnancy (such as true glomerulonephritis).

Have the kidneys in this patient been able to excrete nitrogenous substances in a normal fashion?

STUDENT: There has been no evidence of marked disturbance of nitrogen excretion, at least so far as the chemical tests of the blood indicate. The blood urea nitrogen has varied between 15.4 and 17.4 grams per 100 c.c. of blood.

DR. BARKER: What are the normal figures?

STUDENT: They vary somewhat according to the nitrogen intake, but values of between 10 and 23 grams of urea nitrogen per 100 c.c. of blood are regarded as within normal limits.

DR. BARKER: Yes, those are McLean's figures that you are quoting, and his studies were very carefully made. But urea nitrogen is only one part of the non-protein nitrogen of the blood. What are the other components?

STUDENT: I think it includes ammonia nitrogen, amino-acid nitrogen, and certain other fractions.

DR. BARKER: Yes, you have mentioned the more important components. Another component that is, perhaps, worthy of notice is the indoxyl component, which includes indican, a substance to which considerable attention has been paid in the studies of pregnancy nephropathy.

The total non-protein nitrogen of the blood varies normally, according to McLean and Selling, between 23 and 36 mg. per 100 c.c.

of blood. The concentration of total non-protein nitrogen in normal blood is not constant, but varies within wide limits, corresponding to variations in diet and in amount of fluid ingested.

Was the total non-protein nitrogen of the blood determined in this patient?

STUDENT: I think not. So far as I recall only the urea nitrogen was determined.

DR. BARKER: In normal persons there seems to be a close parallelism between the concentration of urea in the blood and the holding of the blood in total non-protein nitrogen. I am not sure, however, that this parallelism holds in disease, and I think that from the standpoint of research it would be wise, whenever it is possible, to make determinations of the total non-protein nitrogen and of its component fractions. There is some evidence that the amino-acid fraction, the ammonia fraction, and the indoxyl fraction of the total non-protein nitrogen are somewhat increased in the pregnancy nephropathy, though, as a rule, the urea nitrogen is not increased. We know that in the toxemia of pregnancy the liver function is often markedly disturbed, leading to a diminution in the urea nitrogen and an increase in the amino-acid fraction. One observer has asserted that the indican fraction is markedly increased in pregnancy nephropathy and in eclampsia.

Some observers have found a certain disturbance of nitrogen secretion in the severer cases of pregnancy nephropathy, but even in these the capacity to excrete nitrogen does not seem to be markedly disturbed, and in the majority of cases of *nephropathia gravidarum* there seems to be no marked nitrogen retention. Nitrogen retention, you will recall, is most common in glomerulonephritis. In both acute and chronic glomerulonephritis the total non-protein nitrogen of the blood may be greatly increased, with corresponding diminution of the nitrogen output in the urine. In such cases there is hypazoturia and marked azotemia. In the patient before us there has been no evidence of these. We can say, therefore, that we are not dealing with a hypazoturic nephropathy in this patient.

Let us turn next to the excretion of chlorids by the kidneys of this patient. Will you comment upon this point?

STUDENT: The chlorid content of the urine has not been studied, but the chlorid content of the blood-serum has been examined on at least two occasions and was found to be high.

DR. BARKER: Yes; the sodium chlorid of the blood-serum was found, on the first examination, to be 6.55 grams per liter; on the second examination, 5.67 grams per liter. These are rather high figures, somewhat above the normal figures for blood chlorid. This hyperchloremia, together with the occurrence of marked edema (general anasarca), points to chlorid retention. We have to deal then, in this patient, with a hyperchloremic and hypochloruric nephropathy.

It must be remembered that the range of concentration of chlorid in the blood-plasma in normal persons depends to some extent upon the amount of sodium chlorid ingested. The usual range, according to McLean, is from 5.62 to 6.25 grams of sodium chlorid per liter.

You will recall, also, that sodium chlorid is one of the threshold substances; in other words, the concentration in the blood must reach a certain level before sodium chlorid is excreted in the urine. Thus, so long ago as 1912, Widal, Ambard, and Weill found that the threshold for the secretion of sodium chlorid is fairly constant in normal persons at about 5.62 grams per liter. This behavior of sodium chlorid is very different from the behavior of a non-threshold substance like urea. No matter how low the concentration of urea in the blood, so long as it contains any urea, the kidney excretes some, but when the concentration of sodium chlorid in the plasma falls below the threshold value of 5.62 the excretion of chlorid in the urine practically ceases. Though this threshold for sodium chlorid secretion varies somewhat in health, being influenced by the sodium chlorid intake, the administration of drugs, etc., there can be no doubt that this threshold represents an important regulatory mechanism for the maintenance of a tolerably constant composition of the blood as regards chlorids. The French investigators have found that the sodium chlorid content of the urine increases parallel to the square of the value by which the sodium chlorid threshold of the blood is exceeded.

The relation of this sodium chlorid threshold to hypochloruria and to hyperchloremia needs much more careful study, however, before we can value it to any great extent for diagnostic purposes. It is certain that edema is usually accompanied by a relatively increased concentration of chlorids in the plasma and that these relations ordinarily return to normal when the edema disappears. It also seems certain that the functions of chlorid excretion and urea excretion go on quite independently of one another.

Why do you think that this patient has had general anasarca (including edema of the subcutaneous tissues everywhere, with ascites, and a little hydrothorax)?

STUDENT: The fact that the edema of the face appeared early in this patient made us think that the edema was, in part at least, of renal origin.

DR. BARKER: What other origin could it have?

STUDENT: The patient had marked myocardial insufficiency and the edema may have been partly due to this.

DR. BARKER: Yes; the case is a complex one in this respect. I think it certain that a part at least of the edema is of renal origin, but a good deal of it may have been of extrarenal origin. In addition to the myocardial insufficiency we must not forget a possible change in the small blood-vessels (capillaries) all over the body. The extrarenal conditions that are accompanied by edema have been much studied of late, and there is growing interest in the significance of functional changes in the capillary blood-vessels of excretory organs other than the kidneys. The relation of the chlorids in the blood to those in the tissues is an important factor in the production of edema, and there is room for much interesting speculation as to the part played respectively by the kidneys, by the failing heart muscle, and by the changes in the cutaneous and other capillaries. In any case we deal in this patient with a hydropsical nephropathy.

Will you comment upon the blood-pressure in the patient?

STUDENT: When the patient entered the hospital the blood-pressure was 180 systolic and 110 diastolic. At the time when she was delivered of twins the blood-pressure was 200 systolic, 140 diastolic. The pressure remained high, oscillating between 176 and 195 systolic and between 130 and 140 diastolic for some three weeks after the delivery. Then the pressure began to fall. On the twenty-second day after delivery it was 138 systolic and 100 diastolic; on the thirty-second day, 122 systolic and 82 diastolic; on the thirty-third day, 120 systolic and 80 diastolic, and on the thirty-seventh day, that is, two days ago, it was 105 systolic and 70 diastolic.

DR. BARKER: During this first month of the puerperium, then, the patient has passed from a state of very marked arterial hypertension to a state of definite arterial hypotension. Coincident with the improvement of the renal condition and of the cardiac condition this marked change in blood-pressure has occurred. We had to deal

evidently with a hypertensive nephropathy, for it seems probable that the hypertension depended, in large part at least, upon the renal insufficiency, though it may have been contributed to by the myocardiopathy and, perhaps, by other extrarenal abnormalities.

Is it common, do you know, to meet with hypertension in the ordinary pregnancy nephropathy?

STUDENT: I am not sure, but I think it is.

DR. BARKER: Yes. It is very common to meet with hypertension in *nephropathia gravidarum*.

It has for some time now been observed that in the severer cases of pregnancy nephropathy marked arterial hypertension may occur. Even in the milder cases the blood-pressure values are often a little increased. In normal pregnancy, occurring in patients who have had no blood-pressure increase before the pregnancy, the blood-pressure values remain within normal limits, but in pregnant women with simple edema, or with edema with albuminuria, there is often a little increase in the blood-pressure.

The explanation of the arterial hypertension in the pregnancy nephropathy has been much discussed. It is evidently due to hypertonus of the arterioles in the precapillary domains rather than to actual sclerosis of the arterioles, for after delivery and after recovery from the pregnancy nephropathy the hypertension entirely disappears. You have seen that in this patient the very marked hypertension has not only disappeared, but has given place to a definite hypotension, the blood-pressure now being around 105 systolic and 70 diastolic. Some observers maintain that this arterial hypertension associated with the pregnancy kidney may be independent of the nephropathy itself, and may be due to some special pregnancy intoxication. This view has been advanced because the degree of hypertension does not always run parallel to the degree of urinary change (Eckelt).

This marked hypertension in association with the pregnancy nephropathy has recently been discussed by Heynemann, of the Eppendorfer Krankenhaus in Hamburg. He emphasizes the fact that clinical studies have shown that, aside from arteriolar sclerosis, it is diseases of the glomeruli, and especially those that cause anemia of the glomeruli, that are followed by increase of blood-pressure. Loehlein, as well as Fahr, has demonstrated changes in the glomeruli in eclampsias that have complicated pregnancy nephropathy. The

typical finding, according to Fahr, consisted of swelling and of lessened blood contents of the glomerular loops. Heynemann thinks it probable, therefore, that the increase of blood-pressure in *nephropathia gravidarum* is also due to a glomerular disease, and he believes that a rise in blood-pressure during pregnancy, in patients whose blood-pressure was normal before, can be valued for the diagnosis of a glomerular affection. This glomerular change he looks upon as a nephrosis, or degeneration, which effects predominantly the glomeruli rather than the uriniferous tubules. In favor of this view that the pregnancy nephropathy is a nephrosis can be urged: (1) the quick disappearance of the phenomena after the pregnancy has been terminated, and (2) the absence from the urine of red corpuscles in any large numbers. Further facts that may be urged in favor of this view are: (3) the blood-pressure increase, (4) the abnormalities of water excretion and sodium chlorid excretion in so far as they are not due to extrarenal causes, and (5) perhaps also the slight disturbance in nitrogen excretion in the severer cases; moreover, (6) this view can easily be brought into accord with the most recent studies of the pathological histologists. As a result of all these considerations, Heynemann designates the typical renal disease occurring during pregnancy as "glomerulonephrosis of pregnancy" (*Schwangerschaftsglomerulonephrose*). He has chosen this name because it gives expression both to the etiology and the pathogenesis of the disease. The term "glomerulonephrosis," it may be mentioned, was first used by Fahr for certain definite forms of nephrosis, such as the lipoid nephrosis and the amyloid kidney.

The clinical phenomena that have led to this view are met with in their totality only in outspoken cases of the pregnancy nephropathy, but there would seem to be no doubt now that a whole series of degrees of pregnancy nephropathy are met with, all the way from simple albuminuria to the severer cases. Heynemann agrees with Zangemeister, who believes that even the simple edemas of pregnant women belong essentially in this group of the pregnancy nephropathies. If we accept this terminology, the "pregnancy nephropathy" or "glomerulonephrosis of pregnancy" would include a whole series of clinical pictures of which the mildest would be hydrops gravidarum and albuminuria of pregnancy, and the severest would be the eclampsias and the hypertensive states associated with more severe glomerulonephrosis.

When I was writing my book on the *Clinical Diagnosis of Internal Diseases* in 1916 I leaned to the view, then generally accepted, that the pregnancy nephropathy depends upon tubular degeneration rather than upon glomerular change. But I must confess that, on reviewing present knowledge, I am inclined now to accept the view that the pregnancy nephropathy must depend in large part at least upon greater or less injury to the renal glomeruli, in the sense of toxic-degenerative changes (nephrosis) in the capsular epithelium, and perhaps also in the capillary loops of the glomeruli, though not in the sense of a glomerulonephritis with inflammatory, proliferative changes in the glomeruli.

The patient before you illustrates exceedingly well a severe grade of such a glomerulonephrosis of pregnancy. The main features, as you have seen, consist in diminished output of water, in the presence of albumin and casts in the urine, in diminished chlorid excretion, in edema, and in arterial hypertension; whereas, there has been no blood in the urine, no fixation of the specific gravity, and no marked diminution of nitrogen excretion. In technical terms we deal with *an oliguric, albuminuric, cylindruric, hypochloruric, hydropsical, hypertensive nephropathy*; which at the same time is a *non-hematuric, non-hyposthenuric, and non-hypazoturic nephropathy*. The process consists in all probability of a diffuse, toxic-degenerative change in the glomeruli throughout both kidneys, with slight but not marked changes also, in all probability, in the tubules themselves. For if the tubules were greatly diseased there could scarcely be so much re-absorption of the constituents that pass out through the injured glomeruli.

This is not to say that other forms of renal disease never occur in pregnancy. We know that they do. I have already pointed out that a definite glomerulonephritis is sometimes met with in the course of a pregnancy. Recently English observers have called attention to symmetrical, cortical necroses causing suppression of urine in the later stages of pregnancy. These cortical necroses appear to depend upon thromboses of the cortical vessels of the kidneys. They have been well described by E. E. Glynn (1915) and by Jardine and Kennedy (1920). It is possible that such necroses appear as end stages in a toxemia of pregnancy that has also caused pregnancy nephropathy or eclampsia, but in the common forms of pregnancy nephropathy these cortical necroses are not present. They occur

only when the cortical vessels become thrombosed, probably owing to extreme injury to the vascular endothelium.

The hour is nearly up, but we must pay some attention to an analysis of the circulatory conditions presented by our patient. We have seen that this patient has suffered from a high degree of circulatory insufficiency in the course of her pregnancy. Her first symptom was breathlessness at the end of the first six weeks of pregnancy, and later she presented enlargement of the heart due to

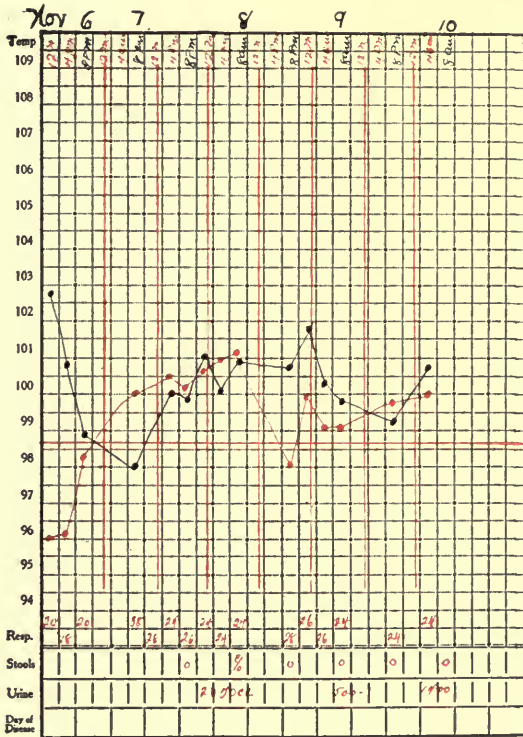


Fig. 30.—Patient suffering from pregnancy nephropathy. Pulse and temperature chart.

dilatation (especially of the left ventricle), definite myocardial insufficiency with chronic passive congestion of the lungs and other organs, and evidences of severe disturbance of the contractility function of the heart muscle (pulsus alternans, gallop rhythm). There has also been a high grade of tachycardia throughout the course of the pregnancy, and, I would point out, without coexisting

signs of hyperthyroidism (see pulse and temperature chart). In addition, as we have seen, there has been a high grade of arterial hypertension persisting through the later months of pregnancy and for about a month after delivery, to be succeeded by the present arterial hypotension (see chart). Obviously, the functions of the cardiac musculature have been profoundly altered. Thus, a disturbance of *chronotropic function* has been manifest in the marked tachycardia, for the number of impulses initiated at the pacemaker at the sino-auricular node has been greatly increased. The disturbances of the function of contractility, or *inotropic function*, have been manifested in the *pulsus alternans* and in the gallop rhythm; the failure of tonicity may perhaps be regarded also as a disturbance of inotropic function, resulting in a dilatation of the heart. The *dromotropic function* of the heart muscle has, apparently, not been disturbed, for the conducting mechanism, as shown by the reports of the electrocardiologist, seems to have been normal.

How shall we interpret these profound disturbances of function of the heart muscle? Evidently we deal with a severe *myocardiopathy*. Moreover, it has been a myocardiopathy that did not reveal itself in electrocardiograms. Do not forget that the electrocardiogram, though very valuable in detecting disturbances of conduction, may be of no help in the recognition of certain other severe changes of myocardial function. Are we to assume that the heart muscle of this patient was normal before the present pregnancy, or had it suffered some injury earlier, which made it give way under the strain of a pregnancy toxemia associated with pregnancy nephropathy and pregnancy hypertension?

It is gratifying to see the improvement in cardiac function and in arteriolar function that have occurred in this patient during the past fortnight. It looks now as though the cardiovascular function as well as the renal function would return approximately to a normal state, though just how complete the restitution will be can only be decided after a longer period of observation.

Certainly it will be important for this patient to get rid of her oral sepsis, since we know now that, at times, absorption from infected teeth and infected gums can have a deleterious effect upon the heart muscle and probably upon the arteriolar walls. It will be well for this patient, too, to reduce her intake of coffee and tea, for she has been overstimulating her nervous and circulatory systems

through too copious an intake of beverages containing caffeine and other methylpurins. I am wondering whether the hypothetical pregnancy toxin may not sometimes have an especially deleterious effect directly upon the heart muscle and upon the arteriolar walls or the nerves innervating them. We have hitherto paid little attention to toxic-degenerative changes in the cardiovascular system in pregnancy, though we have paid much attention to the toxic-degenerative changes in the liver, in the kidneys, and in the nervous system in pregnancy.

Excellent reviews of the toxemia of pregnancy are to be found in Prof. J. Whitridge Williams' *Text-book of Obstetrics*, and in the article by Prof. James Ewing of New York in the *American Journal of Medical Sciences* for 1910. Do look these up in the hospital library when you can find the time.

Whether we deal with a single toxin or with a group of toxins in these abnormal conditions of pregnancy is not yet known. Moreover, the precise source of the toxic substances in pregnancy is still much discussed. Palmer, as you know, believes that the poison is derived from the fetus itself; others say that it comes from the placenta. Palmer thinks that there is evidence that this primary toxic substance originating within the uterus is the cause of the effects upon the distant organs of the mother. Others have assumed that a primary intra-uterine toxin injures first the liver or the kidney, and that these injured organs, in turn, fail to eliminate certain toxic substances or give rise to new toxic substances that secondarily injure the nervous system and other organs. Here there is room still for much study and experimental investigation.

Direct antidotes to the toxic substances produced during pregnancy are unknown. Hofbauer, who believes that hyperemesis gravidarum and eclampsia depend upon overactivity of the hypophysis and the suprarenals in pregnancy, gives ovarian extract with the idea of paralyzing the overactivity of these endocrine glands. He had found, he asserts, that ovoglandol is a specific for the vasomotor disturbances of the climacteric period, which seem to be dependent upon an increased activity of the sympathetic. Accordingly, in every case of eclampsia he gives immediately three vials of ovoglandol and, in addition, injects 0.4 gram luminal-natrium in order to relieve the spasm of the blood-vessels, especially of those in the brain, and to make these vessels less accessible to reflex constriction.

The patient before us makes us wonder whether or not to the severe diseases of the liver that occur in pregnancy, to hyperemesis gravidarum, to the pregnancy nephropathy, and to eclampsia, we may not have to add a pregnancy cardiopathy dependent also upon pregnancy intoxication.

We are as yet wholly in the dark regarding the origin of a toxemia in certain cases of pregnancy and its absence in the majority of cases. Why it is that some women suffer from these serious disorders during pregnancy, whereas others escape, is as yet entirely unknown to us, though doubtless some day an explanation will be forthcoming. In the meantime we cannot do better than to proceed in an orderly way along the paths of accurate, clinical observation of concrete cases and of carefully planned laboratory investigations. Knowledge of the pathological states associated with pregnancy is making rapid progress. We are today familiar with a host of facts that were entirely unknown when Frerich wrote his celebrated work on diseases of the liver and when Leyden described the kidney of pregnancy.

Subsequent History of the Case.—The patient showed remarkable improvement during her stay in the hospital. A sterilization operation was advised, but she objected to it. She was discharged as "improved" on January 22, 1921. The note made on discharge states that the heart was entirely compensated; there was no dyspnea and no more edema. The heart was not enlarged. The eye-grounds were negative. There was slight residual albuminuria.

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DISEASES OF THE MUSCLES, BONES, AND JOINTS

XVIII. SPASMODIC TORTICOLLIS

A MAN OF TWENTY-EIGHT, AFTER SUFFERING FOR TEN YEARS FROM CHRONIC INFECTIOUS ARTHRITIS INVOLVING THE LARGER JOINTS OF THE EXTREMITIES AND THE CERVICAL SPINE, DEVELOPS PAINFUL TONIC-CLONIC MUSCULAR WRY-NECK AND OTHER INVOLUNTARY MUSCULAR CONTRACTIONS.

WE have before us today a patient suffering from a condition that has claims upon our interest partly because it is not at all common, and partly because the question of its treatment is one not yet satisfactorily answered.

The patient's name is William H. He is twenty-eight years old, and has been a farmer all his life until last year, when he became a chauffeur. He entered the Johns Hopkins Hospital on May 1st *complaining of spasm of the muscles of the neck*. This is his second admission, for our records show that he was here eleven months ago suffering from chronic infectious arthritis and oral sepsis.

The *anamnesis*, summarized from the records on both admissions, contains a number of points of interest. His family history is essentially negative. Except for the commoner diseases of childhood his own health was uniformly good up to the age of thirteen. At that time a wood-tick got into his left ear, after which there was, despite treatment, a discharge from the ear for a month. A year later a spider entered the same ear, and this accident was followed by a second period of discharge, lasting from two to three weeks.

Ten years ago, when the patient was eighteen, he, while wading in a stream, got a stone bruise on his right great toe to which he paid no attention for the moment, but the next morning the foot was painful and his toe was so swollen that he could not get his shoe on. This trauma to the toe was doubtless a mere coincidence, for soon after this one after another of his joints became swollen. Thus the metacarpophalangeal joints in his right hand were affected two weeks after his great toe was attacked, and four weeks later his right

ankle became involved. He consulted a doctor and took some medicine, but the pain and redness persisted for two months longer. Six months after the initial attack his left knee became involved, and six months later still, his right knee. After each attack the joint affected cleared up to a considerable extent before another became involved, but the swelling never entirely subsided in any joint and pain in the affected joints returned whenever the weather was cold and damp, and it became increasingly difficult for him to get about.

Two years after the first attack the patient's right hip became involved. The symptoms associated with this joint attack differed, however, from those in the others. There was little or no swelling or redness, though there was considerable pain, which was sharp and shooting in character. Three months later the joint became ankylosed. Six years after the onset of his arthritis the patient's left knee became swollen and painful, and, a year later still, his left shoulder. These two latter attacks resulted in restriction of motion in the joints affected. About two years before this, that is, about six years ago, both tonsils were removed in the hope that the operation might improve his condition; at the same time several abscessed teeth were extracted. Aside from the joint affections described the patient has had no ailments except occasional stiffness of the neck. His habits have been good.

The trouble of which the patient at present complains, namely, the spasm of the muscles of the neck, was insidious in its onset, beginning shortly after last Christmas (about five months ago), when he began to have "pain over the forehead and in the right eye, accompanied by a sticking pain in the right shoulder." A little later his left knee again became painful, and he had a mild attack of stiffness of the neck, on account of which he gave up driving his car. About this time he noticed also "several lumps under his chin and around his neck." These lumps were larger on the right than on the left side. They seem to have been swollen lymph-glands. The muscles in his neck "began to jerk and to knot themselves together," drawing his head to one side. At first these spasms gave him no particular inconvenience, but they gradually increased in frequency and in violence until at last they became very painful, and he says that he could not get comfort in any position, and could not sleep for a long time after he went to bed at night. The only way in which he could obtain relief was to support his chin upon one hand or to lean

against the mantelpiece. Finally, the spasms became practically continuous, except during sleep or when his attention was distracted from his trouble by conversation or otherwise. At such times the spasms were less or ceased for a short time. He became unable to work at all, partly on account of the involvement of the larger joints in the arthritis, partly because of the spasms in the muscles of the neck.

Three months ago he spent two weeks in the Hospital of the University of Maryland, where his condition remained practically unchanged. The spasmodic movements became, however, so violent that his neck and ears became chafed from constant rubbing against the bedclothes. About ten days ago his knees again became painful and swollen, and he decided again to enter the Johns Hopkins Hospital. He has been here a few days, and since his entrance to the ward the muscular spasms have diminished somewhat in intensity.

Physical examination on admission showed marked emaciation. There was considerable atrophy of the muscles of the arms and legs, and, in fact, of the muscles all over the body. Before he began to have the attacks of arthritis his weight was 130 pounds; at present it is only $103\frac{1}{4}$ pounds. The shoulders, elbows, hips, knees, ankles, and spine are all involved in the arthritic process. The periarticular structures are thickened. The right hip is ankylosed. Both knee-joints contain an excess of fluid and there is grating on manipulation of the joints.

The patient has evidently suffered from a severe form of chronic recurring infectious arthritis, which has involved all of his larger joints and the joints of the spine, especially the cervical spine. It seems likely that the primary focus of infection was in the head, either in the abscessed teeth that were removed or in the tonsillar tissues.

The teeth that remain are in good condition. There is slight general enlargement of the lymph-glands of the different regions of the body (cervical, axillary, epitrochlear, inguinal). The lungs are negative. The heart is not enlarged and there are no heart murmurs. The blood-pressure is 110 systolic and 80 diastolic. There is a slight tachycardia, the pulse-rate being around 90. He still has a slight elevation of temperature (100° F.). Nothing abnormal is discoverable on palpation of the abdomen. Examinations of the rectum and of the urogenital system reveal nothing abnormal. The pupils

react to light and on accommodation and the deep and superficial reflexes in the extremities are normal.

An examination of the *blood* shows a marked hemoglobin-anemia (55 per cent. Hb.). The R. B. C. count is 4,280,000, and the W. B. C. count 9800. In the differential count there are: P. M. N., 63.6 per cent.; P. M. B., 0.4 per cent.; P. M. E., 1.2 per cent.; S. M., 27.6 per cent.; L. M. and Tr., 7.2 per cent.

The *urine* is practically normal. The specific gravity is 1020; it contains neither albumin nor sugar; and, on microscopic examination, no casts or abnormal cells are to be seen.

Serious as the chronic arthritis in this patient is, the feature of the clinical condition to which I desire especially to draw your attention in the clinic today is the remarkable disturbance of motility that we observe in some of the muscles, especially those of the neck. We have to deal here with phenomena of motor irritation (hyperkinesis), for we see recurring paroxysms of involuntary, cramp-like contractions of certain of the striped muscles.

The spasmodic contraction of the muscles causes certain definite movements of the head. At first it is drawn backward, and the occiput is rotated toward the right shoulder, while the chin is jerked upward and backward and to the left by a sharp contraction of the right M. sternocleidomastoideus. The M. trapezius (in its clavicular portion), the M. splenius capitis, and the M. semispinalis capitis also take part in the movement, for the right shoulder is elevated, the head is pulled far backward and the chin far upward; and possibly also there is contraction of the M. rectus capitis lateralis (flexing the head markedly lateralward toward the right shoulder). The sternomastoid and trapezius muscles on the affected side are markedly hypertrophied and are stronger than those on the other side. There is an accompanying jerking of the muscles of the face, legs, arms, and abdomen; in fact, many of the muscles of the body are called into action, some of them apparently in an effort to restrain the jerking of the head to the right side. This affection is a very troublesome one, as you see, and it causes the patient a great deal of suffering. (To patient): Have you much pain now?

PATIENT: Yes; a great deal.

DR. BARKER: Do you sleep pretty well?

PATIENT: No.

DR. BARKER: There is an odor of paraldehyd about him now.

It has probably been given him on account of sleeplessness. (To patient): Will you sit up, please? He says he is not able to sit up at all. You observe the position of his head between the paroxysms. It is not held straight, but obliquely, and much more to the right than to the left. The position is not fixed, however; you notice that it is constantly changing. If you watch the neck during the spasms you can see the muscles stand out under the skin. The tonic contractions last for some seconds and then the muscles yield in a clonic manner. We have to deal with a combination of tonic and clonic



Fig. 31.—Torticollis spastica. Photograph during one of the spasms. Occiput and right ear drawn toward right shoulder; face rotated to the left; chin turned upward and to the left; skin of right side of neck wrinkled; lips in whistling position; blepharospasm; frowning.

contractions which subside to some extent when the patient's attention is distracted. I can feel the sternocleidomastoid muscle harden under my fingers during a spasm. This photograph (Fig. 31) shows very well the effects of the spasm. I have also had the moving-picture operator make records of a series of the spasmodic contractions (Fig. 32).

The movements that result from uncomplicated spasm of the sternocleidomastoid muscle alone are threefold:

First, there is rotation of the face toward the opposite side;



Fig. 32.—Torticollis spastica. Cinematographic record of the spasmodic contractions of the muscles of the neck and face.

second, the ear approaches the clavicle of the same side, and third, the chin moves upward and toward the opposite side, the occiput moving backward and lateralward to the side of the contracting muscle.

These three phases of the action of the right sternocleidomastoid muscle in spastic torticollis are observable in our patient, but in this particular case the action of the sternocleidomastoid is complicated by the fact that other muscles of the neck are also involved. The *M. splenius capitis* contracts, causing more extension of the head. The *M. trapezius* contracts, though not so violently, elevating the shoulder and pulling the occiput toward it, and the *M. semispinalis capitis* probably helps to extend the head. The *M. platysma* contracts; you can see its contraction now, under the skin, throwing the skin of the neck into folds.

Aside from these involuntary contractions of the cervical muscles, which account for the spastic torticollis, there are some remarkable contractions of muscles visible in the domain of the distribution of the facial nerves. You notice that the facial muscles contract sometimes on one side and sometimes on the other. There is distortion of the lips (*M. orbicularis oris*); the angles of the mouth are drawn upward (*M. zygomaticus*); there is some blepharospasm (*M. orbicularis palpebrarum*); and there is much frowning (*M. corrugator*). Occasionally there is spasm of the whole right side of the face, but more often the contractions occur in single muscles or in groups of muscles in a haphazard manner. In addition, there are some contractions of the muscles of the trunk (including those of the spine) and of the muscles of the limbs; these latter may be regarded, perhaps, as evidence of a compensatory process rather than as an overflow of the innervations concerned in the main spasmodic process.

As a rule, torticollis is a painless affection, but the condition with which we are now dealing occasions great suffering. (To patient): Are the muscles in your neck tender when I press upon them?

PATIENT: No.

DR. BARKER (to patient): Do the muscles feel sore?

He says that when the jerking comes on there is some soreness at a point that corresponds to the attachment of the sternocleidomastoid muscle. As a rule, when torticollis is painful the pain is due to either myositis or arthritis. This man has had a good deal of trouble with his joints. He has had a chronic arthritis with serous effusion in both knee-joints; indeed, all the large joints of his extremities are affected. He has also had a chronic arthritis of the cervical spine. It is hard to say definitely in how far the arthritis of the spine is responsible for a reflex spasmodic torticollis. It seems to

me probable that there is a central neurogenous element superimposed upon the local arthritic affection.

A "stiff neck" is most often due to a slight myositis, but it may be due to a lesion of the spine. Thus, in the cervical form of Pott's disease, the stiffness of the neck appears only gradually and the head is held straight. When the neck is stiff and painful and the head is asymmetrically placed, the painful lesion that leads to fixation by muscular contraction is usually unilateral. When a stiff neck comes on suddenly, with chills and with a rise of temperature, osteomyelitis of the cervical spine should be suspected.

When the neck is stiff and the head is inclined to one side the condition is known as "wry neck," and there is usually a unilateral lesion of some kind to account for it. A wry neck may be painful, in which event it may be due to unilateral myositis or lymphadenitis; or it may be caused by trauma, causing strain of the ligaments, or by a unilateral spondylitis.

More puzzling, clinically, are the cases of *chronic wry neck without pain*, often referred to as *muscular wry neck* or *caput obstipum*. There is a congenital form of the affection as well as a true rheumatic variety; in the latter there is myositis of the sternocleidomastoid muscle on one side. But in neither of these conditions is there spasm, and the condition is the same whether the patient is asleep or awake. Our patient, on the contrary, is suffering from pronounced spasm that ceases when he is asleep. He has what is known as "spasmodic torticollis" (*torticollis spastica*).

In spasmodic torticollis we have to deal with a neurosis, the cause of which may not be easy to determine. Sometimes it is of reflex origin, that is to say, associated with an arthritis or with some trouble in the eyes or the ears; sometimes it is entirely central in origin, the *torticollis mental* of French writers (Brissaud, Meige and Feindel). In many instances there is, I believe, a combination of local peripheral irritation with a hyperexcitable state of the cerebrum.

In the patient before us the central nervous system is certainly below par, exhausted by chronic infection. The torticollis did not appear until quite a long time after the arthritis began. It is, perhaps, not strange that he should develop a neurotic condition in association with his chronic arthritis. Many chronic "arthropaths" become "neuropaths." At present his nervous system is under the further strain of the severe pain that is associated with the spasms and keeps

him from sleeping. He is, however, very cheerful and good tempered, and interested, as you see, in what is going on around him.

So far as we know the first mention of torticollis is by Rabelais, in the first half of the sixteenth century. He speaks of it as "torty colly." About a hundred years later it is mentioned in a verse by Scarron, and about the same time it began to be discovered professionally by several medical writers, especially Nicolas Tulp, the demonstrator in Rembrandt's famous picture, *The Lesson in Anatomy*. Tulp described the condition anatomically to a certain extent, and even suggested an operation for its relief. From his time on it has received increasing professional attention. You will find interesting historical data in the monograph of Redard (1898) and in that of Cruchet (1907). I would also refer you to the interesting review of wry-neck by Bauer (1913).

Now, the question is, What help can we give this man? He has been getting steadily worse, though there has been some little improvement, as far as the spasms are concerned, during the few days that he has spent in the hospital. The main objectives in the treatment of such a case as this are, in my opinion, (1) the soothing and strengthening of the central nervous system, and (2) the removal, if possible, of the local irritation. To deal with the second objective first, we should try to arrest the arthritis and its local accompaniments, using the measures that I have so often advocated in other clinics that I need not enter into their details today.

As to the methods for attaining the first objective, the soothing and strengthening of the central nervous system, I should like to say something before the end of the hour. To achieve the end mentioned, general reconstructive measures should be adopted. The patient should have a long rest in bed under complete isolation, so as to exclude for some time all exciting influences while we resort to general upbuilding. A general hospital ward is not a very good place in which to carry out such a course of treatment. A private room, with special nursing, is a great advantage. Nevertheless, a good deal can be accomplished, even in the public ward, by prohibiting visitors (even members of the patient's immediate family), and by keeping a screen around the bed so as to exclude, as far as possible, all harmful impressions from the outside. Certain drugs of a soothing nature are helpful. Bromids and other mild sedatives will often secure sleep, but if they should not suffice, I should not hesitate,

with a patient in this condition, to give him sleep for a time with the aid of Schlesinger's solution, say 8 minims hypodermically at bedtime and 5 minims in the morning. The formula for this solution is as follows:

R. Scopolamin. hydrobrom.....	0.0025
Morphin mur.....	0.2
Dionin.....	0.4
Aq. destill.....	10

Sig.—For hypodermic injection, 5 to 10 minims at a dose.

This is a most valuable sedative, especially in the control of pain due to organic disease of any kind. The combination of the three drugs, scopolamin, morphin, and dionin, acts in a really remarkable manner, and the effect lasts longer than that of morphin alone. I have never seen an organic pain that could not be kept under control by it. One may use this mixture instead of morphin alone, and one should be just as careful as with morphin not to prescribe it unless the pains are not sufficiently controllable without it.

Of recent years the so-called psychic treatment of the purely nervous form of torticollis has met with a good deal of success. As yet there is great difference of opinion as to the best form of psychotherapy to employ. Some favor suggestion and hypnotism, others persuasion and re-education, and still others psycho-analysis.

L. P. Clark has recently published several articles upon the subject in which he describes the successful treatment of certain cases. He believes that in order to secure success with this particular class of patients the form of treatment known as "psycho-analysis" must be used, not "suggestion and re-education." When the torticollis is "grafted upon an underlying mental defect" it cannot, in his opinion, be permanently eradicated, but if the make-up is that of a simple neurotic combination, though many of the instinctive trends of the primary intellect and emotion are weak, the condition, in his opinion, can be completely relieved.

General upbuilding, including suitable diet, hydrotherapy, electrotherapy, and psychotherapeutic influences, should be given a thorough trial in every case of spasmodic torticollis. Unfortunately, in many cases the malady does not yield to these measures, and, driven to desperation, the patient is willing to undergo any surgical operation that offers a chance of relief.

Several surgical procedures for the relief of spasmodic torticollis

have been devised. The purpose of all of them is to give rest to the disordered nerve centers by cutting the connections between the central nervous system and the muscles involved. Thus, resection of the N. accessorius has often been undertaken. If this alone does not help, the upper cervical nerves may also be resected. Another operation includes myotomy, neurectomy, and excision of the ganglion of the posterior root of the second (cervical) spinal nerve. Another still more extensive procedure is known as Kocher and De Quervain's operation, in which the attachments, both origin and insertion, of every muscle in the neck on both sides are cut. By this procedure the connections of all the muscles, from the occiput down to the superior aperture of the thorax, are severed. It is a long operation and must be done, of course, under general anesthesia. The head is then put into a plaster cast, with the muscles in the correct position. All movement of the head and neck is rendered impossible for a time because the muscles are completely severed, and while they are reuniting the head is kept rigid by means of the plaster cast. It takes a long time for the muscles to unite, and during this time the nervous system has a chance to rest and to recuperate. This operation is said to have been successful in 7 cases out of 12. There is no doubt that in some cases of torticollis spastica great relief can be gained from this form of treatment. Dr. Finney operated in this way upon a patient of mine who became practically well afterward. In another instance, however, a man from New England, who had had this form of torticollis for years and grown steadily worse as time went on, consented to undergo the same operation. Dr. Finney performed it, but there was no permanent improvement. The patient was, it is true, relieved for a time, but as soon as the severed muscles had reunited the jerking movements recommenced.

Any patient suffering as much as this man before us does is willing to go through even an extensive operation if it promises relief, though I advise a thorough trial by non-surgical methods before resorting to operation. The malady in this patient seems to me closely related to the tic disease. The pathological innervations are widespread. The patient should, if possible, have a thorough rest cure over a long period with psychotherapy and improvement of his nutrition.

[Further History of the Case.]—The patient grew impatient under medical therapy and requested surgical interference. Operation

was performed on May 23d by Dr. Heuer. The spinal accessory nerve on the right side was divided and the right sternomastoid muscle extirpated. The musculature on the right side of the neck was seen to be markedly hypertrophied. The sternomastoid muscle was exceedingly vascular. One or two small glands were visible along its course, and there was some evidence of inflammatory reaction in the glands of the right anterior triangle. One small gland was removed for examination. After extirpation of the muscle the dissection was carried into the deeper planes of the neck, posterior to the great vessels, and the various cervical nerves thus encountered were resected. The same procedure was carried out in dealing with the spinal accessory nerve.

The operation was well borne. The head was put up in the usual cerebellar dressing except that plaster was employed instead of crinolin. An effort was made to overcorrect the original condition by fixing the head markedly to the left. On return of consciousness, soon after the application of the plaster cast, there was no evidence of twitching, proving that severance of nerves and muscular attachments had been complete.

On May 29th, six days later, the cast was removed; owing to the crowded condition of the hospital it became necessary to discharge all patients not absolutely in need of hospital residence, otherwise the cast would have been left on longer. The wound was in good condition, and the stitches were removed. There was a definite area of anesthesia on the lower part of the right side of the face extending from the occiput to the chin and including the ear. Over the site of the right sternomastoid muscle there was a marked depression. The trapezius was rather spastic. The head was tilted to the left, with the chin pointing to the right, forward, and upward. It could not be drawn to the right.

The patient was discharged from the hospital on June 4th. At that date there was no jerking of the head to the right, but at varying intervals it underwent a painful involuntary rotation to the left, with facial contraction on the other side. On the right the trapezius was more spastic than on the left. The right shoulder appeared to be slightly more movable than it was before the operation. The area of anesthesia remained unchanged. The patient's general condition was improved and he was sleeping better. It will, of course, be some time before we shall know how much permanent benefit

has resulted from the operation. Surgical results hitherto have, unhappily, been less satisfactory than one could wish for.]

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XIX. CHRONIC PROGRESSIVE MULTIPLE OSSIFYING MYOSITIS

A COLORED LABORER, NINETEEN YEARS OLD, WITH CERTAIN CONGENITAL ANOMALIES (SHORT SACRUM; POLYDACTYLISM; MICRODACTYLISM; WEB-TOES), WHO BECAME ACUTELY ILL SEVEN YEARS AGO WITH FEVER, DERMATITIS, AND PAINS IN THE VOLUNTARY MUSCLES, LATER DEVELOPING PSEUDOCONTRACTURES IN ALL FOUR EXTREMITIES WITH GENERAL INCREASE IN THE CONSISTENCE OF THE VOLUNTARY MUSCLES AND THE FORMATION OF BONY MASSES IN THE MUSCLES AND IN THE SUBCUTANEOUS TISSUES.

In these clinics we prefer to show you examples of the disease states that you are most likely to meet with after leaving the medical school, as they will be of most service to you in your practical work. But the patient with us today illustrates a condition that is extremely rare—so rare that I thought its very infrequency was, in itself, a

reason for presenting it to you. Indeed, there are not many cases of the disease on record. This is the first one I have ever seen, and it is, I believe, the first instance ever reported in a negro. The case has been a clinical puzzle in the ward, but, on studying it carefully, evidence has been collected that will, I think, convince you that the patient is suffering from chronic progressive multiple ossifying myositis.

The earliest case of this disease to be recorded, as far as I can find, was that reported to the Royal Society by John Freke, F. R. S., in 1740; an account of it was published in the Philosophical Transactions for that year. The patient was a boy, about fourteen years old, who applied at the Out-patient Department of St. Bartholomew's Hospital for advice concerning a number of large swellings on his back which had made their appearance some three years before and had increased in size until one of them was "as large as a penny-loaf." Mr. Freke stated that the case might be considered an exostosis by some persons, but he did not so regard it, because all the cases of exostosis that he had seen arose from "some Part or Parts and have not been found to proceed from a general dissolution of the Bones, as this hath." "The swellings arise," he went on to say, "from all the Vertebrae of the Neck and reach down to the Os Sacrum; they likewise arise from every rib of his Body and joining together at all parts of his Body, as the ramifications of coral do, they make, as it were, a fixed bony pair of Bodices." No further account of the case was given.

In the following year, 1741, a similar case was published in the Philosophical Transactions by the Rev. John Copping, F. R. S. It was described in much detail by himself and by two other persons, who wrote letters concerning it. In this instance the patient, a man named William Clarke, had recently died in County Cork, Ireland, at the age of sixty. He had begun to suffer from stiffness in his joints when about eighteen and the stiffness increased until his body became so completely ossified that it was necessary to take out some of his teeth in order to feed him. At the time of his death the only joints he could move were his knees and his right wrist. "The whole spine," reported Mr. Copping, "is ossified and one entire arch of bone there is from the occiput down to the os sacrum." "It is as difficult," he continued, a little farther on, "to give an exact description of this curious *memento-mori*, as of Calypso's grotto. I am

promised very soon a complete history of his life, and then I shall endeavor to transmit William Clarke's name to future ages." The man's remains came into the possession of a physician in Cork, who prepared his skeleton, now in the Museum of Trinity College, Dublin.

A third case was published in the Philosophical Transactions for 1759 by the Rev. William Henry. The fourth was reported by Abernethy in 1830; and the fifth, which was the first observed in the United States, was reported by David L. Rogers, of New York, in 1833. Since that date about 100 cases have been recorded, each of which has been brought forward as a curiosity. Some of the patients, known to the world at large as "ossified men," have made a livelihood by exhibiting themselves in side shows and other similar places.

The patient before you is a colored man nineteen years of age, a day laborer from West Virginia, who came recently to the dispensary complaining of "weakness and drawing up of the legs and arms, and inability to walk."

His family history and his past history are unimportant, except that his father had an extra digit on one hand, a peculiarity that the patient, as well as one of his brothers inherits, and about which I shall have more to say later on.

The patient's present illness began, according to the account he gives, seven years ago, when he was twelve years old. He first noticed a slight "breaking out," which, lasting about three weeks, spread over the entire body except the palms of the hands and soles of the feet. This eruption consisted of papules each about the size of a mustard seed. They did not become pustular or weep, and there was no itching. When the eruption disappeared his face and body remained more or less pigmented. Since then he has had occasional crops of small "pimples," which, after they appear, develop fluid within them, itch, weep, and then dry up, their whole course lasting from a few hours to a day. He says that he felt a little ill at the time he had the first eruption, though he did not stop work. After it subsided, however, he became acutely ill with irregular fever, cough, hemoptysis, night-sweats, nausea, and vomiting. What do the latter symptoms suggest to you?

STUDENT: Pulmonary tuberculosis.

DR. BARKER: Yes. This point may be of some interest, for pul-

monary tuberculosis has been reported by several observers in association with the disease from which this man suffers.

The patient was so ill at the time mentioned that he went to bed, where he stayed, with a high fever, for several weeks. His muscles soon became sore and tender, so that it hurt him to move any of them, but he thinks they were not swollen. There was so much tenderness, however, that he could not bear the weight of the bedclothes upon his abdomen, and he used to hold his arms over it to keep the clothing from touching him. He has never been able to straighten his arms since. This is an interesting point. He could not straighten his arms, he asserts, on account of the pain. The muscles of the arms soon became very "stiff." Notice what we have here: first, a skin eruption; second, some infection associated with fever, cough, and night-sweats; third, pain and stiffness of the voluntary muscles of the body, interfering with movement and causing contractures.

In the course of the disease there have been periods of exacerbation and of temporary quiescence. His severe illness began about Thanksgiving Day, 1909, and lasted until after Christmas, when he began to feel better. In January, 1910 he was able to return to work, though he found that he had trouble in extending his arms and also had difficulty in walking. His legs, he says, "began to draw up" and he could walk only a short distance before having to stop to try to straighten them out, and this he found very difficult to do. In April the patient found that he could not continue his work because of these "cramps"; moreover, he was sensitive to criticism concerning his disability. He left off work, therefore, and stayed at home, sitting in a chair most of the time. In June he again made an effort to get up and about, but found that he could not straighten his legs at all. Becoming afraid that they would grow still worse he tried at this time to use them as much as he could, with the result, he asserts, that he was able gradually to become more active. I think that there must have been at this period a temporary arrest of the morbid process. Pauses in progress, alternating with periods of aggravation, are characteristic of this disease.

From the beginning of his illness the patient had frequent attacks of subjective numbness and tingling in his arms and legs, and these attacks continued to occur at intervals up to 1913. He has never noticed, however, any areas of definite anesthesia to pain.

By 1912 he had become able to get about on all fours. Since

then his condition has improved still further. He can now chop wood and can, he says, shoot a shot gun with accuracy. He has not, however, regained the ability to straighten out his limbs.

Where does this patient live?

STUDENT: He comes from Northumberland Co., West Virginia. Dr. Futcher saw him first in the Out-patient Department and had him admitted to Ward M.

DR. BARKER: Please read Dr. Futcher's note.

STUDENT: "History of a dermatitis, accompanied by constitutional symptoms at the onset, followed shortly afterward by pains in the muscles, and still later by contractures with flexion of the joints of the extremities, all of which suggests strongly that the patient may have had dermatomyositis, with fibrous changes in the muscles, leading to contracture. The possibility of a neuritis must also be considered. Infectious arthritis seems to be excluded by the *x*-ray examinations."

DR. BARKER: Let us now make a physical examination of the patient during which I shall comment upon some of the more characteristic findings. At first glance you observe the flexion-contractures and the muscular atrophy of the extremities. The head is rather large and the acra are fairly prominent. The soft parts of the lips are thick and the bridge of the nose is rather flat, but we are accustomed to such findings in the negro.

In this disease there is sometimes a pathological thickening of the bridge of the nose. Rolleston has reported a case in which this peculiarity was present and remarks that in Dr. Manson's book on tropical diseases a similar condition is described under the name of *Goundou*, or *Anakre*, there stated to be due to a parasite setting up an inflammation of the bone, though other observers believe it to be the result of periostitis from yaws, and still others regard it as a manifestation of atavism, or reversion to a lower type. The point seems worthy of mention, though I do not feel sure that in our patient the nose has undergone any change as a result of his disease.

The face is rather mask-like. There is some thickening about the eyelids as well as under the ears and in the cheeks, but there is no pitting on pressure. It is more like the thickening one sees in myxedema. There is definite abnormal bulging below the ears and the side of the face looks puffy. The supercilia are sparse. A few shotty lymph-glands are palpable on the posterior triangle of the neck, and also some in the axillary and inguinal regions, but none of them

is larger than a bean; there is thus a slight general lymph-glandular hyperplasia. The thyroid is palpable, but there is no definite struma. The tongue is moderately coated and there is some pyorrhea.

The thorax is fairly well formed and the two sides are symmetrical. The volume of the pectoral muscles is smaller than normal. The chest expands well on inspiration. The lungs are practically negative; there are no signs on percussion or auscultation that make us suspect

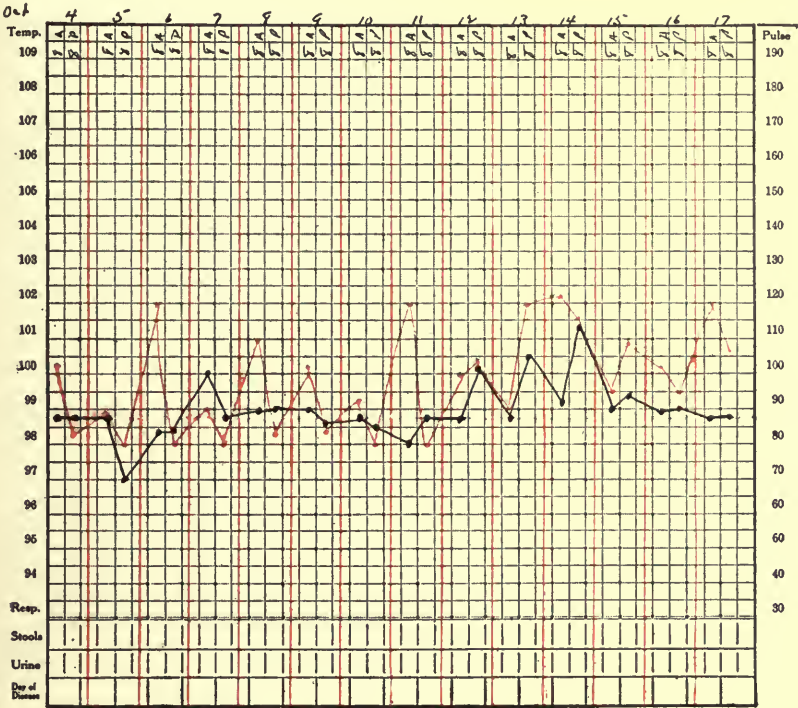


Fig. 33.—Myositis ossificans. Pulse and temperature chart to show tachycardia and slight rises of temperature. The patient was in the hospital for about six months. Period of chart from October 4th to 18th.

the existence of pulmonary or pleural tuberculosis. The position and size of the heart are normal and there are no heart murmurs.

What is the pulse-rate?

STUDENT: The pulse-rate is at present rather slow; about 60.

DR. BARKER: The behavior of the heart of this man is interesting. If we look at the chart we see that his pulse-rate has been very variable (Fig. 33). In one part of the chart the temperature and the

pulse-rate are normal; then there is a part that shows a period of continuous tachycardia with normal temperature; next, a time when he had not only tachycardia but also some fever, and later again a time of quite outspoken tachycardia with some fever. The pulse-rate has at certain periods been above 140. There is, evidently, a marked tendency in the patient to rapid heart action. Tachycardia has been reported in other cases of ossifying myositis. It must be due either to an abnormal condition of the heart nerves or of the myocardium or to some extracardiac influence, though no satisfactory explanation of it has yet been offered.

On examination of the abdomen and of the genitalia there is nothing abnormal to be made out except that the abdominal walls are rigid, and though the patient denies having had any venereal infection, the left testicle is small, soft, and tender.¹

Our patient has, despite his unilateral testicular atrophy, complained of persistent, troublesome erections, but considering his age, race, and lack of activity, I am not inclined to lay much stress upon this symptom.

When we come to examine the flexed, atrophic extremities, we find that the patient is unable to extend his arms beyond an angle of 150 degrees, or his knees much beyond a right angle.

(To patient): Please move your arm; stretch it out as far as it will go.

His arm seems to be very sore and he has pain on trying to extend it. You notice a piece of muscle has been cut out of this arm for histological examination. We have to deal with malposition of the arms due partly to pain and partly to organic changes in the tissues causing shortening. Now let us examine the legs.

(To patient): Straighten out this leg. Does it hurt you?

PATIENT: No.

DR. BARKER: You see he cannot straighten out his lower extremities, though, on trying to do so, he does not at this time suffer pain.

(To student): How many patients have you seen in your clinical work who could not extend their knees or their elbows?

STUDENT: Only a few cases of arthritis.

¹ The latter point is of some interest, since abnormally small testicles, as well as other defects of the genital organs, have been noted in connection with ossifying myositis. Thus, Florschütz, in 1872, reported a case in which both testes were imperfectly developed.

DR. BARKER: The joints are not swollen in this man and he has never had joint enlargement. Roentgenograms of his joints are negative except for atrophy of bones near the joints, due to disuse. We can, I think, rule out arthritis. The hands, as you see, cannot be fully extended at the wrists; the third, fourth, and fifth digits of each hand are held partially flexed. The wrists and the forearms are maintained in a flexion position.

(To patient): Try to move your right arm outward. Now make a circle with your hand. Try the other one, too.

You see, he has relatively free movement at the shoulder-joints, which is unusual in this condition.

The feet are somewhat abducted and are kept constantly in that position. There is some persistent flexion of each foot at the ankle. The toes are abducted and slightly flexed. Notice particularly the positions of these toes. There is a little flexion and a tendency to abduction of the great toes, though not an outspoken hallux valgus, which is present in many cases of the disease.

(To student): When the parts of the extremities, upper and lower, are held in abnormal position as these are, and the patient is unable to extend fully the fingers, wrists, elbows, hips, knees, and ankles, what do you call this condition?

STUDENT: He has contractures.

DR. BARKER: Many would use the term "contracture" here, but I think we shall do better to use another term, namely, "pseudo-contracture." We should, I think, reserve the term "contracture" for conditions in which there is a persistent, involuntary, tonic contraction of one or several of the muscles of the voluntary muscular system. We see such true contractures in the monoplegias, hemiplegias, and paraplegias that accompany those organic diseases of the central nervous system that cause lesions of the pyramidal tract. We see them again in the fixed attitudes due to disease of the extra-pyramidal motor nervous system, such as Parkinson's disease. We see them in tetany and sometimes temporarily in tetanus. We see them sometimes, too, in association with meningeal irritations. But here, in our patient, we are not dealing, in my opinion, with tonic contractions of the voluntary muscles. Feel these muscles, please. Notice that they are not only firm, but their elasticity is greatly diminished. There is a feeling of peculiar hardness, a resistance that differs from that felt in tonic muscle spasm. I feel sure that these

muscles would not relax much or grow softer if the patient were put under a general anesthetic. Some change has taken place in the muscles themselves, which has led to hardening and to shortening.



Fig. 34.—Patient with myositis ossificans. Lateral view. Muscular atrophy. Pseudocontractures. Web-toes.

This condition we call “pseudocontracture.” It is met with in different forms of myositis (one of which this man has), in the myosclerosis of the aged, and in the so-called Volkmann’s malady (or “ischemic paralysis,” due to tight bandages or splints).

I notice something else that interests me very much—something that has not been entered in the notes made in the ward history. Look at the second, third, and fourth toes of that right foot. Are they like other people's—yours, for instance—except for the color?

STUDENT: I do not see anything unusual about them.

DR. BARKER: Well, look at the slit between these two toes and then at that between these other two. Between the third and fourth and the second and third toes the dividing line is shorter than between the others and you find the same thing upon the other foot. We have here a bilaterally symmetrical anomaly in the form of "web-toes" (Fig. 36). The extent of the web formation here is not extreme, but it is definitely positive and the condition has been observed in other cases of ossifying myositis. Carter in 1894 reported in the *Lancet*, a case with this peculiarity, which he speaks of as a "swimming membrane," between the second and third toes of each foot.

In our patient we have also a unilateral polydactylism in the form of a sixth digit on the left hand. The extra finger has two phalanges and a nail, and is attached to the fifth digit only by the skin; there is no bony attachment (Fig. 35).

But, aside from the web-toes and the supernumerary finger in this patient, I am greatly interested in inquiring as to the presence or absence of microdactylism.

Microdactylism, or abnormal shortness of the toes and of the fingers, most often of the great toes and thumbs, is a peculiarity that has been observed in 75 per cent. of the cases of ossifying myositis reported. It was first noted by Gerber and reported by him in 1875, but he regarded it as a malformation accidentally connected with the particular case under his observation. It was Helferich, in 1879, who recognized it as an abnormality definitely associated with myositis ossificans. Microdactylism has almost always been present in the great toes in this disease, and sometimes it has been observed in the thumbs as well. Pincus, in 38 cases tabulated by him, found it present in the great toes in 14 instances; in 2 of the 14 cases the thumbs also were affected. Microdactylism may be present at birth and may exist for years before any signs of the myositis make their appearance; on the other hand, it may not develop until later. In one case where it was observed in the toes when the child was born, it did not appear in the thumbs until the eighth year. Before the introduction of the *x*-ray into medicine it was supposed that the deficiency in the length of the toes in microdactylism was due to an absence of one phalanx in each digit, and many of the earlier cases were so reported, although Manteuffel in 1896 demonstrated a synostosis of the toes upon the skeleton, remarking that, in his opinion, it could easily be mistaken for absence of the first phalanx, to which microdactylism was attributed. The use of the *x*-ray, however, has made it plain that the appearance in microdactylism depends upon a shortening of the metacarpal



Fig. 35.—Patient with myositis ossificans. Anterior view, showing the pseudo-contractures, the muscular atrophy, and the supernumerary digit attached to the little finger of the left hand.

and the metatarsal bones, with, in most cases, a subsequent ankylosis of the interphalangeal joints. Microdactylism in the feet is not confined to the great toes,

instances in which the other toes were shorter than normal having been occasionally reported. Nor are the metacarpal and the metatarsal bones the only bones that may be the site of defective growth in this disease. Elliott has reported a case in which the ulna was an inch shorter than the radius, to which it was attached by a



Fig. 36.—Patient with myositis ossificans. Web-toes and marked striation of skin of legs and feet.

bridge of bone; and Crawford and Lockwood have published a very interesting case in which the *x*-ray showed that the terminal phalanges of the fourth and fifth toes were lacking. Microdactylism of the great toes is usually associated with a condition of hallux valgus, in which the great toe is displaced lateralward and frequently lies either under or above the second toe.

On looking closely at the feet of our patient we see that his great toes are not much shortened, though there is a slight degree of hallux valgus in both feet (Fig. 36). On looking at his hands we see that his thumbs are fairly long, but the metacarpal bones of the thumbs are short compared with the length of the thumbs themselves, and it is this shortening of the metacarpal bones that is the distinctive feature of microdactylism (Fig. 35). We must try to study carefully all of the bones in this patient's skeleton in *x*-ray plates in order to see whether other, and how many, skeletal abnormalities are present.

Although microdactylism is by far the most common of the congenital malformations observable in myositis ossificans, there are a number of others, none of which has been reported in more than a few cases and some of them have been met with in only single instances. From Buenos Aires there has recently been reported a case in which the patient exhibited an unusual number of congenital abnormalities, including some that have never been reported before. The patient was a boy of eight and a half years, in whom the disease began at six, when a swelling appeared over the right scapula. This was operated upon, but no description of the operation is given. It was followed by other swellings in the same situation upon which a second and then a third operation was performed. The patient had microdactylism of both great toes, as well as hallux valgus in an extreme degree, the great toes being directed lateralward and upward to such an extent as to be almost at right angles with the metatarsal bones. The movement in the metatarsophalangeal joint was greater than normal and the joint projected medialward so as to present the appearance of a bunion. The second toes on each foot also had a convex arch on the medial side. On the anterior surface of each of the median upper incisor teeth there was an excrescence extending from the margin of the alveolus to the middle of the tooth. There was also a well-marked depression in the hard palate. On the hands, the thumbs and also the little fingers were shorter than normal, the terminal phalanx being lacking on the latter. There was double ectopia of the testicles. The writer of the article, Dr. D'Ovidio, states that the Wassermann reaction was positive in his patient, and comments upon the fact that this point is not mentioned in reports of other cases. I find that there are, however, in the bibliography a few instances in which it has been recorded as negative. The Wassermann test has been made on the patient before you and is negative. In D'Ovidio's case the patient's father had had a local lesion upon the glans penis a good many years before, which had not been followed, he said, by any secondary manifestations. The boy's two brothers, one older and one younger than himself, were perfectly healthy, and his mother had had no miscarriages.

The congenital malformations that I have found noted in association with myositis ossificans, including those in the above case, are as follows: Microdactylism of the great toes and of other toes and of the thumbs and fingers; hallux valgus; polydactylism; web-toes; curvature of the second metatarsal bone; excrescences on the superior median incisor teeth; shortness of the sacrum; absence of the terminal phalanges of the toes in one case and of the fingers in another; short ulna; thickness of the bridge of the nose; defect in the hard palate; abnormally small testes; double ectopia of the testes; and hypospadias in the third degree. In addition to these, Elliott mentions:

absence of certain muscles; absence of the ear lobules; absence of the testes; absence of the mammæ, and sexual infantilism; but he does not give references to the actual instances.

Another abnormality present in a large proportion of cases of the disease is the formation of exostoses. According to Dr. Walter R. Steiner, these have usually been observed on the medial surfaces of the arms, the anterior surfaces of the tibiæ, the upper parts of the fibulæ, the ribs, and wherever the long bones approach the skin. The frontal bones and phalanges of the fingers are also sites in which they have been noted.

If we continue the examination of the lower extremities of the patient before us we are struck by the long, deep, purplish streaks upon the legs which seem to correspond to the course of the underlying veins. It is an appearance that I have never seen before. Notice, please, how these radiating purplish stripes run down to the foot. Mr. Martin will take some photographs of the condition (Fig. 36). Disturbance of the veins is not one of the peculiarities definitely associated with this disease, though a case was reported by Pincus in 1869, in which a well-marked venous stasis was observed in the lower extremities as well as in the nose and in the hands. It was also noted in his case that the nose was cyanotic. In our patient there is slight cyanosis of the nose and the nails are cyanosed.

Certain other cutaneous manifestations (studied by Dr. Ketron) in our patient deserve mention. The skin on the face has an erysipeloid appearance with a purplish tint, and there is some edema. The changes about the nose and cheeks suggest seborrheic eczema. There is some pigmentation on the arms and the chest. In a few places, especially at the waist and over the lumbar region of the back, there is some loss of pigmentation, and here there is also an absence of the hair follicles. There is some evidence of atrophic changes in the skin over the backs of the hands and on the knees, where the skin is in some places smooth and shiny and thin, like cigarette paper; in other places thicker and showing keratosis.

Calcified nodules in the muscles and in the subcutaneous tissues are demonstrable in this patient both by palpation and by roentgenograms. On the ulnar surface of the left forearm there is a small hard nodule about 2 cm. in diameter, which feels as if it were attached to the bone. The x-ray picture shows it to be a calcareous deposit, apparently separate from the bone (Fig. 37). It is certainly difficult to move over the bone. There is no muscular tissue just here, and it may be either an exostosis or a calcification of the subcutaneous



Fig. 37.—Myositis ossificans. The dark areas on the ulna are calcified masses. Note the rarefaction of all the bones.

fibrous tissue. On the medial aspect of the right arm there is also a nodule which can be freely moved, and is evidently not attached anywhere. Dr. Baetjer and Dr. Waters both report "calcification

in the muscles of the left forearm" in the x-ray plates. The x-ray also shows signs of calcified areas in the tissues on the flexor surface of the knee (Fig. 38). We must make further roentgenograms in this case to see whether other skeletal abnormalities are present.



Fig. 38.—Myositis ossificans. Two small calcareous deposits are visible in the tissues behind the flexed knee. Note the rarefaction of the end of the femur and of the head of the tibia (disuse?).

and, if so, how many. Certainly, as yet, no large masses of bone have formed anywhere. In all the roentgenograms of the bones there is evidence of diminution of lime salts (Fig. 39).

I might mention here that about two weeks ago it was suggested

by some one of the physicians that massage be tried in this case, and it was accordingly given for half an hour at a time. The first treatment was followed immediately by a rise of temperature, which continued until the massage was discontinued at the end of three days. The patient also complained of soreness in the muscles manipulated and of pain in his head after each treatment.



Fig. 39.—Myositis ossificans. The bones are much rarefied.

I mention the injurious effects of the massage because it has been repeatedly noted that any trauma, even palpation of the tissues, may bring on an exacerbation of the disease process in myositis ossificans. In a number of cases it is stated that the original swelling made its appearance after a fall or a blow on the place where it subsequently appeared, and after the disease is once established falls or slight injuries, which, of course, occur frequently as the patient becomes more and more

crippled, are almost always followed by new swellings, accompanied by pain and, occasionally, by constitutional disturbances. This tendency to exacerbation in myositis ossificans after the slightest injury to the tissues was first noted by Abernethy in 1830. In speaking of a case reported by him in Cooper's Surgical Dictionary he remarks:

"The least blow or other injury would cause an exostosis or an ossification of some muscle or ligament, till he was perfectly crippled."

The movements of the spine in our patient are, as you see, not restricted, and there are no curvatures. The sacrum, however, is extremely short and there is a marked increase in its normal curvature.

Shortness of the sacrum has been noticed in other cases of myositis ossificans. The fact that the spine as a whole is not affected is rather remarkable, for in a large proportion of cases of ossifying myositis the muscles of the back and of the neck have been first affected and bony foci, which have various arrangements, have formed in them. Freke and Copping both compare them to the ramifications of coral and Minkewitsch speaks of a case in which they resembled stag's antlers. In Crawford and Lockwood's case they had the form of the letter H. Ossification of the cervical ligaments and of the muscles of the neck may cause the head to be bent forward and the neck to be fixed in that position, and ossification of the gluteal muscles with fixation of the iliofemoral articulation causes the hips to be fixed at the pelvis, in a position that, together with the bending forward of the head, displaces the center of gravity and causes a precipitate stooping gait, like that of an old man. This attitude and gait are very characteristic when present.

Examination of the genito-urinary system yielded negative results. When the patient was admitted to the hospital, it is true, the urine contained some albumin and also numerous casts, but it has since cleared up. On a renal test diet there was no nocturnal polyuria, though there was a slight tendency to hypostenuria.

What was found on examination of the blood? Was there any leukocytosis?

STUDENT: The white blood-corpuscle count was 8000 and the hemoglobin 90 per cent. The Wassermann test was negative. A differential count showed 65 to 70 per cent. of polymorphonuclear cells. There was no eosinophilia.

DR. BARKER: This disposes of the question of trichiniasis—a diagnosis that suggested itself when the patient first entered the hospital on account of soreness and tenderness of the muscles and the edema of the face. Dr. Thomas R. Brown has shown, you will remember, that in trichiniasis we have an outspoken eosinophilia. The blood-pressure is now 160. It has been ranging from 160/90 to 140/88; there is thus a slight arterial hypertension, which, associated

with a history of albuminuria and cylindruria, points to the existence of a nephropathy.

On examination of the nervous system we find that his psyche presents no abnormalities. There are no objective disturbances of sensation. The eye-grounds are practically negative. Motility is restricted because of the pseudocontractures, and there is some muscular atrophy from disuse. All the deep reflexes are somewhat diminished and some of them (periosteal, radial, and knee-jerk) cannot be elicited. The plantar reflexes are normal. The abdominal reflexes are active. There is no disturbance of sphincter function. The pupils react normally.

Let us now summarize the main points of this case: We have before us a young colored man, only nineteen years of age, whose ill health began when he was twelve, with a skin eruption lasting three weeks and followed almost immediately by an illness characterized by pains in the muscles, irregular but high fever, cough, hemoptysis, and night-sweats. The muscular pains began during the attack of fever. He had difficulty in moving the muscles affected, and was bedridden for several weeks. After this he improved and went back to work, though he was handicapped by inability to extend his arms and legs; he was later forced to give up work and to return to bed on account of pain in the muscles and cramps. In this and other later attacks he did not have much, if any, fever. When he again improved he got up and crawled about on all fours. He could, however, feed himself, not being so badly off in this regard as Crawford and Lockwood's patient, whose food had to be placed on a chair so that he could "take it into his mouth like a dog does." Afterward, our patient was able to sit up in a chair, and continued to improve gradually until he reached the point where he is now. Note that the fever began after the eruption had cleared up; then, after it subsided, he developed pseudocontractures due to organic changes in the muscles and connective tissues, causing shortening and permanent flexion malpositions. He has had some pains and paresthesias in the extremities. It was at this stage that he came to this hospital to see if we could help him.

Our examinations showed that the muscles were tender and disclosed the presence of calcified lumps in the muscles and in the subcutaneous tissues of the arms and legs. Massage of the muscles caused marked increase in soreness and some fever. The arms could

not be extended beyond an angle of 150 degrees at the elbows, and the legs could not be extended beyond an angle of 90 degrees, owing to pseudocontractures. The normal elasticity of the muscles is lost, they are decreased in volume, and their consistence is greatly increased, as though they were partly fibrosed. There has been recurring tachycardia with slight irregular fever. There is pyorrhea alveolaris, a slight nephropathy (with albuminuria, cylindruria, and slight arterial hypertension). The superficial reflexes are normal, but the deep reflexes are diminished and some of them are lost. There are certain atrophic and pigmentary changes in the skin and peculiar purplish striæ in the skin corresponding to the course of the superficial veins of the legs. The left testis is small and soft, but there is a history of priapism. A number of congenital anomalies are present, including a short sacrum, web-toes, a slight hallux valgus, moderate microdactylism, and a supernumerary digit attached to the little finger of the left hand, the last-mentioned anomaly having been observed in at least two other members of his family.

Evidently, in this man with a series of interesting congenital anomalies, we have to deal also with a crippling chronic disease which presents exacerbations and remissions, which leads to pigmentary and atrophic changes in the skin, and which causes fibrosis and calcification of the voluntary muscles and the connective tissues with formation of pseudocontractures.

From a study of this case, and of others more or less resembling it reported in medical literature, we can make only one diagnosis: It is a chronic myopathy and dermatopathy; it is probably an ossifying myopathy because, in cases that have come to autopsy, the microscope shows that the calcified nodules in the muscles are of the character of true bone; it is a progressive myopathy because the disease advances slowly for years, exhibiting periods of striking exacerbation and of quiescence; and it is a multiple myopathy because it affects a number of different muscles in various parts of the body one after another. In this particular case the degree of calcification is much less than one would expect after a course of seven years' duration.

We have before us, then, a case of chronic progressive ossifying multiple myopathy, a disease first observed in 1740. The name *myositis ossificans progressiva multiplex* was given to the disease by Münchmeyer in 1869, the term having been suggested to him by von Duysch. I have used the word "myopathia" in preference to

the term "myositis," since there is some doubt as to whether the disease is to be regarded as a true inflammation or as a neoplastic change accompanied by inflammatory reactions on irritation.

The disease seems to have a preference for the Anglo-Germanic race, only a few instances having been reported in the Latin races or in the mixed Latin peoples. Péteri and Singer, on analyzing 53 cases, found it distributed as follows: Germany, 23; England, 21; Russia, 5; Hungary, 2; Sweden and Austria, each 1. Goto in 1913 reported the first case in Japan.

It is emphatically a disease of early life, almost all cases beginning before the third decade. Lorenz found that 38 cases out of 45 began before the fifteenth year of life. One case, however, has been reported in which the symptoms did not make their appearance until the patient was fifty-four years of age.

There seems to be a general agreement that the disease is a congenital malady, though not hereditary. Kümmell reported a case in which the symptoms were noticeable fourteen days after birth, and in which the disease must, he thinks, have developed during intra-uterine life. In only one case, that reported by Burton-Fanning, has there been any history of inheritance; in that instance the patient's father had the same disease. There is another case on record where the father of the patient had microdactylism of the great toes, but presented no symptoms of "myositis." Our patient, you will remember, inherits his extra digit from his father, who did not have the disease of the muscles from which this patient suffers.

The disease occurs much more often in males than in females. Rolleston gives the proportion as 5 to 1. Some writers think it begins earlier in life in girls than in boys, but the evidence on this point is inconclusive.

The first manifestations of the disease to be noticed are, as a rule, swelling and pain confined to certain muscles with edema of the overlying tissues, some redness of the skin, more or less constitutional disturbance, and a slight elevation of temperature. These symptoms subside in a few days, but the affected muscle remains indurated, and finally, a hard tumor-like mass appears in it. In most cases a bony deposit eventually forms in this mass, but sometimes it remains as a fibrous tumor, though occasionally the mass disappears altogether and the muscle undergoes fibroid degeneration. In a few rare instances the muscle seems to return to its normal condi-

tion. Fibrillary twitching in the affected muscles, just as the morbid process sets in, was described by Münchmeyer, and has since been observed by Pincus and by Crawford and Lockwood.

After the first attack the disease usually remains stationary for a varying period, but sooner or later the same process involves other muscles, accompanied by the same symptoms, except that the recurrences may not be attended by a rise of temperature. The process of ossification proceeds very slowly, usually requiring from two to eight months, though Ferraton has reported a remarkable case in which the patient, who had been able to eat normally on going to bed, found when he woke in the morning that he could not open his mouth on account of the involvement of the masseter muscles. It is, of course, inconceivable that ossification or even calcification could take place this quickly. Eventually, if the patient live long enough, all the muscles in the body are likely to become involved. Even the muscles and connective tissues of the eye may be affected; Billroth and Zollinger have reported a case in which there were calcified plates in the choroid. In Crawford and Lockwood's case there were signs of ossification in the lower part of the *M. orbicularis palpebrarum*.

Let us now consider some of the diseases with which a chronic progressive multiple ossifying myopathy may be confounded. The first attack, or any acute exacerbation, might, like other forms of myositis, be taken to be trichiniasis on account of the pain and tenderness in the muscles associated with fever. Indeed, acute polymyositis is sometimes spoken of as "pseudotrachiniasis." Examination of the blood for eosinophilia and histological examination of a bit of excised muscle will determine the presence or absence of trichiniasis.

Our own patient, when first seen, was supposed to have arthritis deformans, but this diagnosis was excluded by both the general physical and the *x*-ray examinations, which showed that the joints are not involved.

The leontine expression of the face, associated with skin lesions, suggested leprosy, and this idea received some support from the fact that, on palpation, one of the ulnar nerves was found to be thickened. But the fact that the patient had never been out of Maryland and Virginia, and that closer examination showed the changes in the face to be due to edema, disposed of the idea of leprosy.

The skin in certain localities is rather firm and a little glossy, and scleroderma was thought of as a possibility; but the skin is nowhere attached to the subcutaneous tissue. Sclerodermal changes have been known to occur in connection with myositis ossificans. In our case the changes in the skin are doubtless due to the early dermatitis, followed by pigmentation and atrophy. In the various forms of myositis it is common to have an associated dermatitis, and the term "dermatomyositis" is frequently met with in the literature.

The pains and paresthesias with disability made one think of polyneuritis. The glossy skin in places, as well as the changes in the deep reflexes, might give further support to the idea. But the muscular atrophy is here an atrophy of disuse, not a degenerative atrophy, and there are no objective disturbances of sensation. What is the electrical condition of the muscles?

STUDENT: They have not yet been tested electrically.

DR. BARKER: We should have a careful electrical study of them. A combination of myositis and polyneuritis seems sometimes to occur, as in the neuromyositis described by Senator.

Lydia de Witt, who has written an excellent article on myositis ossificans, asserts that electrical tests, wherever they have been applied, have seemed to indicate an entire absence of any neuropathic factor, except in the cases of Pincus and of Kümmell, in which the faradic excitability was much reduced in the affected muscles; she considers this an additional reason for regarding the disease as purely myopathic. Goto tested the electrical reactions of individual muscles in ossifying myositis and found that the faradic and the galvanic excitability of those affected were definitely either increased or diminished, whereas the reactions of the apparently sound muscles were normal.

But, in addition to the demonstrable changes in the muscles themselves, what is most important of all as regards the differential diagnosis between myositis and polyneuritis in this case is the fact that there are no areas of objective sensory disturbances. Polyneuritis, therefore, can be readily ruled out as a cause of the main trouble. That is not to say that the nerves are wholly uninvolved in this patient. No doubt some of the little terminals of the sensory nerves in the muscles have been involved because of the pain, but this involvement is doubtless due to the muscular, fascial, and connective-tissue changes rather than to a primary neuritis.

Charcot's joint (tabetic arthropathy) and spondylitis deformans

are conditions that have, in certain instances, been confounded with myositis ossificans, but they would scarcely be thought of as possibly existent in our patient.

Osteitis deformans (Paget's disease), which has presented difficulties in diagnosis in some cases, does not appear until late in life, and when it develops it involves only the bones. On careful physical examination there should be no difficulty in discriminating between Paget's disease and ossifying myositis.

It must be clear to you, then, that in this patient the diagnosis must lie between chronic progressive ossifying multiple myositis (myopathy) and some other form of myositis that has led to fibrous changes and calcified areas in the muscles.

Acute hemorrhagic polymyositis, which is characterized by the presence of hemorrhagic foci in and between the muscles, is a rare disease. It usually follows tonsillitis and it often involves the myocardium. Few of the cases recover. My colleague, Dr. Thayer, reported an interesting case at the Association of American Physicians in 1902, and I would refer you to his article for an excellent clinical description of the disease.

The other forms of polymyositis (dermatomyositis, polymyositis with erythema multiforme, etc.) might also be confused with the ossifying myopathy. They may occur in childhood, but more often they begin late in life; they are not, as a rule, associated with congenital anomalies (though Dr. Walter Steiner (1900) has described a case of dermatomyositis in which there was a rare muscle anomaly), and they terminate after a short period (a few months to a year and a half) either in recovery or in death.

The form of myositis that we have under consideration, on the contrary, begins almost invariably during the first two decades of life, and in some instances has begun shortly after birth. In the large majority of cases it is associated with congenital malformations of some kind, about 75 per cent. of all cases being accompanied by microdactylism, in addition to which there may be hallux valgus, web-toes, and other abnormalities. Finally, recovery never takes place, though death may not occur for an indefinite period.

Now we have here today a man in whom the disease began at twelve years of age. It has lasted seven years and he is quite crippled by it. In his case the disease of the muscles is accompanied by microdactylism, hallux valgus, polydactylism, web-toes, a congenital

defect of the sacrum, and an abnormally small testis. He also presents the characteristic signs of a progressive disease in recurrent attacks of swelling of the muscles, accompanied by soreness, pain, and sometimes by fever, as well as by pigmentation and atrophy of the skin. The x-ray examination shows calcified areas under the skin with evidence of involvement of the muscles with calcification in different parts of the body. The clinical picture is complete, and I believe there can be no doubt that we have here a case of *chronic progressive ossifying multiple myopathy (myositis)*.

The clinical diagnosis being established, we have next to consider the exact nature of the pathological-anatomical process in the disease. There has been much controversy for more than half a century as to how the pathological-histological findings in this particular affection are to be interpreted. Two main opinions have been advanced: (1) that the bone formation is the sequel of an inflammatory process; (2) that it is the result of a definite tumor formation. Virchow regarded the disease as being upon the borderline between inflammation and new growth. Goto has recently, like Virchow, avoided the tumor theory, on the one hand, and the inflammatory theory on the other; he asserts, also, that we are dealing not with a primary disease of the muscles, but with a disease of the fibrous tissue in the muscles—a *hyperplasia fascialis*, and suggests that the name “hyperplasia fascialis ossificans progressiva” be substituted for the term now in use to designate the malady. There is much, I think, to be said in favor of this terminology.

Some other theories of minor importance concerning pathogenesis have been advocated. Nicoladoni, Eichhorst, and others believed the disease to be a trophoneurosis accompanied by changes similar to those seen in progressive muscular atrophy or hypertrophy, except that the process is more extensive and that the final result is ossification. Stoneham considered it a rheumatoid arthritis. Brehnson considered it a reversion to a lower type of tissue due to atavistic influences. Michelsohn believed that it represents a blood anomaly due to chemical and bacteriological irritants, and Krause and Trappe have asserted that it is a chronic infectious disease from the origin of which lues cannot be excluded.

The histological findings at different stages of the disease are very interesting. The first microscopical examination of tissue removed from the affected muscles was made by Cesar Hawkins in

1844, and the second by Minkewitsch in 1857. The descriptions were fragmentary, however, until Münchmeyer's classic article appeared in 1869, in which he described the process of bone formation with accuracy and recognized three stages in its morbid anatomy. His description is so clear that it has been accepted as valid ever since. He divides the morbid process into three stages:

1. A stage of infiltration with cells of embryonic type
2. A stage of connective-tissue induration.
3. A stage of ossification.

The first stage he regarded as a definite inflammation of both intramuscular and intermuscular connective tissue, with marked proliferation of embryonic connective tissue. In other words, there is at this stage, in his opinion, a fairly acute interstitial myositis, the muscle-fibers themselves being affected only secondarily. In the second stage the embryonic connective tissue becomes organized with formation of adult connective tissue, which later undergoes contraction, giving rise to a hard fibrous swelling, which, on section, resembles the tissue of a fibroma. Toward the middle of the fibrous swelling there are small angular spaces in which lie formative cells that later become osteoblasts and bone corpuscles. In the third stage ossification actually takes place in the fibrous tissue. Compact or spongy bone is formed in fascia, ligaments, and tendons; this resembles true bone both histologically and chemically.

Poggiale made a chemical analysis of dried portions of the new formations removed, and in 100 parts found 58 per cent. of organic matter and 42 per cent. of inorganic, proportions that agree with the view that the bone thus formed is softer comparatively than normal bone.

On thinking over the problem of the nature of the disease, it seems to me that the mode of onset, with fever, local swellings and tenderness in the muscles, and general lymph-gland hyperplasia, betoken an acute inflammatory process at the onset, probably of infectious origin. But this becomes later a chronic productive inflammation, first giving rise to granulation tissue, and later to adult fibrous tissue. The calcification and ossification can, I think, be viewed as a metaplasia rather than a neoplastic process. It is, of course, conceivable that an acute polymyositis of infectious origin may be the starting-point of another disease that is not inflammatory, say a hyperplasia fascialis in the sense of Goto.

The occurrence of this ossifying interstitial myopathy practically always in association with microdactylism, web-toes, or other congenital abnormalities is a very interesting feature of the disease. It indicates, I think, that there must be a congenital disposition to this particular malady. The congenital abnormalities point to a faulty development of the mesoblastic tissues, and probably the peculiar susceptibility to fascial and interstitial inflammations is also dependent upon a faulty mesoblastic development.

Rolleston, who has also been struck with the part played by the mesoblast in this disease, says that:

"Myositis ossificans depends upon (a) a congenital weakness and want of resistance and (b) a tendency to aberrant growths on the part of the mesoblast. As the result of diminished resistance the muscles are most susceptible to inflammation, while the tendency to aberrant growth subsequently shows itself in the calcification and ossification of the inflammatory products. . . . The mesoblast is very much more prone to irregularities of growth than either the superficial skin layer (epiblast) or the lining of the alimentary canal (hypoblast). Growths of the mesoblast tend to be multiple. A number of diseases seem to depend on some congenital aberration of development and growth in the mesoblast."

Rolleston, in discussing diseases of the mesoblast, points to the fact that it can be divided into two layers, namely, a tegumentary layer and a skeletal layer, each of which may again be divided into two, thus:

(1) *Tegumentary layer:*

- (a) Superficial layer. Junction of epiblast and mesoblast. Affected by molluscum fibrosum and generalized neurofibromatosis.
- (b) Deep layer. Affected by multiple fatty tumors.

(2) *Skeletal layer:*

- (a) Muscular layer. Affected by myositis ossificans and by the atrophic myopathies.
- (b) Bony layer. Affected in multiple exostoses and in enchondromata.

Thus, according to Rolleston, there is a very interesting group of mesoblastic diseases, each of the four sublayers being affected by its own special group of pathological conditions.

Some excellent pathologists, however, among them Steiner and De Witt, regard myositis ossificans as a true tumor formation. Warthin also believes that the bony growths are true neoplasms in the progressive form of the disease. though he admits that in the localized variety (myositis ossificans circumscripta) the process of ossification is an inflammatory one. The exercise and rider's bones that occur in the circumscribed form are, he thinks, an atavistic reversion to the splint bone of lower animals.

In regard to the *etiology* of the disease nothing definite has been established beyond general acceptance of the view that influences

of congenital nature are of importance, in the sense that the disease depends upon some congenital aberration of growth. The malady is not hereditary, but some authors assert that the congenital deficiency underlying it is likely to occur most frequently in those who have a family history of certain diseases, especially tuberculosis, cancer, rheumatism, and possibly lues. But the evidence on this point is scanty and imperfect. Since tuberculosis, carcinoma, and rheumatism are frequently present in family histories in general, it seems probable that we might find the same amount of evidence concerning them in the histories accompanying any disease, or even taken at random. The evidence for lues as a causative factor is almost *nil* except in D'Ovidio's case, already mentioned, in which the Wassermann reaction was positive. Pincus was strongly of the opinion that obstetrical injury is a frequent cause, but he does not bring any evidence in support of his view, nor have I found anything in favor of it in cases reported since the publication of his article. It is conceivable, of course, that trauma at birth, like trauma later, may act as an exciting cause, for there can be no question that trauma plays by far the largest part among exciting causes. In a number of cases the initial symptoms have followed definitely upon a fall or a blow, the swelling appearing at the site of the injury. The number of instances in which subsequent exacerbations have followed such accidents is smaller, though by no means small, and when we consider that the symptoms, both local and general, have been provoked by injuries so trivial as palpation of the tissues, massage, the removal of bits of muscle for microscopical examinations, or even by subcutaneous injection, it seems reasonable to suppose that there may not infrequently be cases in which the attacks are excited by trauma so slight in its nature as to pass unnoticed. Unsanitary surroundings, exposure to cold and to dampness have been cited as predisposing causes, and in one case the first attack took place after the patient, who was wet through, had sat for some time in his wet clothes.

The *prognosis*, so far as recovery is concerned, is hopeless. As a rule, the patient dies before many years, generally from some intercurrent affection of the respiratory organs resulting from the fixation of the ribs and consequent interference with breathing. Pincus mentions 3 cases in which death took place from miliary tuberculosis. The characteristic periods during which the disease remains stationary

sometimes extend over a considerable length of time. Cases have been reported in which the malady remained *in statu quo* for six, ten, or even, in one instance, for twenty-three years. Gibney reports a case in which the disease made no progress for ten years, during which time the patient was able to earn her living in a factory. The only instance in which actual improvement has been reported is one mentioned by Stephen Paget, who, when reporting a case of his own, alluded to one of his father's, in which ossification had proceeded so far that the ribs were firmly fixed, in spite of which the patient, ten years later, was able to write to the following effect:

"The whole front from throat to pelvis is better. I remember your gesture of despair when you found no movement of chest and sides on my drawing a breath. Now the chest and sides move very well, not properly, of course, but not badly."

No form of *treatment* has proved of any avail. Various drugs have been tried at different times, among them mercury, iodid of potash, colchicum, lactic acid, and phosphoric acid, but all without any beneficial results. Paget's patient had taken salicylate of soda steadily during the ten years in which he had improved, though how much it had to do with the improvement is doubtful, as it has been given in other cases without benefit. Of late years thyroid extract has been tried, and in Weber and Compton's case a subcutaneous injection of Merck's fibrolysin was employed, but it was followed at once by the appearance of bony plates at the site of the injection. Counterirritation has been found to give some relief in attacks of fresh swelling and pain.

Operation was first tried by Cesar Hawkins in 1844. He removed a bony mass, situated between the trapezius and the rhomboid muscles and intimately associated with both, in the hope of giving freer movement to the arm. The operation was followed by excessive hemorrhage from which the patient was a long time in recovering, and there was no improvement in the mobility of the arm. No further attempts at operative treatment in the progressive form of myositis seem to have been made until 1891, when a New Zealand surgeon, R. G. MacDonald, made an effort to give relief by means of operation in a case in which the arms were completely fixed. The *teres major*, which was completely ossified, was removed *en masse*, but without any improvement in mobility. The following year, 1892, Pollard, an English surgeon, removed a lump of bony deposit from

the teres major, with apparently good results, the operation being followed by increased movement of the arm, but this was soon lost again. In 1894 Gibney, of New York, divided an ossified tendon of the right latissimus dorsi and took out a dense, hard piece of bone about an inch wide, but a new bony mass, larger than the first, formed within the cavity in a short time. In 1913 the Japanese surgeon, Goto, operated repeatedly upon a case, which he reported that year, partly in the hope of improving the mobility of the arms and partly to obtain material for histological investigation. The first operation, at which a piece of bone was excised from the tendon of the right latissimus dorsi with a hammer and chisel, was followed by a fresh swelling at the site of the wound. A second operation was done in order to obtain a specimen of the new material then forming for examination, and this was repeated until five operations in all had been performed, each one being followed by fresh manifestations of the disease at the site of the incision. There was no improvement in the condition of the patient. Goto claims that microscopic examination of the fresh specimens supports his view that the disease is a simple hyperplasia of connective tissue without true inflammation.

[*Further History of the Case.*—The patient remained in the hospital for some months. A piece of skin and a piece of muscle were excised from his arm and a gland from the axilla. No marked signs of chronic inflammation were found in the tissues excised, doubtless because unaffected areas were excised. A culture made from this specimen showed a non-motile, Gram-positive, pleomorphic bacillus.

Electrical examination in the dispensary showed the biceps in both arms to be normal in their response to both the faradic and the galvanic current. The other muscles of the arms manifested some decrease of response to both forms of current. The legs gave practically no response in the quadriceps group. Other muscles showed a decreased reaction to both currents. There was no true reaction of degeneration.

After examination in the Orthopedic Department it was decided to try forcible extension in the hope that a better position of the lower extremities might be obtained. Both legs were accordingly extended under general anesthesia and put up in casts at an angle of about 115 degrees. There was some pain afterward, which subsided next day. Two weeks later the forcible extension was repeated, the right knee being now held almost straight. The patient had

some pain in the back after this second extension of the legs. After an interval of nearly four weeks the legs were manipulated and straightened to an angle of 160 degrees. This treatment was followed by considerable pain in the back and legs, which subsided in the course of a few days. At this time it was noted that the tachycardia still continued and the temperature often reached 99° F. Four weeks later the casts were removed. The skin was in good condition and the position of the legs was corrected to some extent. The patient was discharged a little later, with instructions to return in two months for further observation. He has never reappeared, and at the time of publication (1922) no further information concerning him has been obtained.]

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DISEASES OF THE NERVOUS SYSTEM

XX. A PSYCHONEUROTIC PRESENTING THE CHRONIC INVALID REACTION

ASTHENIA, ANOREXIA, NAUSEA, AND OTHER SYMPTOMS OF A REACTION OF CHRONIC INVALIDISM IN AN EMACIATED YOUNG WOMAN OF NEUROPATHIC ANCESTRY; DISCUSSION OF THE TREATMENT AND PREVENTION OF SOME OF THE PSYCHONEUROSES.

AMONG the more striking advances in medicine during the past thirty years has been the increase in knowledge concerning psychoneurotic states.

At the time of my graduation in medicine (1890) most medical men had but little, if any, conception of the importance of psychiatry. The attention of medical students was focussed by clinical instructors upon the detection of evidences of pathological-anatomical changes in the organs. Interest centered in changes in structure rather than in alterations of function. No one thought of studying psychology or sociology as a preparation for medicine. Indeed, the academic psychology and sociology of that time would have been of little help to the prospective physician. Even later on academic psychology was divorced from life, being interested mainly in so-called physiological psychology and pure introspective psychology rather than in characterology and in the personality studies that have in recent years become so interesting and so important for medical men. New life was, however, soon to be infused into psychology from two main sources: (1) that of the comparative psychologist and (2) that of the psychopathologist.

The comparative psychologist, studying the behavior of animals, supplied us with a wealth of detail regarding the fundamental animal instincts, and this knowledge was gradually applied to human beings, and was supplemented by the behaviorists, who laid all emphasis upon conduct—upon what a man does as contrasted with what he thinks and feels. Many old adages, such as "Actions speak louder than words"; "As a man acts, so he is"; "By their deeds ye shall know them," received the approval of the behaviorists. The ob-

servational method of studying conduct in man was thus greatly helped by the growth of animal psychology. Biologists, in general, were interested in studies of adjustment of adaptation of organisms to their environment. Growth and the capacity for adjustment is characteristic of the development not only of an individual, but of a race, and the students of social psychology soon found that many social problems, for example, crime, insanity, delinquency, vagabondage, prostitution, and neurosis, are intimately related to failure on the part of individual members of society to make adequate reactions of adjustment.

The second important source of the newer knowledge of psychology has been the study of behavior and of mental phenomena in diseased human beings. Just as the study of normal physiology received a great impetus from the study of human pathology, so knowledge of normal psychology has of late years been greatly enriched by students of psychopathology. The observations of febrile deliria, of toxic-infectious psychoses, and of human behavior in dementia paralytica and in arteriosclerotic dementia, had a revolutionary effect upon the attitude of medical men toward psychology.

In addition to these two main sources of the newer psychological knowledge there are other contributory sources that are scarcely less important. Thus, studies of childhood psychology, of the psychology of adolescence, and of the comparative psychology of individuals led to a rapid increase in the general knowledge of human psychology, and to a growth of interest in the genesis of mental states and their associated behavior. Through all these studies it gradually came to be recognized that researches bearing upon the affective life and upon the conative functions are fully as important as those bearing upon cognition. The domain of the subconscious began to be explored. The importance of race psychology and of folk psychology for the understanding of human motives and human behavior began to be realized.

Medicine as a whole was not in a position to profit by the newer studies in psychology until medical students could be taught psychology and psychiatry in the medical schools. It meant a real step forward for medical practice when psychiatric clinics developed in Europe and, later on, in this country. Still later, psycho-analysis, as a method of study and as a form of treatment of the psychoneuroses, came into vogue and gave rise to violent discussions that

have stimulated medical men in all countries to greater interest in the psychic life of their patients. This last thirty years, then, has been a most interesting period for mental pathology, as well as for pathological physiology and biochemistry. The practitioner of today, in his work as trouble-adjuster, considers not only the soma, but also the psyche and the social *milieu* of his patient.

In this hospital we try to study the mental side now as well as the physical side of our cases. Even in the public wards of the hospital the mental states as well as the physical states are considered, but it is in the private wards that we gain, perhaps, our largest experience in the treatment of psychoneurotic states and of the minor psychoses. The private wards of the medical clinic always contain a number of cases that belong in the borderland between internal medicine and psychiatry, and in the psychiatric clinic, of which Professor Adolf Meyer has charge, you have opportunity as students of observing not only similar borderland cases but also patients manifesting outspoken major psychoses that cannot well be cared for in the medical clinic proper. You who study medicine today have thus a great advantage over students of earlier times for whom no such facilities for psychic and psychiatric studies were provided.

The hour of the clinic today is to be devoted to a consideration of a patient who was under treatment in the private ward last year. Unfortunately, I cannot bring the patient before you; but I shall ask the resident physician, Dr. John Dorsey, who had immediate charge of the case in the private ward, to tell you of the history.

DR. DORSEY: The patient, a young married woman, aged twenty-two, entered the private ward service complaining of "nausea, weakness, and total lack of appetite."

Though she had never been strong, she dated the onset of her present severer symptoms to a period following an operation for the removal of tonsils and adenoids some eighteen months before. There seems to have been considerable loss of blood at the operation. She stated that she became very weak, lost her appetite, and had continuous nausea for four months. Then she had a three months' respite, but after this the nausea returned and continued for another three months. The patient then became a little better and married. She felt fairly well for the first four months after marriage. But the nausea again returned and persisted for another five months, at the end of which time she applied to Dr. Barker for treatment.

Her symptoms had by this time become distressing. The nausea was sometimes very severe and not infrequently was accompanied by vomiting. On one occasion she vomited no less than eight times in twelve hours, and the vomitus was once streaked with blood. She stated that she had some epigastric pain which was unrelated to meals, and not relievable by the ingestion of food. More distressing even than the pain was a feeling of "faintness" in the epigastrium. Gaseous eructations were also troublesome. The symptoms complained of included headaches, especially at the menstrual period, frequent attacks of faintness, occasional dizziness, frequent night-sweats, nervous rigors, especially under excitement or when meeting strange people, palpitation and pain about the heart, indigestion, backache, recurring urticaria, fatiguability, emotionalism, a tendency to worry, and unpleasant dreams. As a result of her anorexia and nausea she had taken very little food, and had steadily emaciated. Though her ideal weight was around 116 pounds, she had remained below 100 pounds in weight for some months, and shortly before admission she had been losing flesh rather rapidly. The patient declared that her symptoms had made her an invalid for at least eighteen months.

Asked regarding her health before the onset of the present illness, the patient stated that she had never been strong. In childhood she had measles, mumps, chicken-pox, whooping-cough, diphtheria, and repeated attacks of malaria. Some seven months before admission she suffered from a rather severe attack of influenza. She was subject to frequent sore throats, and for this reason underwent the operation for tonsillitis and adenoids already referred to. Some four years ago she went through a severe attack of colitis. Throughout life she had had a feeble digestion, and she gave a history of two attacks that were strongly suggestive of appendicitis. In the hope of improving her digestion she had about nine months before admission undergone appendectomy.

She stated that she was happily married; that she was fond of her husband and he of her. She has never become pregnant. Her menstruation had begun at the age of fifteen, but was never regular. Slight changes of climate would interfere with the menstrual flow, and there was considerable dysmenorrhea and menorrhagia. At the time of the period she was always exhausted and had to stay in bed. Her increasing weakness interfered with her participation

in activities of various sorts. Even riding in an automobile was followed by exhaustion, and for three years before admission she had stopped playing tennis, a game that she had formerly enjoyed.

At the first physical examination made by Dr. Barker on her admission to the private ward she was found to be very much undernourished; had a gracile, bony framework, and thin, pale, moist skin. There was fine tremor of the extended fingers, but no tachycardia and no struma. There were slight eye signs of hyperthyroidism, and there was general hypotrichosis, though the distribution of the hairs was normal. Aside from the scar of the appendix operation the examinations of the abdomen and thorax were negative. There were no discoverable signs of organic disease of the nervous system; the deep and superficial reflexes and the pupils reacted normally, and the eye-grounds looked healthy.

A pelvic examination made by Dr. E. H. Richardson revealed nothing abnormal except a moderate hypoplasia of the genital organs and a few hemorrhoids.

The eyes were examined by Dr. Alan Woods, who found hyperopic astigmatism, but normal eye-grounds.

DR. BARKER: Will you tell us of the laboratory tests that were made?

DR. DORSEY: The *blood* was normal except for a slight secondary anemia. R. B. C., 4,204,000; hemoglobin, 80 per cent., and W. B. C., 8500. The differential count showed: Polymorphonuclear neutrophils, 70 per cent.; eosinophils, none; small mononuclears, 24 per cent.; large mononuclears and transitionals, 6 per cent. There was no anisocytosis and no poikilocytosis. The platelets seemed to be present in normal numbers.

On examination of the *stomach contents* there was a slight subacidity. Free HCl, 2 ac. per cent.; total ac., 33 ac. per cent. No occult blood; no lactic acid. A second examination of the stomach contents made a little later showed free HCl, 18 ac. per cent.; total ac., 36 ac. per cent.; no occult blood; no lactic acid.

The examination of the *feces* revealed nothing abnormal.

The *urine* was quite normal except for a faint trace of albumin, demonstrable at times; but no casts were found and no red blood-corpuses. Occasionally a few white corpuscles could be seen in the urine. The urine was free from sugar. The renal function was good, the phthalein output being 67 per cent. in tw^o hours.

DR. BARKER: What x-ray examinations were made?

DR. DORSEY: Roentgenograms of the paranasal sinuses of the skull, of the lungs, and of the gastro-intestinal tract were made. Except for signs of a few possible adhesions in the right lower quadrant of the abdomen (the site of the preceding appendix operation) nothing abnormal was demonstrable.

DR. BARKER: You did not mention the Wassermann reaction. Was the test made?

DR. DORSEY: Yes; a Wassermann test is made on every patient entering the private ward for study and treatment. It was quite negative in this patient.

DR. BARKER: Had she any trouble with the teeth or gums?

DR. DORSEY: She was sent down to the dental clinic for examination. The consulting dentist reported that there was non-suppurative gingivitis that should be treated, as it might be a slight focal factor. There was no evidence of periapical infection of any teeth. The wisdom teeth were unerupted, but were not impacted.

DR. BARKER: On account of the tendency to palpitation, the sweating, the nervousness, the emaciation, and the eye signs, the thyroid functions were investigated. Will you tell us the result?

DR. DORSEY: In addition to the signs you have mentioned, there was marked fine tremor of the fingers and, under observation in the hospital, there were periods of slight tachycardia. There was no demonstrable struma. The Goetsch test for epinephrin sensitivity was, however, positive.

DR. BARKER: Was the rate of basal metabolism measured?

DR. DORSEY: Yes; Dr. John H. King, Jr., tested the basal metabolism and found it 0.4 per cent. below the average for the patient's age and sex, indicating a strictly normal metabolic rate.

DR. BARKER: You stated that the tonsils and some infected adenoid tissue had been removed before the patient came to the hospital. Were there any signs of nose and throat disease, or of disease of the paranasal sinuses on examination here?

DR. DORSEY: Dr. Crowe went over the nose and throat very carefully. He found no evidence of any infection of the nose, throat, or paranasal sinuses. She had complained of some pain in the ears, but the examination of the ears was negative.

DR. BARKER: I lay great stress upon a thorough, general, diagnostic survey preceding the institution of treatment in every patient

exhibiting a psychoneurotic state. It would be a great mistake to start in with the treatment of a psychoneurotic patient before ruling out, by careful diagnostic methods, the existence of demonstrable somatic disease. When the findings are negative not only is the patient greatly reassured, but the physician can go ahead with the general treatment in full confidence that nothing important on the somatic side can have been overlooked. The establishment of this confidence at the very beginning of treatment of a psychoneurotic case is of real importance both for the patient and for the physician. Many psychoneurotic patients fear the existence of some obscure disease that the physician has not discovered. The removal of this fear is most helpful to many of these patients. Moreover, I can scarcely understand how a conscientious physician can willingly enter upon a long upbuilding and psychotherapeutic cure of a patient before he has satisfied himself that he has ruled out discoverable somatic disease by careful diagnostic methods. His ability to reassure the patient from time to time would otherwise be hampered by a personal feeling of insecurity regarding the matter; he would himself always be wondering whether he might not have overlooked something of importance on the somatic side, and the patient would sooner or later become conscious of this feeling of insecurity on the part of a physician. If somatic disease be found in a psychoneurotic patient, it is important to do all that is possible to get rid of it, for organ inferiority in the patient is prone to be accompanied by feelings of inferiority. Sometimes there is organ inferiority that cannot be relieved, and when this is true, the problem of mental adjustment is made more difficult. In the patient under consideration the marked undernutrition, the gastric subacidity, the secondary anemia, the genital hypoplasia, the refraction error, the slight oral sepsis, the slight thyreopathy, and the accompanying autonomic disturbances are all of interest and merit due consideration.

Was there anything especially interesting in the family history of the patient?

DR. DORSEY: Yes; the patient comes of neuropathic ancestry. Her father, though a successful business man, had what she calls a nervous breakdown. He was under treatment for four months in the private ward of this hospital not long ago. He made a good recovery and, according to the patient's report, has been well ever since.

DR. BARKER: I remember this patient's father very well. He was undernourished and depressed and showed many inhibition symptoms. I thought that he suffered from a mild form of a manic-depressive psychosis.

How about the patient's mother?

DR. DORSEY: The mother of the patient, according to the daughter's account, suffered from "nervous prostration" about twenty years ago. She has been exceedingly nervous ever since, though she lives at home and is at present getting along fairly well.

DR. BARKER: Considering the history of the parents of this girl is it any wonder that she herself has nervous symptoms? With the fusion of germ plasms from two parents of this sort she must certainly have inherited a neuropathic predisposition.

I lay great stress upon neuropathic heredity. It is much more important than many people seem to think. There is a tendency on the part of some to discount heredity altogether, and to lay all the stress upon environment. There is a tendency on the part of others to attribute everything to heredity, and to minimize the effects of environmental influences. Both attitudes are wrong. Heredity and environment are, of course, both important.

In this connection I should like, however, to emphasize one point particularly, and that is this: Much that is attributed to heredity may, in reality, be due to psychic contagion during childhood. A child born of nervous parents is all too likely to be subjected to most pernicious influences of example in childhood. As you have heard, this young woman's mother has been a nervous invalid for twenty years, and her father has had a nervous breakdown, a mild melancholy of some months' duration. You can easily imagine the family influences to which, as a child, our patient has been subjected. So important are such influences upon children that I thought it worth while, some time ago, to write about the subject two articles, namely, *The Principles of Mental Hygiene Applied to Children Predisposed to Nervousness* (1911) and *How to Avoid Spoiling the Child* (1919). I think you may be interested in reading these two articles. Many general practitioners have told me that they have found the pamphlets helpful for the instruction of parents whose children are predisposed to nervousness.

Let us turn next to a brief consideration of the personality of our patient. To become well acquainted with a patient's personality

requires some time. The preliminary rest cure that many of these patients need gives opportunity for the establishment of a personal *rapproch* with the patient and for the gradual acquisition of insight into the patient's psyche. It is, however, desirable during the general diagnostic survey made at the very beginning to inquire into a whole series of points regarding the preceding mental and social life of the patient. We are very fortunate here in having the hearty co-operation of the staff of the Psychiatric Clinic in our general diagnostic surveys. I have been greatly helped in the understanding of many of my patients by reports on the mental state from one or another member of the psychiatric staff. In the present instance Dr. Esther Richards was good enough to examine the patient from the psychopathological side. Will you please read her report?

DR. DORSEY: Dr. Richards' report was as follows: "The patient is the victim of an unfortunate environment and training. She has been brought up to believe that she is by natural endowment too frail to face any of the concrete issues of life. The mother has, to a large extent, lived the patient's life for her, planning her activities and making her decisions. The husband is the only member of the family who has interfered with the mother's domination. The patient wavers between these two influences, being quite willing to make her nerves the scapegoat. Her dreams are somewhat poorly disguised escapes; either she is being kidnapped from her family or they meet with disaster and die. The patient's condition appears to belong to a chronic invalid reaction on a situational basis."

DR. BARKER: Such a report gives a number of clues for the psychotherapeutic handling of the patient after treatment has been begun. Though brief, such a report gives you an idea of the help that a psychiatric consultation can yield. Let me urge upon you during your student period in the medical school to take advantage of every opportunity offered you in the Psychiatric Clinic. You will be surprised, when you come, later on, to engage in general or in special practice, how helpful the training you have received in the Psychiatric Clinic will be to you.

I shall ask Dr. Dorsey to tell you now of the treatment that has been followed in the case under consideration.

DR. DORSEY: After the diagnostic study had been completed the patient was told fully and frankly of her condition. An effort was made to explain the situation to her in as simple a manner as

possible. Nothing of importance that had been found out was withheld from her, and she readily consented to follow the treatment that was outlined for her.

DR. BARKER: After the patient's condition had been explained to her, I told her that I saw no reason why she should not recover; that we had found no serious organic disease; that her bodily health could be very much improved, and that I believed that, if she would co-operate, she would be able gradually to get back to a much more normal life. She asked, of course, of what the treatment would consist. I told her that it would be necessary for her to stay for at least some weeks under treatment, away from her family and without direct communication with the family. The reason for this isolation was carefully explained to her. She was told that she would stay in bed at first under the care of a special nurse in the daytime, who would assist the physician in building her up and making her gain weight. The presence of the special nurse makes the isolation easier to bear. Though allowed no visits and no letters, she was told that, if anything went wrong at home that she should know, we would tell her, and that her nurse would report regularly to her family of her condition. If she got no word of anything going wrong at home she was to understand that this was the equivalent of having a message each day that everything was all right at home.

As the patient feared food and suffered much from nausea and vomiting, she was placed at first upon "Dubois diet," which, as you know, consists of milk every two hours and no other food. Many of the psychoneurotic patients assert that they cannot take milk, but it is rare that we find a patient who is really unable to take it. There may occasionally be an idiosyncrasy, but the majority of people who believe that they suffer from this idiosyncrasy do not do so at all. After a few days of milk diet most of these patients can be placed upon a full diet regardless of choice, and find that they can bear it very well. Other patients are not able to go, at once, upon full diet. A trial was made of full diet with this patient early in the treatment, but she had so much difficulty in eating the food, and in keeping it down, that we returned to a milk diet and kept her on 3 or 4 liters of milk per day for a longer time. Occasionally she would vomit the milk, but even if she did so, milk was again administered at the next regular period. She was told that it did not matter if she did vomit occasionally, that she was to take the

milk any way, whether she vomited or not. After a few days the patient was able to retain most of the milk and she gradually began to gain weight, though she complained bitterly and continually of nausea and of anorexia.

I have found the use of this form of milk diet at the beginning of the treatment of the undernourished psychoneurotic most valuable. With the psychoneurotic it is essential to establish medical obedience at the very beginning, and the easiest way to establish it is by means of some such régime as I have mentioned, instituted after the patient's confidence has been gained through the thorough diagnostic survey and the judicious manifestation of interest in and sympathy with the patient.

Once you get the patient to co-operate, even in such matters as the taking of food, rest in bed, and isolation, you have gone far toward success in the upbuilding treatment. It is not at all uncommon to see patients gain from 3 to 6 pounds per week during a rest-cure period. Weir Mitchell, in his *Fat and Blood and How to Make Them*, followed this technic of fattening the undernourished patient.

Not that all psychoneurotics are undernourished. We get some fat psychoneurotics, and have to reduce them. But there are far more undernourished than overnourished psychoneurotic patients.

Many of the patients have a morbid fear of becoming fat, and we always assure them that we do not intend to make them gain beyond their calculated ideal weight. We also tell them that we will do our best to distribute the fat in a suitable way over the body. Many of the patients complain that the increased amounts of food give them indigestion; that they suffer from abdominal pain; that they feel distended; that they have much gas; or that milk constipates them. We listen to these complaints, but we ask the patient to ignore them. We point out to them that they are under close observation, that no indications for surgical treatment have been discovered, but should they appear they will be met. We tell them that we want them to bear the symptoms for the time being, and explain to them that they have so long been accustomed to taking an insufficient amount of food that they must expect some unpleasant sensations on taking larger quantities of food.

After the milk period is over and solid food is given we usually prescribe an all-round mixed diet and tell the patient to eat every-

thing that comes to them on the tray, regardless of choice or inclination; in other words, to ignore their likes and dislikes and their food fears. It is surprising how many people suffer from food phobias and show a distaste for one or more wholesome foods. Of late years we have all learned the dangers of an ill-balanced food ration. I feel sure that much of the good of rest cures and fattening cures depends upon the re-establishment of balanced food rations.

Constipation and insomnia are two symptoms that often have to be combated during this period. Constipation is usually easily overcome, for people who eat liberally are rarely constipated. Until a regular habit is established, mineral oil at night or an occasional enema may be necessary, but we rarely have to make long use of such measures. Insomnia may be intractable over a considerable period. At the beginning it may be wise to give the patient a good night's sleep occasionally with the aid of veronal or other hypnotics, though we prefer to depend as much as possible upon reassurance, upon temporary forbearance, and upon hydrotherapy. Nothing is gained, and much is lost, by the prolonged use of hypnotics in these cases. The more experienced physicians of the resident staff are always amused by the tendency shown by younger house officers entering upon their work to make use of drugs for the relief of symptoms such as insomnia and constipation. After a brief apprenticeship the drug giving rapidly diminishes.

Massage and occupation therapy are helpful adjuvants during the rest-cure period. They help to chain the patient's attention and to divert it from the symptoms. Moreover, if the masseur and the teacher of occupational therapy have good nervous systems themselves, and are persons experienced in the treatment of psychoneurotics, they exert, by example and by precept, a wholesome influence upon the patient during the treatment.

Good team-work is necessary in the management of these patients during the rest-cure period. All that co-operate in the treatment (physicians, nurses, masseurs, attendants, etc.) should understand the importance of surrounding the patient with an atmosphere of cheerfulness, optimism, and favorable suggestion. Though every one is kind and judiciously sympathetic, the patient soon finds that the régime is maintained consistently by everyone who comes into contact with them, and that there is no yielding to the whims and caprices of patients.

These patients often urge the physician to tell them how long it will take them to get well. They say: "If I can just know how long it will be before I am well the date will be a goal to which I can look forward." It is, in my opinion, a mistake to make any prophecy as to the length of time that will be required, for the course is so different in different cases that even large experience with these patients does not permit one to prophesy with accuracy. My answer is, "I wish I knew, but no one knows enough about medicine as yet to be able accurately to foretell. Some patients recover much more quickly than others. This much we will promise you: we shall try not to leave anything undone that will favor your recovery and we shall proceed just as rapidly as possible."

In the case under consideration the nausea was a most persistent and troublesome symptom. It was many weeks before sufficient food could be retained to permit the patient to gain materially in weight. Nevertheless, the régime was steadily maintained and the patient gradually began to gain in weight. At the end of about four months of treatment the weight had reached the calculated ideal of 115 or 116 pounds. During this long period psychotherapy and occupation therapy were regularly employed, and, thanks to the co-operation of the patient and her desire to get well, real progress resulted from the application of these methods of treatment. In many frank and free discussions the psychic conflict was brought clearly into the consciousness of the patient, with the result that she gradually became better able to meet her concrete problems.

Toward the end of her stay in the hospital the régime of *protection* was gradually replaced by a régime of *exertion*. After the period of rest in bed had been completed we began to get her up and about. In the transition from bed to exercise we always go very slowly and gradually. Thus this patient was permitted to sit up one hour the first day; two hours the second day; three hours the third day, and on the fourth day she was permitted to walk about a little. The walking was gradually increased until the patient walked one hour in the forenoon and one hour in the afternoon. The amount of rest in bed was gradually diminished until the period of so-called "half-rest" was reached. By half-rest I mean remaining in bed until 10.30 in the morning; then rising and dressing for the day; resting for an hour or two lying down after the midday meal, and a return to bed by 9 P. M. It is often desirable to keep up such half-rest for several

weeks, sometimes for several months, in cases in which there have been great exhaustion and asthenia.

No rigid scheme dare be followed in the treatment of these patients. One must individualize the therapy at all stages according to the special needs of the particular patient in hand. Much of the opprobrium pertaining to the old-fashioned rest cure was due, I think, to the following of rigid schedules independent of individual needs. The physician must use his own head in the conduct of rest cures, upbuilding cures, and psychotherapeutic cures, and not rely upon the general pronouncement of any so-called "authority."

Régimes of this sort can rarely be carried out with success in the patient's own home. Removal to a hospital or nursing home is necessary, and, in the severer maladies, preferably in a town other than that in which the patient lives.

The physician must be able to inspire confidence not only in his professional ability but also in his integrity and good will. A certain *rapprochement* between the patient and the physician must be established. You all know how easily those we like can influence us, and how negative we are to the suggestions of those whom we dislike. The same is true in greater degree of psychoneurotic patients. They must *like* their physicians or their physicians cannot help them. And here, of course, great care is necessary to make sure that this affective relation is kept within proper bounds. The successful psychotherapist should have a strong character himself and be able to keep his own emotions well bridled. As he gradually leads the patient to become self-directing he should also see to it that any strong affective relation that has been established shall be gradually modified until the patient's affects are distributed over a wider area than the physician's personality.

It is important not to let these psychoneurotic patients return to their home environment too soon. They should learn to live with gradually increasing independence, first in the neighborhood of the physician, later at a little distance away, and then finally in their home surroundings. After returning home these patients should report, from time to time, at least for a year after apparently full recovery, to the physician in order that backsliding may be prevented. The fact that the physician still keeps them under his supervision goes far toward giving these patients the confidence they require and to insure the ultimate establishment of complete self-direction.

In this discussion I have said but little about the different varieties of the psychoneuroses, or of the borderland states between the psychoneuroses (which are minor psychoses) and the outspoken major psychoses. Time will not permit me this morning to dwell upon the differences among the "neurasthenic," the "hypochondriac," the "hysteric," and the "anxious neurotic," nor to give you the criteria that permit of the recognition of the mild "manic-depressive" or the suspect "schizophrenic." Your studies in the psychiatric clinic will, however, help you in these directions.

You should read as widely as you can in the modern literature of the neuroses and the psychoses, though to attain to skill in their management you must yourselves gain a large practical experience extending through a period of years. The bibliography of the subject of the psychoneuroses is now large and cumbersome. Let me direct your attention, however, to a few references that I think you may find especially helpful. For careful descriptions of some of the mental states of these patients the works of Pierre Janet can be highly recommended; you will enjoy his *Mental State of the Hystericals*, and especially his volumes entitled, *Les obsessions et la psychasthénie*. For a general introduction to the subject of abnormal psychology in relation to the psychoneuroses I may refer you to Kempf's *Psychopathology* and also to Hollingsworth's *Psychology of the Functional Neuroses*. For an understanding of the fictitious gold of the psychoneurotic and the meaning of the symptoms that psychoneurotics manifest, you will find much of interest in this English translation of a volume by Alfred Adler, entitled *The Neurotic Constitution; Outlines of a Comparative, Individualistic Psychology and Psychotherapy*. Adler's discussion of the inferiority complex, of the absence of a sense of security, of the tendency to maximize the ego, and of the so-called masculine protest, are exceedingly interesting and helpful to one who would understand psychoneurotics. For the special psychology of sex, you may refer to these six volumes by Havelock Ellis, to this treatise by I. Bloch, and to this well-known brief monograph by S. Freud, entitled, *Three Contributions to the Theory of Sex*. For Freud's special ideas of the neuroses you may read this volume in English by Hitschmann, and also Freud's *General Introduction to Psycho-analysis* (1920). For the technic of psycho-analysis itself you may study Ernest Jones, A. A. Brill, and S. E. Jelliffe; also the writings of Jung, of Zurich,

and those of Freud himself. On the rest-cure as applied to the treatment of the undernourished patient who is nervous I would strongly advise you to read Weir Mitchell's *Fat and Blood and How to Make Them*, and Dercum's *Rest Cures*. There are two very interesting French treatises on this subject, namely, Camus and Pagniez's *Isolement et psychotherapie*, and Dejerine and Gauckler's *Les psychoneuroses*. The latter is obtainable also in English translation. Of the treatises on persuasion as a mode of treatment this book by DuBois, of Berne, contains much that is helpful. Let me call your attention, too, to this short article by Esther Richards on the *Invalid Reaction*; you will find it illuminative. From the standpoint of prevention and the management of the nervous child you will enjoy reading W. A. White's book on *Mental Hygiene*, Pfister's *Psycho-analytic Method*, Wile's *Mental Hygiene During Childhood*, Evans' *Problem of the Nervous Child*, and perhaps the pamphlets of my own already referred to. With the aid of the literature mentioned you will be well started in the study of the bibliography, and from the references given you can easily gain access to the further literature of the subject.

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XXI. HEREDO-FAMILIAL CEREBELLAR SYNDROME

DISTURBANCES OF THE EQUILIBRATORY AND NON-EQUILIBRATORY SYNERGIC MOTOR MECHANISMS WITH SLIGHT INVOLVEMENT OF THE PYRAMIDAL TRACT, SUBJECTIVE NUMBNESS ON THE LATERAL SURFACE OF THE RIGHT THIGH, AND OPTIC ATROPHY IN A MAN OF THIRTY-FOUR IN WHOSE FAMILY THE MOTHER, TWO SIBS, AND TWO OF HIS OWN CHILDREN HAVE BEEN PROBABLY SIMILARLY AFFECTED.

DR. BARKER: The resident physician, Dr. V. R. Mason, has called my attention to a patient in Prof. Thayer's service who exemplifies an

interesting cerebellar syndrome, and we are to have the opportunity of seeing and examining him this morning. The clinical clerk, Mr. Ruben, will give you a summary of the history of the patient.

STUDENT: The patient, Lawrence G., is a white man, thirty-four years of age, by occupation an automobile agent. He was in this hospital for three weeks in the spring of 1920, and was readmitted four days ago (on February 4, 1921) complaining of "staggering" and of "flickering before the eyes."

The first symptom of his *present illness* appeared some twelve years ago, when he began to notice a feeling of numbness in the right thigh, on its lateral aspect, a symptom that has persisted ever since. Some ten years ago, while telephoning during a thunder storm, he was struck by lightning, or, rather, the telephone wire was struck, and he received a slight burn on his left arm and left ear, with singeing of the hair. Since then he has been somewhat deaf in his left ear. He states that three months after the electrical shock his vision became blurred and remained so for a month, when it cleared up and remained good until he began to have visual disturbances about two years ago. He states also that the electrical shock killed the nerves in several of his teeth and that the pulps of these teeth had to be removed.

About five years ago the patient noticed that on marked physical exertion he became dizzy and staggered slightly. This dizziness and staggering gradually increased until, after a year, the symptoms would appear on only slight exertion. These disturbances were all the more embarrassing to him in that his friends thought that he was drinking and would ask him where he had "got his load." As the condition progressed he began to stagger and to become dizzy on ordinary walking, though he says that he never actually fell. He noticed that if he rose suddenly he would be dizzy, and that he would sometimes stumble over objects in his path. These symptoms seemed to be aggravated on exposure to cold.

About two years ago a peculiar visual disturbance appeared. He would notice that the objects before him would "begin to flicker" unless he held himself very still. On account of this he had difficulty in reading unless he held the paper rigidly and kept his head very quiet.

Certain peculiar digestive disturbances appeared fourteen months ago. He began to have paroxysms of vomiting in which he would

vomit six or seven times per day for two or three days. The vomiting stood in no relation, apparently, to the ingestion of food; from the descriptions he gives it would seem that the vomiting was not projectile. He had some six attacks during the following six months. Recently there has been no vomiting.

For the past two years he has complained of roaring in both ears, and for the past ten months of frequent night-sweats. He has also noticed, lately, difficulty in starting the urinary stream and, occasionally, dribbling of urine.

His speech seems to have been disturbed for a number of years, but about one year ago he noticed what he called "marked stuttering," which lasted for a while and then disappeared. At that time he also had marked tremor of his arms and lips. Any emotional strain would make him feel nervous and tremulous, and he states that he frequently had laughing spells that were difficult to control. These troubles have since disappeared.

He was under observation in the Johns Hopkins Hospital in March, 1920, and left after a few weeks without improvement in his symptoms. By August, 1920, however, he felt much better and continued to be fairly well until January of this year, when his symptoms again became worse, though he states that his condition is not nearly so bad now as it was when he was here last year. At that time he was compelled to use a cane when walking; now he can walk without a cane and staggers much less than formerly.

His *past history*, aside from this main illness, presents but little of interest. He had measles and mumps in childhood. He underwent two nasal operations for hypertrophied turbinates, and was operated upon for hernia twice, once in 1906 and once in 1910. He has always been well nourished; in fact, he has been somewhat obese. During 1919 and 1920 he suffered from headache and dizziness. He denies venereal disease. His habits have been good as regards alcohol, tobacco, coffee, and tea. He has lived much of his life in the open air.

His *family history* is of considerable interest. Though his father is living and well at the age of seventy-six, his mother died at sixty-four of what he calls "paralysis," but her disability seems to have come on gradually twenty years before her death, and to have progressed until she had to sit in a chair or remain in bed. The patient is one of a large family. Four sisters and three brothers are said to be well, though in the light of the family history to be given they

should, we think, be carefully examined. One brother died at forty-four of "heart trouble and pleurisy." One sister, now forty-eight, has suffered from what he calls "paralysis" for about eighteen years. A second sister died at the age of twenty, and a third at the age of twenty-five of a trouble that the patient feels sure is the same as his, since they suffered from staggering, dizziness, headaches, and flickering before the eyes. Still another sister died at twenty-five with what was called "tumor in the head." One of these sisters, Lizzie G., came under the observation of Dr. William G. Spiller, of Philadelphia, a few years ago. In a letter to Dr. Thayer Dr. Spiller states that she complained of numbness of the feet and legs extending up to the trunk as far as the umbilicus and of weakness in the lower extremities. At times she had pain in the lower limbs. This was chiefly soreness, but occasionally there was sharp pain. Walking was difficult. Later she became numb in the upper extremities and had continuous pain also in the arms. The grasp was weak on both sides. There was an ankle-clonus on the left, but the knee-jerks were normal. She gradually became so that she could not stand without support. As there was a 1+ Wassermann in the blood-serum and a positive Noguchi reaction, it was supposed at the time that she was suffering from a luetic ascending meningomyelitis.

The patient himself married ten years ago and has four children living. His wife has had no miscarriages. Two of his children, one aged nine, the other aged four, are, he says, very clumsy.

DR. BARKER (to patient): How does this clumsiness show in your children?

PATIENT: They fall down very easily; much more easily than other children do. They will stumble over the least little obstacle, and sometimes they will stumble and fall when there is no obstacle in the way. It seems to me that they do not use their arms and legs right. The older one goes to school, however.

DR. BARKER: These children should certainly be carefully examined from the neurological standpoint.

(To student): Will you tell us first the findings on physical examination other than the neurological findings in this patient?

STUDENT: Notes have been dictated upon the physical status by the house officer, Dr. Telinde, and by the resident physician, Dr. V. R. Mason. Outside the nervous system there was very little abnormal, except for moderate obesity, the scars of the former hernia

operations, and a few dead teeth. The blood and urine were normal on this admission as on the previous admission. The blood Wassermann was negative. On his earlier admission lumbar puncture was done and the cerebrospinal fluid showed 30 cells with a 2+ globulin, with a low parietic gold curve. The Wassermann, however, was negative. There had been no history suggestive of epidemic encephalitis.

DR. BARKER: Full neurological notes have been dictated on this patient by Dr. V. R. Mason, the resident physician, and by Dr.

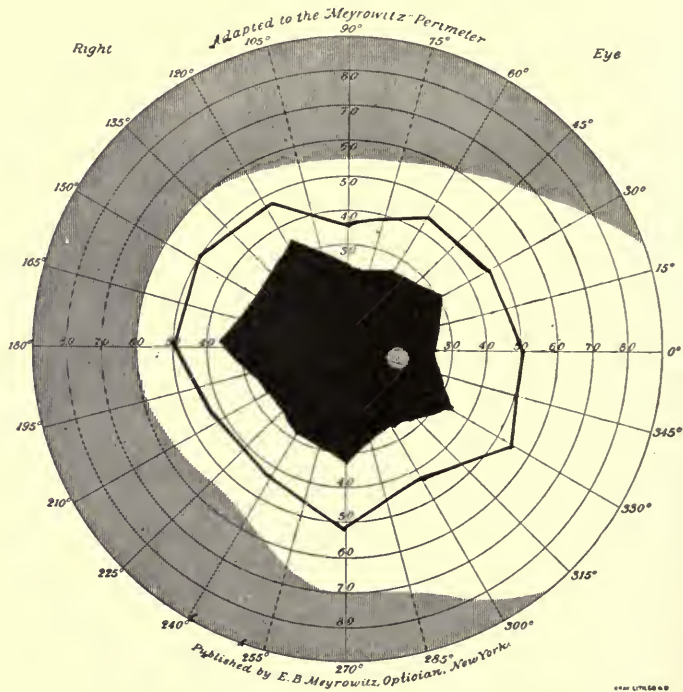


Fig. 40.—Disturbance of visual field of right eye.

H. M. Thomas, Sr., the visiting neurologist, and we have reports on the eyes from two of the ophthalmological staff. Would you mention the principal positive findings?

STUDENT: The patient has a peculiar disturbance of speech, nystagmus, and slight inco-ordination of the upper extremities. He tends to stand with rather a broad base, though he can stand, without falling, with the feet close together. He sways a little more

with the eyes shut than with them open. He staggers somewhat on starting to walk and on quick turning, and he is totally unable to walk a straight line placing one foot before the other; he quickly loses his balance when he attempts to do so. Despite the subjective numbness on the lateral surface of the right thigh, there is no objective disturbance of sensation. The senses of touch, temperature, pain, position, and movement are normal on objective testing. There is deafness and tinnitus in the left ear, though the deafness is slight. His vision in the right eye is 15/200, and in the left eye 20/40. Per-

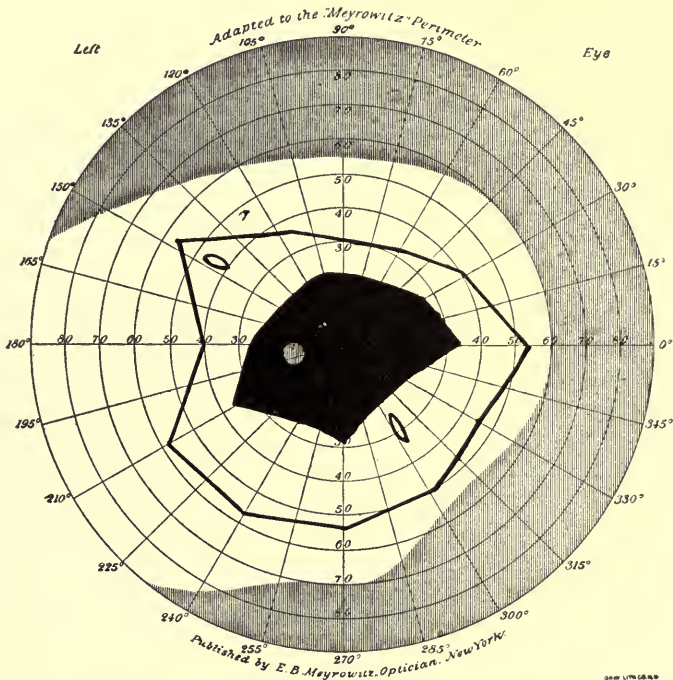


Fig. 41.—Disturbance of visual field of left eye.

imetry shows concentric contraction of both visual fields and two scotomata (Figs. 40, 41). There is a little opacity of the right cornea; otherwise the media are clear. The optic disks are pale, especially in their temporal halves, and particularly in the right eye. One of the ophthalmologists believes that this is a primary optic atrophy; the other thinks that the atrophy may have been preceded by a mild optic neuritis; in other words, that it is a secondary atrophy,

though he admits that the case is a borderline one in which it is almost impossible to make the distinction between primary and secondary atrophy. Dr. H. M. Thomas thought that the edges of the disks were fairly clean cut and rather favored the idea of a primary atrophy.

The deep reflexes were all normal. The pupils were equal in size and reacted promptly to light and on accommodation. There is a little inco-ordination of movement in both the upper and the lower extremities, though it is not marked. The Babinski reaction is sometimes positive in the right foot; it is equivocal on the left. Aside from the nystagmus, the optic atrophy, and the left deafness and tinnitus there were no disturbances in the domain of the cerebral nerves.

DR. BARKER: An interesting history with important physical findings. He has numbness on the lateral surface of the right thigh beginning twelve years ago; deafness and tinnitus in the left ear; blurring of vision; staggering gait, noticed first five years ago; nystagmus; disturbance of speech; difficulties of urination; recent loss of sexual potentia; optic atrophy; slightly positive Romberg sign, and a demonstrably positive Babinski on the right side.

Well, let us now examine the patient for ourselves, and, particularly, let us test the motility, since there are no objective sensory disturbances, and we have the reports of specialists upon the condition of the hearing, of the vision, and of the visual mechanisms.

In the first place, the volume of the single muscles and muscle groups is unchanged. There is nowhere any muscular atrophy or muscular weakness. We can be sure, then, that the lower motor neurone groups are unaffected. The so-called *idiodynamic control* is normal.

On passive movement of the arms and of the legs there is certainly no increase of the resistance, nor do I think there is any decrease. In other words, there is neither hypertonicity nor hypotonicity to be made out here. The *tonic control* of the musculature, as far as it can be tested by passive movement, seems normal.

(To patient): Please make the following movements as I mention them. (A large number of movements involving the principal groups of muscles were designated.) You see he performs all these movements immediately upon request. He appears to have good *volitional control* of the musculature.

(To patient): I am told that you have a good sense of humor and I can see that you smile readily.

(To class): You notice that the patient has an exceedingly mobile face. His face gives expression easily to the emotions that he experiences.

(To patient): Please make a fist with your right hand. With your left.

(To class): You notice that the normal associated movements occur on the making of a fist. The hand becomes extended at the wrist, but does not become overextended.

Still other tests of the normal association of movement have been made in this patient. There seems to be no discoverable disturbance of the *automatic associative control* of movements.

Now let us turn to an examination of *synergic control*, the kind of control in which we know that the cerebellar mechanisms are of greatest importance. We may test first his equilibratory control on standing and on walking, and afterward we may test his synergic control of certain movements of the extremities and of the head, neck, and trunk.

(To patient): Please stand up; stand as steadily as you can.

You notice that he is just a little awkward on rising, and that he stands with his feet somewhat apart and somewhat everted; but he stands fairly steady.

(To patient): Please place your feet close together.

He still stands steadily.

(To patient): Now close your eyes.

You see there is very definite swaying, though it is not of high grade. He has a slightly positive Romberg. This increase of swaying when the eyes are shut, when there is no swaying when the eyes are open, is an extracerebellar rather than an intracerebellar sign. The swaying that is due to disease of the cerebellum itself is not increased, as a rule, by closing the eyes, for visual stimuli are incapable of compensating for oscillation that arises as the result of intracerebellar disease. On the other hand, when there is degeneration of the posterior funiculi, as in tabes dorsalis, visual impulses can compensate markedly for the loss of influence of the sensory impulses passing up through the posterior funiculi.

(To patient): Please sit down again. Now will you arise quickly and walk across the room?

Again he has a little difficulty in rising and in starting, but his spontaneous walking across the room is very good. He does walk with a somewhat broad base, but there is no staggering at present. I shall ask him, on walking, to turn quickly to the right, also quickly to the left, and to stop suddenly in the course of his walking. He does these three things also very well. When he was here a year ago he was quite incapable of such normal performance. The disturbance of gait is obviously much less marked than it was.

Now let us ask him to walk a crack, placing one foot before the other.

Here the equilibratory disturbance becomes very noticeable. On attempting to place one foot before the other his whole body oscillates from side to side; his movements are uncertain, and he would fall were it not for the support of the clinical clerk.

We will ask the clinical clerk to act as a control in making several of our tests.

(To student): Mr. R., will you please walk this crack?

You see he can do so without difficulty.

(To patient): I shall spread this blanket on the floor and ask you, if you will, to walk on all fours and to creep. He does this very well also. He does not oscillate from side to side as he would do if he had, at present, a high grade of equilibratory disturbance.

Next, let us make the test for major cerebellar asynergy. That is to say, let us observe whether, on walking, his legs tend to run ahead of his center of gravity. You will recall that Babinski first called our attention to the tendency of the upper part of the body in cerebellar syndromes to remain, on walking, behind the lower extremities. He described this condition as "giving the appearance as though the legs were running ahead of the center of gravity." The symptom is not manifest in this patient at the present time.

We owe, too, to Babinski several easily applicable tests of other synergic movements. These tests are usually grouped together as "minor tests of cerebellar asynergy." They include: (1) The leg-lifting test, (2) the sitting-up test, (3) the foot test, (4) the kneeling test, and (5) the leaning backward test. Let us try each of these in this patient and on our control.

(To patient): Please lie down on your back on the rug and lift your right leg; afterward, please lift your left leg. You observe that he does not lift the extremity as a whole, but first flexes the

thigh and then extends the leg. There is a decomposition of the single act into its two components. Possibly he has not understood exactly what I wish him to do. I shall now explain to him that I wish him to lift the leg as a whole. He does it a little better now, but still seems to be unable to lift the leg as a whole. There is a certain decomposition of the synergic movement into its two components.

Next, we shall try the "sitting-up test."

(To patient): Please lie on your back again; fold your arms across your chest and sit up.

You see, he flexes his body, although he is not able to sit up completely. His lower extremities are kept straight and are lifted a little off the floor. Our control, as you see, is able to sit up; and with the flexion of the trunk he also flexes the thigh and flexes the leg, and he does not allow his feet to go up into the air as the patient does. The patient has a certain disturbance of his trunk-leg-flexion synergism.

The "foot test" comes next. We shall ask the patient to sit in this chair and to touch my hand with his foot. You notice that he flexes the thigh before extending the leg, but our control does this almost in the same way as the patient does. On explaining the test to both of them, however, the control performs the movement smoothly without hip flexion, whereas the patient still tends to flex the hip-joint first. He avoids the hip flexion, however, much more now that he knows what the test is intended for.

Next, we may try the "kneeling test."

(To patient): Please stand beside this chair and grasp the back of it with your hands and then place your knee on the chair.

You notice that he does not dissociate the two movements of hip flexion and knee flexion much more than does the control.

The "leaning backward test" is one of the best of these minor tests for cerebellar asynergy.

(To patient): Please stand up and then lean backward as far as you can without falling. We shall stand behind you and make sure that you do not fall. I want you to hold your head back and to bend your body backward in the form of an arc.

You see he does this very well, and he does not fall as he does it. He has the normal associated movement of flexion at the knee-joint. If he had any high grade of cerebellar asynergy this associated movement would not occur. He would keep his lower extremities straight,

and as he curved his back the center of gravity would be so displaced that he would fall. You will find a very good illustration of this asynergic disturbance in Babinski's article in the *Revue mensuelle de médecine interne et de thérapeutique*; I have copied them in the third volume of my book on the *Clinical Diagnosis of Internal Diseases*, where you will find them pictured on pages 248 and 249.

Considering the history this man gives us of cerebellar symptoms, it is interesting to see how far they have receded. His *integrative synergic control* is now very good when we consider what it must have been last spring.

We owe to another French neurologist, André Thomas, certain methods for testing a patient's judgment of the distance, force, and time of muscular contractions. In cerebellar disease this judgment seems to be much disturbed, so that the patient makes marked mistakes in the distance of the excursion, in its force, and in the time of muscular contraction. Such mistakes of measurement are referred to as "dysmetria." Let us try the finger-nose test, the heel-knee test, the grasping test, and the hand-reversal test.

(To patient): Close your eyes, please, and touch your nose with your forefinger, first with the right hand and then with the left.

He does this very well, and without much error. There is, perhaps, a slight error on the left.

(To patient): Close your eyes and place your left heel on your right knee; now do the same test with the other foot.

He performs this test with both lower extremities exceedingly accurately.

(To patient): Please drink from this glass of water, using your right hand first, then your left hand.

He does this perfectly well with his right hand, but there is rather marked hesitation with the left, though he finally accomplishes it satisfactorily. Some patients with dysmetria are wholly unable to grasp a glass of water and to carry it to the mouth.

(To patient): Please extend your arms and turn the palms upward as I am doing. Now close your eyes and turn your hands over so that the backs are up. He does this also very well, though the left hand is held a little obliquely. If there were more asynergy the hands would be held much more obliquely. There is very little asynergy here now. The dysmetria that exists affects the left upper extremity.

Another cerebellar sign that we should test for is that of inability to make rapid movements in succession (adiadochokinesis).

(To patient): Place the palm of your hand on your thigh and then the back of your hand, and make these two movements in succession as rapidly as you can, just as I do, first one hand and then the other.

He makes these movements rather clumsily, with a good many failures, and the failures are more marked on the left than on the right.

(To patient): Extend your arms as I am doing and make the two hands go up and down rapidly.

He does that very well.

(To patient): Now flex and extend your two forearms rapidly, as I am doing.

He does that very well also. There is a little adiadochokinesis here, however, more marked on the left than on the right.

The "rebound phenomenon" of Gordon Holmes is another interesting feature of certain cerebellar syndromes. I shall have the patient hold his forearm flexed while I try forcibly to extend it. See what a difference there is in the rebound between the two sides. The arm rebounds somewhat more than normal on the right, but a great deal more than normal on the left. The left forearm flew back, as you saw, into his face.

(To patient): I hope it did not hurt you.

PATIENT: No, it did not hurt. It surprised me.

DR. BARKER: On our control there is considerable rebound, too, but much less than in the patient. Now, normally, the cerebellum checks this rebound; in cerebellar asynergy the rebound is more marked than normal.

The patient has no tremor at present, though he had some tremor when he was here before, and tremor is not uncommon in cerebellar syndromes. It is usually a rather coarse oscillation.

Let us next examine his eyes for nystagmus. When he looks straight forward there is no nystagmus at present; on strong deviation to the right there is slight nystagmoid movement, but not much; on strong deviation to the left, however, there is very marked nystagmus. The quick movement is to the left and the slow movement to the right. On looking upward the nystagmus is most marked. It is an up-and-down nystagmus and a rotary nystagmus combined; on looking down there seems to be no nystagmus.

I hope that our otologist, Dr. S. J. Crowe, will be able to make a careful analysis of this nystagmus, for nystagmus is a very important symptom for valuation in disease of the vestibular apparatus and in disease of the cerebellum. Robert Bárány, of Vienna, has made many beautiful experiments that have thrown light upon the nature and meaning of nystagmus. You will find a good account of his work in this volume by Jones, of Philadelphia. For a brief account you might read Bárány's own article on localization in the cortex of the cerebellar hemisphere; it was published in the *Deutsche medizinische Wochenschrift*, April 3, 1913. You will find there a very clear epitome of his views.

A series of special tests for the integrity of the vestibular mechanisms may be employed. By means of the rotation test one can find out whether there is disease beyond the extramedullary vestibular paths, and by means of the caloric test, that is, injection of warm water or cool water into the external ear (a strictly unilateral test), one can draw conclusions regarding the pathology of the labyrinth itself. Even more interesting in this case would be the application of the test for pointing errors during a caloric nystagmus. If one injects cool water into one ear when the labyrinth is normal, a horizontal nystagmus to the opposite side will occur and will continue for one or two minutes after the irrigation has ceased. If, for instance, one thus produces a horizontal nystagmus to the left, and then tests for a pointing error, he will find, normally, a deviation to the right during the continuance of the artificially produced nystagmus. This error is due to a reaction of the cerebellar hemisphere of the same side. If the functional area concerned in the right cerebellar hemisphere be not functioning, owing to disease, the past-pointing does not occur. I cannot go into the details of this test here, but you should familiarize yourselves with it, especially if you desire to make careful studies of patients suffering from vestibular or cerebellar diseases.

We may in this patient, however, right now test for any spontaneous past-pointing error. I allow the patient to put his index-finger in contact with the under surface of mine held above his thigh, then I tell him to close his eyes, to let his hand fall to his thigh, and then raise it again so that it will come into contact once more with the under surface of my index-finger. He does this on the right side without error; he does it also on the left side perfectly well.

There is, therefore, no spontaneous deviation of Bárány. As I have said, however, it will be interesting to test for past-pointing during caloric nystagmus.

Next, let us test this patient's ability to turn his head upward, downward, to the right, and to the left. You see he makes all of these movements perfectly smoothly and without oscillation or tremor. There is, therefore, no cephalogyric synergic disturbance.

This patient presents an interesting disturbance of speech. You have had the opportunity of hearing him talk during the clinic, and I am sure that you must have noticed certain peculiarities of enunciation. In the first place, his speech is rather slow (bradylalia), with a tendency to scanning, though it is not a regular scanning. In the second place, though the speech is, in general, somewhat monotonous, there are sudden and unexpected variations in the force and explosiveness with which syllables are pronounced. At times the patient sounds a little like a stutterer, and he described his own symptoms as those of "stuttering" when his speech disturbance was much more marked than it now is. It would seem that he presents a definite asynergic speech disturbance, a kind of dysmetria of the movements involved in speech. There has not been any asynergy of the masticatory movements as far as we can make out.

Finally, let us test the reflexes. His pupils react to light promptly and they are equal in size. The deep reflexes in the upper extremities are normal; they are not hyperactive. The knee-jerks are active, but there is no clonus of the patella or at the ankle. I shall let him sit on the table for a moment and test for the so-called "pendular knee-jerk." Ordinarily when one taps the patellar tendon when the patient is in this position there are one or two marked oscillations and then the leg quickly comes to rest, owing to the check on the movement due to cerebellar activity. Here the oscillations continue somewhat longer than normal, but the leg of our presumably normal control, as you see, also oscillates to about the same degree as does that of the patient. I think we can draw no conclusion from this tendency to pendular knee kick in the present instance. The abdominal reflexes are normal. The Babinski reflex on the right, as you see, is positive; on plantar stimulation the great toe is extended dorsalward and the small toes are spread like a fan. On the left side the Babinski is equivocal; it is not definitely positive. It

is rather interesting that this pyramidal-tract sign is more marked on the right than on the left; whereas, as we saw, the cerebellar asynergy is more marked in the left upper extremity than in the right.

(To student): What localizing value has this positive Babinski sign?

STUDENT: It indicates a lesion of the upper motor neurones whose medullated axones form the pyramidal tract.

DR. BARKER: Yes, certainly, the upper motor neurones must be involved in this patient. Possibly the disturbance of bladder function may also depend upon upper motor neurone lesion, though this is not certain. The disturbance of *potentia cœundi*, of which the patient complains, may be due to a beginning lesion of the posterior funiculi of the spinal cord.

To what does the subjective numbness in the right thigh point?

STUDENT: To a disturbance of function in the sensory conduction path. This might be in the peripheral sensory neurones, in their continuation upward in the spinal cord, or in the higher sensory neurones anywhere above the cord, between it and the cerebral cortex.

DR. BARKER: Yes; in the absence of any objective disturbance of sensibility we can scarcely attempt any finer localization of the process causing this numbness, though when you recall that other members of the patient's family had outspoken numbness, the distribution of which pointed to the posterior funiculi, we can think of the possibility of a similar localization for the very slight disturbance of cutaneous sensibility in this patient.

What localizing value has the Romberg sign?

STUDENT: It could depend upon some lesion in the sensory paths going to the cerebellum.

DR. BARKER: Yes, I think it points to some cerebellipetal path rather than to an intracerebellar lesion. In the absence of signs definitely pointing to the posterior funiculi one might think of the fasciculi spinocerebellares, either the dorsal fasciculus or the ventral fasciculus. You will remember that the dorsal spinocerebellar tract is made up of medullated axones, the cells of origin of which are situated in Clarke's column of cells in the gray matter.

To what does the optic atrophy point?

STUDENT: To degeneration in the optic nerve; and it would

seem likely that the degeneration is a primary process rather than a process secondary to an optic neuritis in this patient.

DR. BARKER: That is an important point, for a primary optic atrophy would favor the diagnosis of some toxic-degenerative process or some heredo-familial degenerative process, whereas a secondary optic atrophy would suggest increased intracranial pressure due to a neoplasm, an inflammation, or a cyst.

How would you value the nystagmus in this patient from a localizing standpoint?

STUDENT: I think we would need more study of the nystagmus to determine that point.

DR. BARKER: Yes, and I hope that that study will be made by Dr. Crowe, whose opinion in such matters I value highly.

The connections of the vestibular paths are very important, and you will, perhaps, enjoy reviewing them after the clinic. Sensory impulses from the semicircular canals have an important influence upon the tonus of the musculature, especially on the adaptation of tonus to certain positions of the head, of the body, and of the eyes. Every change in the position of the head alters the tonus of the neck muscles and of the body muscles. Each labyrinth acts on the muscles in both sides of the neck. The vestibular fibers, as you know, go to certain nuclei of reception in the pons (including Deiters' nucleus) and also to the cerebellum of both sides. Axones from Deiters' nucleus run upward in the fasciculus longitudinalis medialis to the eye-muscle nuclei and downward in the same bundle to the neck muscles, and, indeed, to the muscles of the body through the intermediation of the anterior horn cells. This important vestibular mechanism is, therefore, sometimes known as the "optostatic system."

Finally, how do you value the disturbances of equilibratory and of synergic control in this patient for localizing purposes?

STUDENT: There must be injury to the cerebellum itself or to the paths leading to or going from the cerebellum.

DR. BARKER: Yes; the statotonic functions and the synergic functions generally are mediated principally by the cerebellum and by the cerebellipetal and cerebellofugal paths. The whole mechanism is a very complicated one, but, thanks to clinicians, to histologists, and to experimental physiologists, our knowledge of the cerebellar mechanisms has, during the past quarter of a century, been much increased.

I would like to call your attention to a few collective reviews that you may find valuable for reference. The architectonics of the nervous system, as far as they were known up to 1899, you will find fully described in my own book, *The Nervous System and Its Constituent Neurones*, but great advances in our knowledge of this subject have been made since 1899. Very interesting in this connection is this article by L. Edinger, which I shall pass around the class. It was published, as you see, in the *Deutsche medizinische Wochenschrift*, April 3, 1913. It contains a brief but clear account of our general knowledge regarding the structure of the cerebellum and its connections, and the simple illustrations that accompany the article you will find illuminating. These two collective reviews in the *Ergebnisse der Physiologie* (vols. vii and xii) by van Rynberk will give you the main facts from the standpoint of experimental physiology, but for the physiology and morphology you should look over, in addition, Bolk's important papers. On the clinical side, you will want to read Babinski's original articles, A. Thomas' monograph (English translation), and these excellent articles by Gordon Holmes, of London. You will find also very interesting clinical articles published in this country, especially these that I am passing around, namely, that of Archambault, of Albany (1918); this one, by Mills and Weisenburg, of Philadelphia (1914), and this one by Wilson and Pike, of Chicago (1915). Above all, let me recommend to you the study of this new volume, *The Form and Functions of the Central Nervous System*, by F. Tilney and H. A. Riley, of New York. In connection with this clinic you will want to read especially the part on the cerebellum; but this book by Tilney and Riley is one that I would advise each one of you to buy early for your libraries, for you will frequently want to refer to it not only during your student careers, but afterward as practitioners. It is, at present, the best book in English on the structure and functions of the nervous system. It is very recent, having been published only a couple of months ago. You will find particularly valuable in it the clear descriptions of the clinical syndromes that correspond to lesions of different parts of the nervous system. I use this book much for reference in my own work. On the blackboard you will see a number of other references that may be helpful to you in connection with the study of cases like the one before you.

Though the cerebellum is a large organ, has multiple connections,

and must have very important functions, it is surprising how ignorant we are of the exact nature of its functions and their localization despite the arduous labors of experimental physiologists and of the combined activities of pathologists and clinicians. A vast deal of work has been done in this field, but the harvest thus far has been relatively smaller than might have been expected.

The studies of the comparative anatomists upon the cerebellum have been interesting and important. They have shown us that the vermis must be the most fundamental part of the cerebellum, since it appears much earlier than the other parts of that organ in the phylogenetic series. You will recall that in the animal series as a whole the cerebellum is a comparatively late development. There are even some vertebrates (*e. g.*, certain salamanders) that have no cerebellum at all. Wherever there is a cerebellum, however, there is a vermis. Cerebellar hemispheres do not appear until the mammal stage has been reached. In the higher mammals these cerebellar hemispheres develop to enormous proportions, so that in whales, in elephants, and in man the cerebellar hemispheres quite overshadow in their development the phylogenetically more important vermis. Evidently, these cerebellar hemispheres must be of very great significance for the functional activities of the nervous system of the highest animals.

All students of the cerebellum agree that the main functions of the organ are (1) the maintenance of equilibrium (*statotonus*), and (2) the synergic control of muscular activity.

A host of cerebellipetal impulses have their origin in the sense organs of the muscles and joints, on the one hand, and, on the other, in the sensory apparatus of the semicircular canals and labyrinth. The centripetal impulses from the muscles and joints pass through the posterior roots of the peripheral nerves into the spinal cord and are transferred, through collaterals, to the cells of Clarke's column; hence, spinocerebellar conduction paths (the *fasciculus spinocerebellaris dorsalis* and the *fasciculus spinocerebellaris ventralis*) conduct the impulses to the cerebellum, especially to the vermis of the same side and of the opposite side, the fibers terminating in end-arborizations around the Purkinje cells of the cerebellar cortex, which thus becomes a great receptor apparatus. The impulses from the upper extremities and from the muscles of the neck pass by way of the ventral spinocerebellar path into the frontal portion of the

vermis, whereas the impulses from the trunk and from the lower extremities (muscles and joints) end in the more dorsal and more caudal parts of the vermis. The impulses of vestibular origin (semicircular canals and vestibule) pass through the vestibular nerves, and their nuclei of termination in the pons to be distributed also among the Purkinje cells of the cortex of the vermis of both sides. The cortex of the vermis of the cerebellum is thus continually under bombardment by cerebellipetal influences that depend upon (1) contractions of the muscles and movements of the joints, and (2) changes in the position of the head in space that stimulate the nerve endings in the semicircular canals and the vestibule. So much for the cerebellipetal influences reaching the vermis.

But what about the cerebellipetal impulses that reach the cortex of the cerebellar hemispheres, for the vermis is the old part of the cerebellum (*paleocerebellum*), whereas the hemispheres represent the phylogenetically newest part of the cerebellum (*neocerebellum*). The comparative anatomists have shown us that the cerebellar hemispheres develop *pari passu* with the development of the cerebrum and its cortex. A great mechanism has thus been developed which throws the cortex of the cerebellar hemispheres under the influence of sensory impulses that arise primarily in the muscles and joints, though these impulses take a very roundabout path in reaching the cerebellum. They pass from the muscles and joints through the posterior funiculi of the spinal cord to the nuclei of Goll and Burdach in the medulla, where they undergo relay; the axons from the cells in these nuclei cross in the sensory decussation of the medulla and pass toward the brain in the medial lemniscus, undergoing relay in the ventrolateral nuclei of the thalamus on each side; thence the impulses pass through thalamocortical paths to the frontal, parietal, and temporal lobes of the cerebrum. These impulses are then reflected from the cerebral cortex downward through the cerebro-cortico-pontile paths, which terminate in the nuclei pontis, or, rather, undergo relay there. The axons from the cells of the nuclei pontis pass to the cerebellum through the brachii pontis and terminate in end-arborizations among the Purkinje cells of the cerebellar hemispheres. You see what a circuitous path is taken by these impulses, and, of course, manifold modifications and combinations of the impulses may occur in the different relay centers that have been described. Evidently, this roundabout path that intercalates the

cerebral cortex between the muscles and joints and the cerebellar hemispheres must be of high importance for the higher vertebrates, including man.

Next, let us consider briefly the cerebellofugal paths. They, too, are rather complicated, but an understanding of these paths is very important for our clinical studies of cerebellar disease. The axons from the Purkinje cells of the cerebellar cortex end predominantly in certain nuclei of the cerebellum. It is probable that most of the axons from the cortex of the cerebellar hemispheres end in the nucleus dentatus, whereas most of the axons from the cortex of the vermis end in the more medially situated nuclei, namely, the nucleus emboliformis, the nucleus globosus, and the nucleus fastigii, or nucleus of the roof. In accord with this view is the fact that the nucleus dentatus undergoes development *pari passu* with the development of the cerebellar hemispheres. Now the axons from these several intrinsic cerebellar nuclei constitute the principal cerebellofugal paths, and they terminate in certain large motor nuclei in the tegmental regions of the medulla oblongata, the pons, and the midbrain. The aggregate of these more or less widely distributed motor cells is often spoken of as the motor nucleus of the tegmentum (nucleus motorius tegmenti). In higher forms, and especially in man, these motor cells in the tegmentum tend to form fairly definite groups. Two of these groups are quite large, the lower one being known as Deiters' nucleus (nucleus nervi vestibuli lateralis), and the upper one as the red nucleus of the tegmentum (nucleus ruber). Now these large motor cells of the tegmentum seem to be of great importance for muscle tonus throughout the body. When the paths from these motor nuclei are destroyed, hypotonia results; when the paths are irritated, tonus increases up to outspoken spasm. Cerebellofugal impulses from the cerebellar hemispheres pass to the nucleus dentatus and thence through the brachium conjunctivum (superior cerebellar peduncle) to the midbrain, where they cross over and end in the nucleus ruber of the opposite side. Similarly, impulses from the vermis pass through the medially placed nuclei of the cerebellum to Deiters' nucleus. Furthermore, paths descend from the nucleus ruber, on the one hand, and from Deiters' nucleus, on the other, through the brain-stem into the spinal cord to influence the lower motor neurones that innervate the striped muscles. The path from the nucleus ruber to the spinal cord is known as the rubro-

spinal path (von Monakow's bundle); it is, you will recall, a crossed path. The path from Deiters' nucleus to the spinal cord, known as the vestibulospinal path, is homolateral. Another very important path connected with Deiters' nucleus is the fasciculus longitudinalis medialis (or posterior longitudinal bundle), which runs upward to throw the eye-muscle nuclei under the influence of the cerebellum, and downward to the spinal cord to throw the neck muscles and trunk muscles under the same influence. By means of these nerve-paths the movements of the eyes, of the head, and of the trunk are co-ordinated (optostatic system).

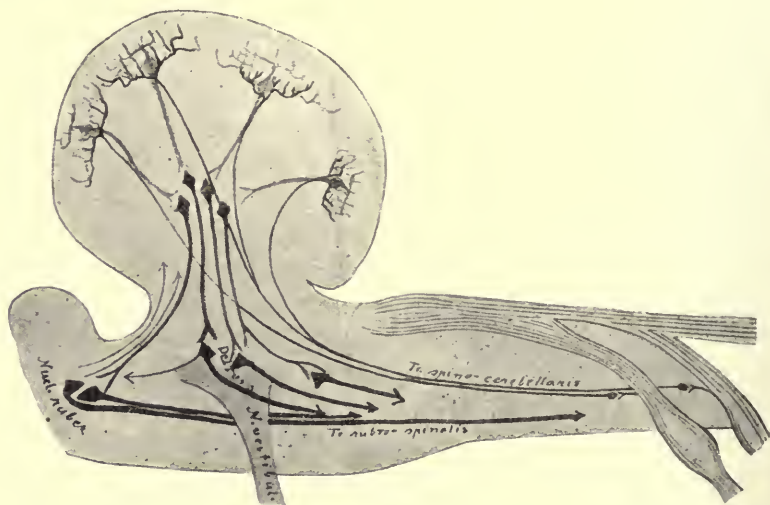


Fig. 42.—Diagram of the cerebellar apparatus and its connections. (After L. Edinger, *Deutsche med. Wchnschr.*, 1913, p. 634, Fig. 1.)

Very good illustrations of some of these cerebellipetal and cerebellofugal paths will be found in these simple diagrams that I have copied from Edinger's article (Figs. 42-44). The two figures copied from André-Thomas' book are also excellent (Figs. 45, 46).

From the study of the architectonics of the cerebellum and its connections, and from a consideration of the results of the experimental physiologists, we must assume that the cerebellum, as a part, at least, of its functions, represents a great apparatus for the maintenance of statotonus. For stimulation of the cerebellar nuclei, of their cerebellofugal axons, or of the motor nuclei of the tegmentum, leads to a marked increase of the muscle tonus, or even to outspoken

spasm, whereas interruption of the afferent spinocerebellar paths, or destruction of the cerebellar cortex, or injury to the motor nuclei of the tegmentum, results in marked hypotonia. The stimuli from the muscles and joints and from the labyrinth, then, seem to keep up through the intermediation of the cerebellum and of the motor nuclei of the tegmentum, the degree of muscle tonus and the co-ordination of muscular contractions that make standing and walk-

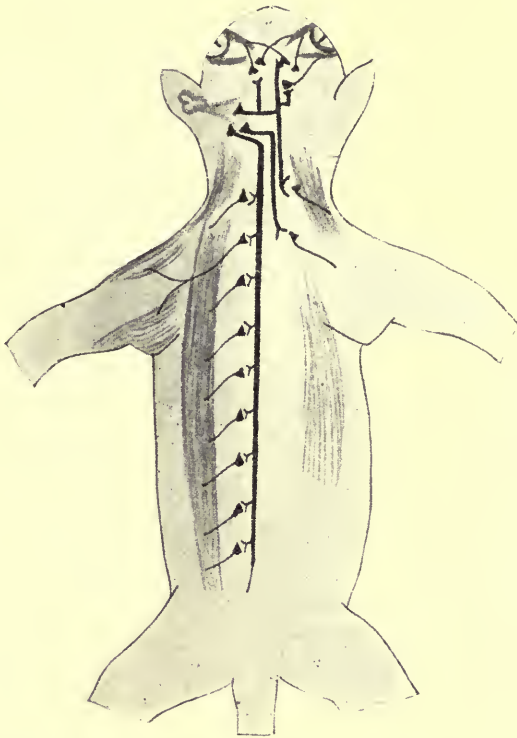


Fig. 43.—Diagram of the nucleus motorius tegmenti and its connections. (After L. Edinger, *Deutsche med. Wchnschr.*, 1913, p. 635, Fig. 2.)

ing possible. It is probable that the vermis is the essential statotonic portion of the cerebellum.

This statotonic mechanism mediated by the cerebellum and the motor nuclei of the tegmentum is, furthermore, thrown under inhibitory control by centers higher up. We know that there is an important bundle of fibers, the tractus tectocerebellaris of Edinger, that extends downward from the midbrain to end in the cortex of

the vermis and in the nuclei connected with it. Now, if this path be severed just below the midbrain, there is an enormous increase of ipsilateral tonus, and this hypertonicity becomes even more marked on joint movement. If the path on both sides be severed the whole body goes into the pronounced muscle spasm that constitutes the "decerebrate rigidity" of Sherrington. It is evident, therefore, that under normal conditions the total statotonic apparatus of the cere-

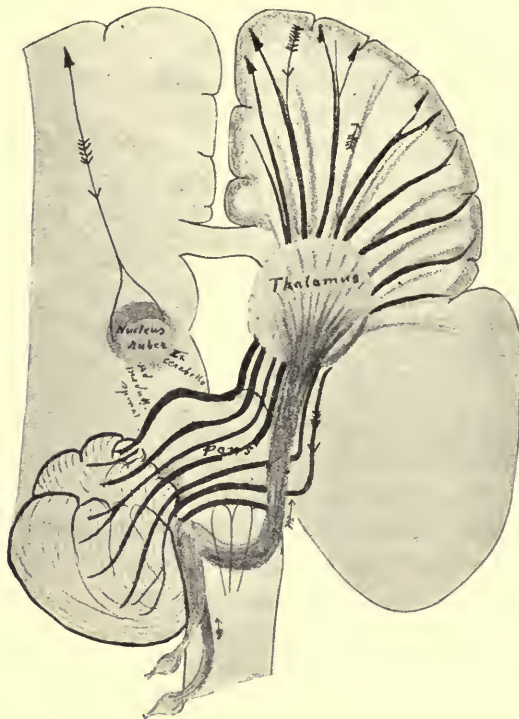


Fig. 44.—Diagram of the conduction paths from the posterior funiculi to the homolateral half of the cerebellum by way of the pons. (After L. Edinger, *Deutsche med. Wchnschr.*, 1913, p. 636, Fig. 3.)

bellum is subject to inhibitory impulses that descend from the mid-brain region.

Though the vermis seems to be mainly concerned, as I have said, with the maintenance of statotonus, it is the hemispheres of the cerebellum that appear to exercise synergic control of muscular activity other than that concerned in the maintenance of ordinary equilibrium. In the exercise of this control the hemispheres make

use of cerebellofugal paths, namely, the rubrospinal path, the vestibulospinal path, and, perhaps, other spinopetal paths in common with the vermis. The cerebellar hemispheres are, also, as we have seen, thrown under the influence of the great proprioceptive system

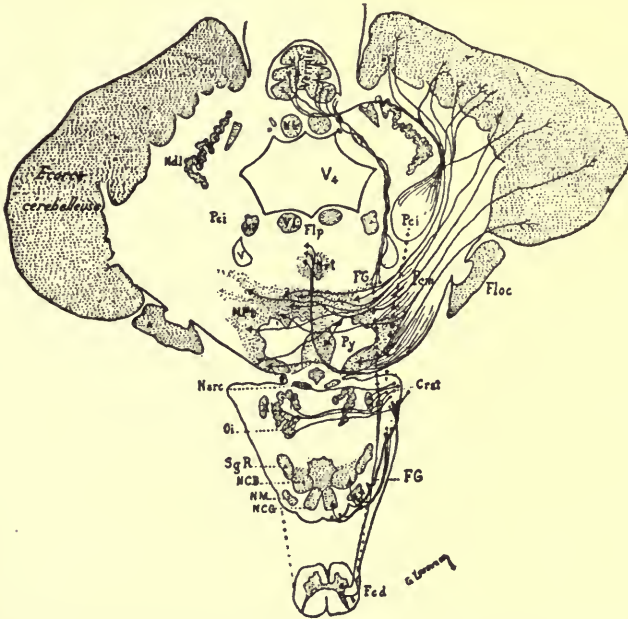


Fig. 45.—Afferent fibers of the cerebellum. (After André-Thomas, *Cerebellar Functions*, 1912, p. 39, Fig. 28.) *Cip*, Posterior segment of the internal capsule; *Cisl*, retrolenticular segment of the internal capsule; *Crst*, restiform body; *Fcd*, descending cerebellar bundle; *FG*, tract of Gowers; *Floc*, flocculus; *Flp*, posterior longitudinal bundle; *Ln*, locus niger; *Na*, *Ne*, *Ni*, anterior, external, and internal nuclei of the thalamus; *Narc*, arciform nucleus; *NC*, caudate nucleus; *NCB*, nucleus of the column of Burdach; *NCG*, nucleus of the column of Goll; *ND*, Deiters' nucleus; *Ndl*, dentate nucleus; *Nl*, nucleus of the lateral column; *NL₁*, *NL₂*, *NL₃*, first, second, and third segments of the lenticular nucleus; *NM*, nucleus of Monakow; *Npt*, pontine nucleus; *NR*, red nucleus; *Nrl*, nucleus reticularis tegmenti pontis; *Nt*, nucleus of the roof (fastigii); *Oi*, inferior olive; *P*, cerebral peduncle or crus; *Py*, pyramidal bundle and pyramid; *Pci*, *Pcm*, *Pcs*, inferior median and superior cerebellar peduncles; *SgR*, gelatinous substance of Rolando; *Th*, thalamus; *V₄*, fourth ventricle; *III*, nucleus of N. oculomotorius; *V*, descending branch of fifth nerve; *VI*, nucleus of sixth nerve.

(muscle sense, joint sense, vestibular sense), but this proprioceptive system, you will recall, influences the cerebellum only in a very roundabout way through the medial lemniscus, the thalamocortical paths, the cerebrocorticopontile paths, and the pontocerebellar paths.

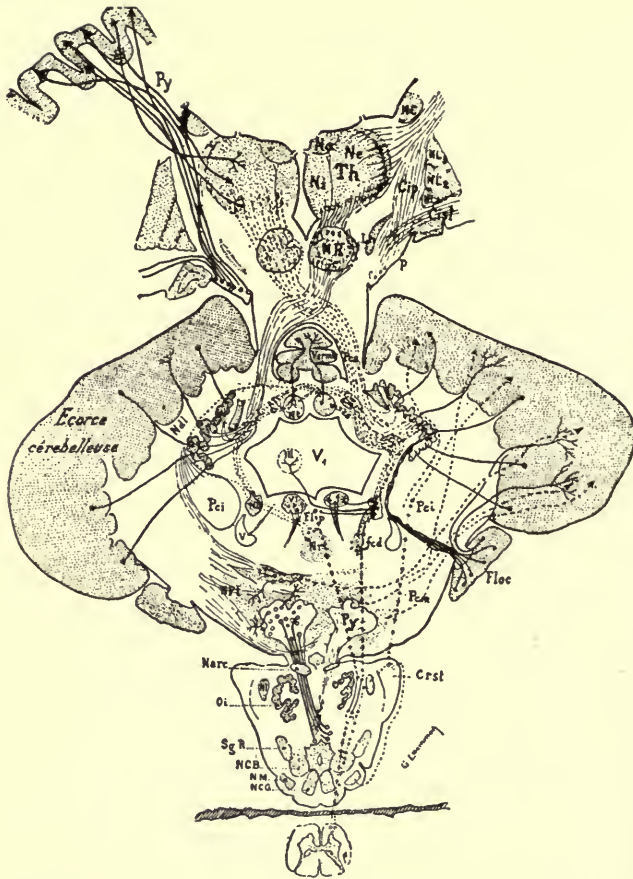


Fig. 46.—Efferent fibers and fibers of projection of the cerebellum. (After André-Thomas, *Cerebellar Functions*, 1912, p. 41, Fig. 29.) *Cip*, Posterior segment of the internal capsule; *Cisl*, retrolenticular segment of the internal capsule; *Crst*, restiform body; *fcd*, descending cerebellar bundle; *FG*, tract of Gowers; *Floc*, flocculus; *Flp*, posterior longitudinal bundle; *Ln*, locus niger; *Na*, *Ne*, *Ni*, anterior, external, and internal nuclei of the thalamus; *Narc*, arciform nucleus; *NC*, caudate nucleus; *NCB*, nucleus of the column of Burdach; *NCG*, nucleus of the column of Goll; *ND*, Deiters' nucleus; *Ndl*, dentate nucleus; *Nl*, nucleus of the lateral column; *NL₁*, *NL₂*, *NL₃*, first, second, and third segments of the lenticular nucleus; *NM*, nucleus of Monakow; *Npl*, pontine nucleus; *NR*, red nucleus; *Nrt*, nucleus reticularis tegmenti pontis; *Nt*, nucleus of the roof (fastigii); *Oi*, inferior olive; *P*, cerebral peduncle or crus; *Py*, pyramidal bundle and pyramid; *Pci*, *Pcm*, *Pcs*, inferior median and superior cerebellar peduncles; *SgR*, gelatinous substance of Rolando; *Th*, thalamus; *V₄*, fourth ventricle; *III*, nucleus of oculomotor nerve; *V*, descending branch of fifth nerve; *VI*, nucleus of sixth nerve.

It would seem that the minor forms of cerebellar asynergy and the past-pointing errors of B \acute{a} rány depend upon interference with the functions mediated by the cortex of the cerebellar hemispheres and their connections.

If these several views be correct we can, then, think of the vermis and its connections as subserving especially statotonus, and of the cerebellar hemispheres and their connections as subserving especially synergic control. It seems probable that in the cerebellar hemispheres the movements of each of the joints in the several directions in which movements occur are represented by definite local functional areas. The studies of Bolk and of B \acute{a} rány point to such a view.

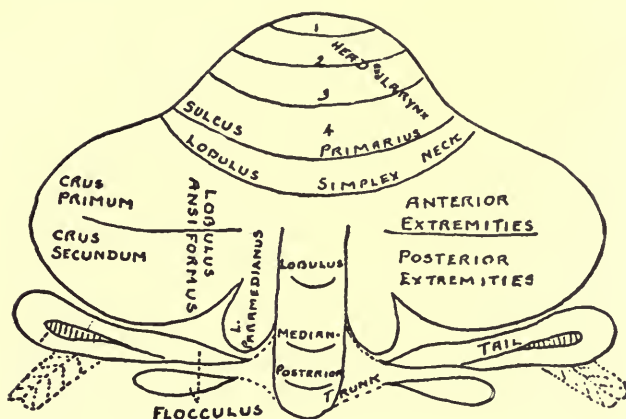


Fig. 47.—Bolk's diagram of the mammalian cerebellum; on the left half, the new anatomic names; on the right half, the functions of special areas. (After Bolk as modified by von Bechterew.) (Copied from the article by Mills and Weisenburg, Jour. Amer. Med. Assoc., Chicago, 1914, p. 1816.)

The tendency of late has been to consider the representation of the functions of the vermis and of the cerebellar hemispheres together as a whole, making divisions of the organ in a transverse direction and emphasizing less than formerly the separation between the middle part (vermis) and the lateral parts (cerebellar hemispheres). In Fig. 47 I have copied a diagram that illustrates von Bechterew's modification of Bolk's scheme of the mammalian cerebellum.

In 1913, at the meeting of the 17th International Congress of Medicine, Dr. C. K. Mills, of Philadelphia, gave an excellent review of the newer work on cerebellar function. In Figs. 48 and 49 are copied two diagrams that represent the views of localization in

the human cerebellar cortex that have been based upon the newer studies. Let me quote a paragraph from the article by Mills and Weisenburg (1914): "How then shall we apply the known facts of

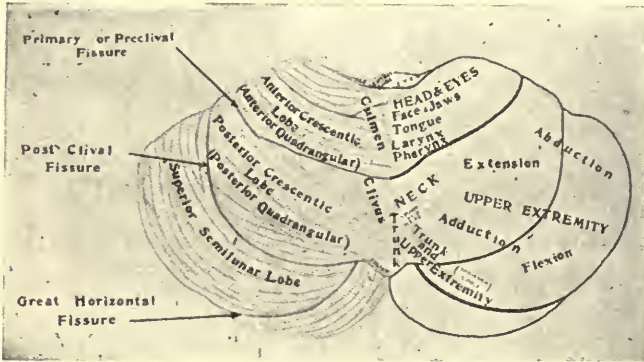


Fig. 48.—Cerebellar localization; zones and centers of the superior surface of the cerebellum. (After Mills and Weisenburg, Jour. Amer. Med. Assoc., 1914, p. 1817.)

cerebellar localization in neurologic diagnosis? Simply by bearing in mind that when the trunkal movements and those movements of the limbs which must act with them to preserve static and dynamic

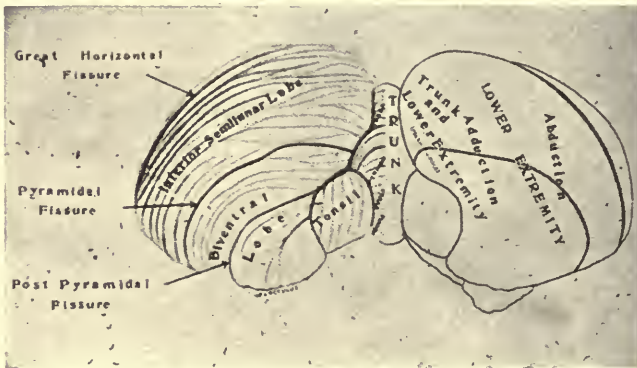


Fig. 49.—Cerebellar localization; zones and centers of the inferior surface of the cerebellum. (After Mills and Weisenburg, Jour. Amer. Med. Assoc., 1914, p. 1817, Fig. 3.)

equilibrium are affected, the vermis must be involved in whole or in part.

"The associated involvement of one lateral lobe in the vermal

lesion will be largely determined by unilateral dysmetric phenomena, the extent of the anteroposterior involvement of the inferior vermis by the preponderance of asynergy in either the lower or the upper limbs."

Great difficulty is often encountered in distinguishing the symptoms of labyrinthine disturbance from the symptoms of cerebellar disturbance, especially in mixed cases. Attempts have been made, however, to set up labyrinthine criteria and cerebellar criteria for the pure cases; that is, cases in which the labyrinth or the cerebellum is alone diseased. It would take us too far to discuss this subject in detail. At your leisure you should, in this connection, read the excellent article by Wilson and Pike (1915). Their views may be summarized in a single paragraph: "Labyrinthine lesions differ from cerebellar: (1) In the existence of Romberg's sign in labyrinthine lesions; (2) variations in the attitude of the head influence, the lack of equilibrium of the body in labyrinthine and not in cerebellar lesions; (3) an affection of the labyrinth does not definitely involve those movements of isolated parts which result in dysmetria; (4) in labyrinthine disease movements of rotation or disorientation are not so readily perceived."

Our time is more than up, but we must consider for a moment the localizatory significance of the symptoms in the patient before us, and we may try to form some guess as to the nature of the lesion or lesions present.

Let me summarize the principal facts regarding our patient:

1. There is optic atrophy, probably primary, though the ophthalmologists disagree on this point.

2. There is a pyramidal tract lesion, certainly on the right, and possibly on the left, as shown by the positive Babinski sign.

3. There is a subjective disturbance of sensation on the lateral surface of the right thigh, of many years' duration, but no objective disturbance is demonstrable. This must be due to some disturbance of the afferent or sensory conduction path (possibly in the posterior funiculi of the cord).

4. There is nystagmus, but this nystagmus has not yet been carefully analyzed for determination of its labyrinthine or cerebellar origin.

5. There is a positive Romberg sign, which points to extracerebellar rather than to cerebellar disturbance.

6. The patient a year ago exhibited typical cerebellar titubation, and even now he is unable to walk a crack. This symptom points to disturbance of the statotonic mechanism, but it could depend either upon a lesion in the cerebellum itself (vermis) or upon lesions in the cerebellipetal or cerebellofugal paths.

7. Some of the minor signs of cerebellar asynergy are present (adiadochokinesis, rebound phenomenon, etc.) and there is asynergy of the speech movements. These signs point to lack of synergic control. They are more marked in the left half of the body than in the right, and they are more pronounced in the left upper extremity than in the left lower. They point to a disturbance of the complex apparatus for synergic control, which, as we have seen, is mediated largely by the cerebellar hemispheres and their centripetal and centrifugal connections.

8. The history suggests the occurrence of several cases of a similar disease in this man's family, not only among his sibs but also, perhaps, in his mother and in two of his children. Though examinations of several members of the family should be made to make sure of this point, it seems very probable that the disease with which we are dealing is one of the heredo-familial diseases of which several groups are now known (Friedreich's ataxia; heredo-ataxia of Marie and of Sanger-Brown; primary cerebellar degeneration of Holmes; olivopontocerebellar atrophy of Thomas).

Obviously, further study of this patient and of his family will be necessary: (1) for more exact localization of the lesions and (2) for a decision as to the precise nature of the disease from which he suffers. Sometimes a slowly developing tumor of the nervus acusticus gives rise to a mass in the cerebellopontile angle that causes symptoms similar to those in our patient, but a recession of symptoms would scarcely have occurred with tumor. The history of the family and the obvious involvement of several of the extracerebellar paths (optic nerves, pyramidal tracts), in addition to the vestibulocerebellar symptoms, make it seem likely that we are dealing either with a progressive primary atrophic process or with a progressive degenerative process of wide-spread distribution.

[*Subsequent History of the Case.*—The patient was discharged as "improved" on February 10, 1920, two days after the clinic, with instructions to return if his symptoms became worse. Nothing was heard from him up to November 1, 1921.]

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XXII. HYPERKINETIC FORM OF EPIDEMIC ENCEPHALITIS

A COLORED MAN OF THIRTY-EIGHT SUDDENLY ATTACKED SEVERAL MONTHS BEFORE THE CLINIC WITH PAIN IN THE HEAD, DIZZINESS, AND LEFT HEMIPARESIS, AFTER WHICH DIPLOPIA, PUPILARY DISTURBANCES, AND VIOLENT SHAKING OF THE LEFT ARM DEVELOPED; CRANIOTOMY AND EXCISION OF AN AREA OF THE CEREBRAL CORTEX; DEATH; AUTOPSY.

THE patient before you illustrates a peculiar neurological syndrome and presents an interesting problem not only in topographical

diagnosis but also in the diagnosis of the nature of the underlying malady. I shall ask the clinical clerk, Mr. Andrus, to give us a brief account of the patient's history.

STUDENT: The patient, John D., is a colored laborer, aged thirty-eight, who applied for examination recently at the Out-patient Department of this hospital complaining of "shakes and paralysis."

On brief examination by Professor H. M. Thomas in the Neurological Clinic, such an interesting syndrome was found that the patient was admitted to Ward M of the stationary clinic (Professor W. S. Thayer) for thorough study and for a period of observation.

The family history of the patient revealed nothing of importance for his present illness.

The patient himself has been a hard-working negro. In childhood he had measles and chickenpox, but no other serious illness. In 1918 he had an attack of influenza. He asserts that he has never had gonorrhoea or syphilis. He has been subject to frequent colds in the head and has had a slight morning cough for years, but this has been unproductive of sputum and there has never been any hemoptysis. The patient has neglected his teeth and has had a great deal of trouble with his gums and with dental caries, so that a number of the teeth have from time to time been extracted. He has suffered from chronic constipation, and states that he has had to rise two or three times at night to pass urine. He has presented no nervous symptoms, however, until the present illness. His weight has been variable. At one time he weighed as much as 180 pounds, but he has lost a good deal of weight during the present illness.

He has used alcohol to excess, and states that he got drunk for many years whenever he had an opportunity to do so. He has been drinking quite heavily during the week preceding the present illness. It is difficult to know how much to rely upon his statements, for the patient seems, mentally, to be decidedly inferior. He made a number of contradictory statements during the taking of the anamnesis, and he is very poorly informed about things in general, stating that Mr. Taft is, at present, the President of the United States. He seemed also unable to give his own address or the addresses of members of his family. Nor did he know the name of the hospital in which he now is.

When asked about the onset of the present illness, he states that it appeared suddenly, six or eight months ago, while he was at work

shoveling dirt on the railroad. He felt a severe pain in the head, more marked on the left side and in the back of the head than elsewhere. He became dizzy and noticed a feeling of weakness in the left arm and leg. He was compelled to stop work. Some one told him that during the first week of his illness his left eye remained open while he was asleep. Occasionally he saw double. From five to seven days from the onset he noticed that his left hand began to shake. There was twitching, at first, in the fingers of the left hand, but this soon spread up the arm. Two or three weeks later he noticed shaking of the left foot, the shaking extending upward so as to involve the whole of the left lower extremity. He thinks that the arm and leg remained weak from the onset until the time the shaking began. The shaking has gradually grown more violent and is very troublesome while he is awake. Owing to this shaking he cannot go to sleep until late at night, but he says that others have observed that the shaking does not occur when he is asleep. The headaches ceased at the end of three months, but the shaking on the left side continued to be violent and to be constantly present except when asleep. He has a constant feeling of discomfort in the shaking left side owing to the continuous movement, and he has what he calls a "drawn-up feeling" in the arms. Four months before admission he noticed, temporarily, a slight disturbance of his speech. On trying to call out to some man he found, he says, that he could not make his tongue and lips work. This phenomenon seems to have been transitory. He states that he cannot stop the shaking no matter how hard he tries to do so. The shaking of the left arm is so violent that for some time while awake he has held his left hand with his right in order to control the shaking, or rather to limit the excursions. For some time his left arm has been strongly flexed at the elbow as well as at the wrist, and he states that efforts to straighten the limb are painful. The only other symptoms noticed during the present illness have been a little difficulty in starting the urinary stream and a persistent constipation.

On admission to Ward M the patient's temperature was 99.8° F., pulse-rate 84, and his respiration rate 28. Though muscularly well developed, he is now markedly undernourished. The striking thing about him is the violent shaking of the left side of the body, well marked in the foot and leg, but most violent in the hand and forearm. He tries to control this shaking, as you observe, by holding

the left hand with his uninvolved right hand and by crossing the legs. The shaking is rhythmical, the rate about 230 to the minute, that is, approximately, 4 oscillations per second. When the left arm is left free the excursions of the hand are at first from 3 to 5 inches, but if the patient be at all excited more extensive excursions are made and the left forearm and hand are thrown back and forth violently, like a flail. The head is turned somewhat to the right and flexed lateralward toward the right shoulder, an attitude that tends to be maintained, though it can be voluntarily overcome.

A general physical examination outside of the nervous system reveals but little. The throat and chest are negative, both lungs and heart seeming normal. There is no thickening of the radial arteries, nor are there any signs of arteriosclerosis elsewhere in the body. The blood-pressure is 130 systolic, 100 diastolic. The patient has marked pyorrhea alveolaris. The abdomen is quite negative on physical examination. Neither the spleen nor the liver is palpable, and no abnormal masses can be felt in the abdomen. The testes are normal. There is no scar on the penis. The prostate shows no marked thickening.

There is a little general muscular atrophy of the left side; the exact measurements are given in Fig. 50.

DR. BARKER: What did the neurological examination reveal in addition to the violent shaking on the left side, the forced attitude of the head, which you have already described, and the slight muscular atrophy on the left side?

STUDENT: There seems to be some paresis of the lower part of the face on the left side. The angle of the mouth is drawn somewhat to the right. There is no disturbance in the upper facial domain except that the right lid-slit is wider than the left, possibly the right eye is a little more prominent than the left. The muscular strength does not seem to be impaired on either side, though voluntary movements are interfered with in the left upper and lower extremities, owing to the violent involuntary contractions. The flexion contractures of the left elbow and of the left wrist are evident, and there is rather marked rigidity of both arm and leg on the left.

There is no dysarthria nor dysphagia at present. There is no paralysis in the domain of distribution of the cerebral nerves except for the weakness of the lower left face already mentioned, certain pupillary disturbances (to be described in a moment), and a slight

exophoria (though each bulb can be moved far to the right and far to the left). There is no inco-ordination except that which the tremor will account for. The heel-knee test is well performed on both sides.

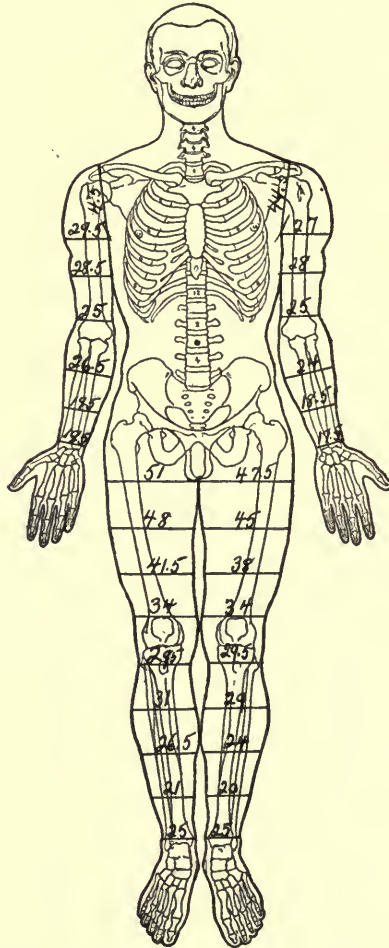


Fig. 50.—Patient with epidemic encephalitis. Comparative measurements of the circumference of the extremities at different levels, showing slight atrophy on the left side.

The finger-nose test is also well performed on the right, but, on attempting this on the left, the tremor is violent. When the patient tries to stand there is a little tendency to fall, owing to his inability properly to use the muscles of his left side.

No disturbances of cutaneous sensibility can anywhere be made out by applying light touch, the prick of a pin, or hot and cold test-tubes. Nor is there any general disturbance of deep sensibility, for he detects and names correctly the direction of slight passive movements on the right side. Smell, taste, and hearing are unaffected. A little dizziness has been the only disturbance in the vestibular domain. His eyesight is not impaired and the eye-grounds are negative on ophthalmoscopic examination; no signs of choking of the disks or of retinal arteriosclerosis can be detected.

The deep reflexes are present on both sides. The left knee-jerk is more active than the right. The deep reflexes of the upper extremities are approximately equal on the two sides. The superficial abdominal and cremasteric reflexes are active and equal on the two sides. Plantar stimulation of the sole of the left foot yields either no reaction or a slight plantar flexion of the great toe. The other four toes on this side have been amputated. Plantar stimulation of the sole of the right foot causes plantar flexion of the great toe and rather marked tickle response. However, on testing on the right for the Oppenheim reflex by stroking the skin over the medial surface of the tibia, there is pronounced dorsal flexion of the great toe. The Gordon reflex is also positive on the right, yielding dorsal flexion. The Oppenheim and Gordon reflexes are negative on the left.

The pupils are equal in size and stand midway between dilatation and contraction. Neither pupil reacts to light, though each pupil contracts a little on accommodation and on convergence. Even this contraction is slight, so that there is a tendency to absolute pupillary rigidity rather than typical Argyll-Robertson pupils.

On testing for the hip-trunk flexion synergy, it is found that the right leg is raised from the bed higher than the left, but that the right shoulder is drawn further forward than the left and is directed somewhat toward the left leg, an atypical result.

DR. BARKER: What laboratory tests have been made upon this patient?

STUDENT: The blood, the urine, the stools, and the cerebrospinal fluid have been examined.

The red cell count is normal; the hemoglobin 85 per cent.; the white cell count varies between 7340 and 8040; the differential count reveals nothing abnormal.

The Wassermann reaction in the blood-serum is negative.

The examination of the stools is negative, as is also that of the urine.

The cerebrospinal fluid was not under increased pressure, and there were only one or two cells. The Wassermann reaction in this fluid was negative.

DR. BARKER: This is indeed an interesting array of symptoms, especially in neurological domains. The man seems to have been suddenly attacked while at work with violent pain in the left side and back of the head, with dizziness, and with weakness in the left arm and leg. Within a week shaking of the left hand and arm appeared, to be followed two or three weeks later by shaking of the left leg. This shaking in the two extremities on the left side has been violent and has continued ever since, ceasing only when the patient is asleep.

The tongue shows a faint tremor, as you see, and, interesting enough, the tremor is much more marked in the left half of the tongue than in the right. It may be that the little tremor on the right is transmitted from that on the left. You note the forced attitude of the head; the face is turned to the right and the head is flexed lateralward toward the right shoulder. The muscular atrophy on the left side is not very marked. I doubt if you would notice it unless you looked very closely or made measurements, such as Mr. Andrus has made. The flexion contracture at the left elbow is obvious. As I try to extend the arm, you notice what resistance is offered; there is a marked increase in tonus of the flexor muscles. I can flex the arm, however, easily after it is extended; there is very little hypertonus in the extensor muscles of the elbow. You observe, however; that there is marked hypertonus in all these muscles of the lower extremity. The whole limb is rigid and attempts at manipulation cause exacerbation of the shaking.

(To patient): Please let go of your left hand and let the arm shake as it will.

Notice how violent the shaking now becomes and how wide these excursions are; now his whole forearm is shaking like a flail. Note, too, how rhythmical the shaking is and the rate of the oscillations. It resembles a Parkinsonian shaking, except that it is much more violent and the excursions are much wider. There is no choreatic disturbance of motility here. The disturbance reminds me of what was described as "hemiballismus" by Kussmaul.

Now, let us retest the reflexes. You see that the periosteal, radial, the biceps, and the triceps reflex are present on the right. I get them, also, here on the left, although the shaking interferes with the tests. Note how feeble this knee-jerk is on the right, even with reinforcement. It is well marked on the left. The superficial abdominal reflexes are active and equal on the two sides.

Plantar stimulation, first on the left where only the great toe is left, causes scarcely any response. When the toe moves at all it moves slightly downward. Oppenheim and Gordon tests yield a similar response here. Now, let us try on the right. You notice that plantar stimulation causes plantar flexion of the great toe here. But on testing for the Oppenheim reflex, as I pass my thumb down the medial side of the left leg, you notice how very definite the dorsal response of the great toe is. The Gordon reflex, as you see, also gives a dorsal flexion of this great toe. This is a curious dissociation, for usually the Oppenheim and Babinski tests yield the same response; but here the Babinski test is perfectly negative, whereas the Oppenheim test is positive.

Let us next try the hip-flexion synergy test.

(To patient): Please lie flat on your back; stretch your legs wide apart; hold your arms folded across your chest, so. That's right. Now please sit up.

Note that both legs are raised, but that the right leg is raised much higher than the left. Note, however, that the trunk is rotated to the left so that the right shoulder is directed toward the left lower extremity. Ordinarily, with this test, when the right leg rises more than the left, the trunk is rotated in the opposite direction, so that the left shoulder passes farther forward than the right and is directed toward the right leg. Here again we have a peculiar discrepancy to record.

I desire to test these pupils again in your presence. The pupils now are certainly about equal in size and are midway between dilatation and contraction. Neither pupil contracts to light, either directly or consensually.

(To patient): Please look closely at my finger as I bring it toward your face. There is a little contraction of each pupil on convergence and on attempts at accommodation, but very little. It is, indeed, a very sluggish reaction. There is, therefore, almost total pupillary rigidity here, though I must admit that there is a little contrac-

traction on accommodation and on convergence. The reaction to light is absent entirely. I suppose we shall have to call it an Argyll-Robertson pupil, though it stands midway between the typical Argyll-Robertson pupil and absolute pupillary rigidity.

We shall not repeat the sensory tests here, for they have been carefully gone over in the ward and were entirely negative. Even the stereognostic sense has been tested and was found normal in both hands.

There is no real inco-ordination here; you see he can easily touch his nose with his forefinger of the right hand; with that of the left he cannot do so on account of the flail-like shaking. You note that he does the knee-heel test perfectly well on both sides and he can run his heel accurately down the front of his shin.

The only sphincter disturbance he has complained of is a slight difficulty in starting the flow of urine.

(To student): Let us try to *localize the lesions* that account for these clinical disturbances. Let us begin with the disturbances of motility. Do you think these motor disturbances are due to a lesion of the central nervous system or of the peripheral nerves?

STUDENT: Of the central nervous system.

DR. BARKER: Do you think the lower motor neurones or the upper motor neurones are principally concerned here, or are still other motor neurones involved.

STUDENT: The muscular atrophy might make one think of lower motor neurone lesions, but the atrophy is slight and there is no fibrillary twitching. The test for reaction of degeneration has not yet been made, although with the reflexes active, everything points to the integrity of the lower motor neurones.

DR. BARKER: Is there anything pointing to injury to the upper motor neurones, that is, to the motor neurones the medullated axons of which form the pyramidal tract?

STUDENT: Yes; the paresis in the lower facial domain suggests a supranuclear lesion of the corticomotor path to the face. The positive Oppenheim on the right might also suggest a pyramidal tract lesion, but the Babinski is negative. I do not know how to interpret this.

DR. BARKER: Nor do I; I wish I did. It is strange, too, that the knee-jerk on the right is less marked than that on the left. You remember that the patient complained of some weakness of the left arm and of the left leg immediately after the onset of his illness, and

he stated that this weakness continued until the shaking began. It is quite possible that this patient did have a left hemiplegia of upper motor neuron origin. If so, the signs have largely passed off now. The resident physician, Dr. Mason, who made a careful neurological note soon after the patient was admitted, thought that there had been a left hemiplegia and that also there was a slight involvement of the pyramidal tract on the right side.

What about this violent shaking?

STUDENT: It is a symptom of motor irritation and would be grouped among the hyperkinetic phenomena.

DR. BARKER: Yes. One wonders whether this hyperkinesia is due to direct irritation or due to injury to some inhibitory mechanism. The condition reminds one somewhat of the agitation in unilateral Parkinson's disease, but the shaking is much more violent.

Dr. J. Ramsay Hunt, of New York, as you know, has described lesions of the cells in the globus pallidus of the nucleus lentiformis in Parkinson's disease. The so-called extrapyramidal motor system has become very interesting to clinicians in recent years, for when it is injured so-called amyostatic syndromes make their appearance. The term "amyostatic" is not very happily chosen, however.

Where are the lesions that have caused these disturbances of the pupillary reactions?

STUDENT: I should think somewhere in the midbrain.

DR. BARKER: Yes, I think so too. The patient sees perfectly well, and the eye-grounds are negative. The visual paths to the occipital cortex seem to be intact. The oculomotor nerves are not paralyzed. Even the autonomic fibers innervating the intrinsic muscles of the eye are still functioning, although very sluggishly. The pupillary contractions are sluggish on accommodation and on convergence, and do not occur on exposure to light. The lesions seem to be, therefore, in the midbrain, but proximal to the cell-bodies of the neurones that give origin to the fibers of the oculomotor nerves. These lesions are in the corpora quadrigemina or in the cerebral peduncles below them. They may be in the terminals of the optic fibers that go toward the nuclei of origin of the oculomotor nerves or in the little neurones intercalated between these optic terminals and the cells in the nuclei of the oculomotor nerves, that is to say, in the *Schaltneurone* of von Monakow.

Precise localization of the lesions in this man's brain is not easy.

We have evidence, however, of lesions involving (1) the pupillary innervations on both sides, (2) the extrapyramidal motor innervations, and (3) the pyramidal motor innervations also. These lesions are probably rather diffuse lesions in the midbrain region, and in the region of the basal ganglia.

A word should be said perhaps regarding the structural basis of the psychic inferiority exhibited by this patient. But first let me ask you, was this psychic inferiority manifest before the onset of the present illness, or has it developed only since then?

STUDENT: We have not been able to find out. We are trying to get in touch with friends and relatives of the patient in order to ascertain whether or not there has been marked psychic deterioration since the illness began.

DR. BARKER: Yes. It would be interesting to know whether there is a constitutional psychopathic inferiority here, or whether there has been mental deterioration that appeared only during the present illness.

What part of the brain would you say might be especially concerned in such a hypophrenia?

STUDENT: Since normal mental functioning depends largely upon integrity of the cerebral cortex and of the association paths, I should think the forebrain would be concerned.

DR. BARKER: Yes; either there has never been a proper development of the cerebrum, or, if the deterioration is due to the present illness, then there must have been lesions involving either the cortex or the association paths during this illness.

Let us consider next the *nature* of the pathological changes underlying the patient's present condition.

Do you think the pathological anatomical changes are of circulatory origin, of toxic degenerative origin, of inflammatory origin, or of neoplastic origin?

STUDENT: I do not feel sure.

DR. BARKER: If they were of circulatory origin, what are some of the common disturbances of circulatory conditions that might be considered?

STUDENT: Cerebral hemorrhage, cerebral thrombosis, and cerebral embolism.

DR. BARKER: Is there anything in the history or the physical examination pointing to cerebral hemorrhage?

STUDENT: No, I think not. Though the onset was sudden, while he was at work, with pain in the head, dizziness, and a feeling of weakness in the left arm and left leg, still a week later the shaking in the upper extremity developed and two or three weeks after that the shaking in the lower extremity. This history points to some progressive process. If he had had a cerebral hemorrhage one would expect most of the symptoms to appear at once and to see some recession of the symptoms later.

DR. BARKER: Quite so. Moreover, his blood-pressure is low (systolic 130), and there are no signs of arteriosclerosis anywhere in the body. Could he have had cerebral thrombosis?

STUDENT: I suppose so; but at his age cerebral thrombosis, or cerebral occlusion, is most often due to syphilis, and I do not think he has had syphilis.

DR. BARKER: We shall discuss the question of syphilis as an etiological factor a little later. Certainly it would not seem likely that he could have had an occlusion of a cerebral artery due to an arteriosclerotic process, nor is embolism a likely explanation of his symptoms.

Could an inflammatory process account for the symptoms?

STUDENT: Yes; I think it could. Syphilis is the first inflammatory process I would think of. Tuberculosis is possible, especially as he is a colored man. Epidemic encephalitis should be kept in mind as a possibility.

DR. BARKER: What, among the facts, do you think, favor the idea of syphilis?

STUDENT: Syphilis is common in the negro, and cerebral diseases in young people are often due to syphilis.

DR. BARKER: Yes, that is true; but so far as we know the patient has never had syphilis. There is no scar on the penis. There is no history of "secondaries." The Wassermann reaction in the blood-serum is negative, and that in the spinal fluid also. The cell count in the spinal fluid is not increased. There is, however, one sign present here that makes one think of the possibility of a pre-existing syphilitic infection. What is it?

STUDENT: The pupillary rigidity.

DR. BARKER: Yes; changes in the pupils such as this patient presents make one think of cerebral lues or of paralues—a *tabes dorsalis* or a *dementia paralytica*.

It is certainly very uncommon to meet with the Argyll-Robertson pupil outside of tabes dorsalis or general paresis, both of which are due, we believe, to pre-existing syphilitic infection.

Do you know of any condition other than lues in which the Argyll-Robertson pupil occurs?

STUDENT: It is said that it is sometimes met with in chronic alcoholism.

DR. BARKER: Yes; there are some reports in the literature to that effect. This patient has been addicted to alcoholism. Still, the Argyll-Robertson pupil must be exceedingly rare in chronic alcoholism. I do not remember having met with a single instance in which I felt sure that chronic potatorium had given rise to an Argyll-Robertson pupil. Do you know of any other condition that might be responsible?

STUDENT: I do not think of any.

DR. BARKER: Well, it is interesting that in the reports that are coming in on epidemic encephalitis, there have been a few instances in which an Argyll-Robertson pupil has been due to the encephalitis. I have with me here the August number of the *American Journal of Ophthalmology* (1920). In it is an article by Guilford Dickinson entitled "Ocular Notes on Lethargic Encephalitis," with 2 case reports. In 1 of these cases there was a typical Argyll-Robertson pupil on the left side which was due to the encephalitis, and which disappeared as the symptoms of encephalitis passed off. There was no history of lues in the case, and the Wassermann reactions were negative. Moreover, in the European reports considerable stress is now being laid upon the pupillary disturbances in lethargic encephalitis.

I do not think that this man has syphilis now. If he were a general paretic he would almost certainly have a positive Wassermann reaction in the blood-serum and also in the cerebrospinal fluid. If he had tabes dorsalis, though the blood Wassermann reaction might be negative, the cerebrospinal fluid Wassermann would probably be positive, and the cell count would be increased. One could think, of course, of a so-called "burnt-out tabes"; that is, of a tabes that has been wholly arrested. But this is rare in the absence of anti-syphilitic treatment. Therefore, I must conclude that these pupillary changes are probably due to the same trouble that has caused this shaking on the left side, and the other symptoms that have recently developed.

Though there has been but little fever, and no definite eye-muscle paralysis, it is quite possible that the whole abnormal condition has been due to an encephalitis.

Parkinsonian forms, myoclonic forms, and other hyperkinetic forms of epidemic encephalitis have been manifoldly reported both in this country and in Europe. Encephalitis epidemica can simulate almost any neurological syndrome. Everything depends upon the situation of the encephalitic lesions.

Neoplasm is very improbable in this case. The mode of onset does not suggest neoplasm; it was too sudden. Of course, one does sometimes see symptoms suddenly appear when a hemorrhage occurs into a neoplasm. A slowly developing glioma may be latent as far as the symptoms are concerned until there is a hemorrhage into it, when symptoms may suddenly appear. It is some eight months, however, since this trouble started. One would think that a neoplasm sufficiently large to cause the symptoms present would be accompanied by signs of increased intracranial pressure. Were any such found?

STUDENT: The patient has had some dizziness and some headache. He has had no nausea and no vomiting, and there has been tachycardia rather than bradycardia. Moreover, there has been no sign of choked disk.

DR. BARKER: The patient is to remain some time longer in the hospital under observation. It may be that we can secure further data that will help us in arriving at a final conclusion. For the present I am inclined to think that the underlying malady has been a special form of epidemic encephalitis, and that this disease has been responsible for lesions in the midbrain and in the interbrain. Whether or not it is also responsible for the psychic inferiority now exhibited we do not know.

This violent shaking, especially of the left arm, is most troublesome to the patient. Have you any therapeutic suggestions to offer?

STUDENT: I cannot think of any satisfactory remedy.

It would be scarcely feasible to control the shaking by drugs, though hyoscin or coniin might be tried.

DR. BARKER: As I entered the clinic our Professor of Neurology, Dr. H. M. Thomas, suggested that if the violent shaking of the left arm continued to be such a source of annoyance to the patient as

it now is, it might become necessary to extirpate the arm area in the right cerebral cortex. That is an interesting therapeutic suggestion. Life is certainly a torture to this man as he now is. Moreover, when the hyperkinetic disturbance continues many months, as it has here, one begins to despair of a spontaneous recession. Many encephalitic symptoms clear up entirely, but there are occasionally permanent residuals. If this violent shaking should continue much longer I think Dr. Thomas' suggestion should be acted upon. Either Dr. Heuer or Dr. Dandy could extirpate the portion of the cortex containing the pyramidal cells that innervate the left arm. This arm is of no use to the patient as it is. He would be much better off with a quiet arm than with this violently shaking member.

[*Subsequent History of the Case.*—As there was no improvement in the patient's condition he was transferred to the Surgical Service a few days later. On October 30th Dr. George Heuer removed what he believed to be the motor cortex of the left arm, the area excised being of nearly the same size and shape as that removed by Sir Victor Horsley in 1896. Twenty-four hours later the contractions had ceased and the patient seemed to be in fairly good condition, though he was stuporous and could not be easily roused. His expression was apathetic. On the second day after the operation his temperature rose to 103° F. On the third day, immediately after the wound was dressed, the patient had a jacksonian epileptiform convulsion, beginning with twitching of the left face, the eyes and the head being turned to the left side. The seizure was confined to the left face for about a minute, after which the left arm began to jerk furiously, though the left leg was not affected. Ten minutes later a similar convulsion began, which extended to the right arm and leg. The right pupil was larger than the left. Neither of them reacted to light. The twitching continued and finally became continuous. The patient's temperature rose to 107° F.; the pulse was 180 per minute; the respirations 45 per minute. At 11 P. M. on the third day the patient was given 100 c.c. of hypertonic Ringer's solution, administered intravenously. Two hours later (1 A. M.) on the fourth day another injection of the same kind was begun, but before 10 c.c. had been received the pulse became imperceptible and respiration ceased.

Report of Autopsy (Made by Dr. Putnam).—“Craniotomy. Removal of sensory cortex. No lesions found. Subdural hemorrhages.

The brain was removed as a whole and placed in a solution of 10 per cent. formalin for further study."

Neuropathological Report on Brain (Made by Dr. V. R. Mason).—"The brain shows the effects of general congestion. The convolutions are flattened; the sulci closed; there is herniation of the cerebellum and the vessels, particularly those of the cortex, are engorged. There is a large subdural clot which pressed upon the right frontoparietal region causing an induration.

"In the upper right paracentral area an operation was performed to remove the motor cortex with a view to relieving the left-sided myoclonic spasm. After localization by stimulation the cortex of the arm area was removed. The spasms were not relieved. Examination shows the area removed to be directly posterior to the motor area.

"The brain was cut horizontally in many slabs, but nothing was found to account for the myoclonic spasms of the left arm or of the left leg.

"Sections for examination were taken from:

"(1) *The Operation Block.*—The absence of giant-cells shows that it is not taken from the motor cortex. The shallower plexiform layer and the more prominent external large bone show the characteristics of the posterior central cortex.

"(2) *Cortex Inferior to the Site of Operation.*—This shows giant-cells; a broader plexiform layer; and a less prominent external pyramidal layer.

"(3) *Central Ganglia.*—Normal.

"(4) *Cerebellum.*—Normal.

"(5) *Medulla.*—Normal.

The tissue from different parts is to be very carefully studied histologically in the Phipps Psychiatric Clinic.]

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XXIII. THALAMIC SYNDROME APPEARING SUDDENLY IN A PATIENT UNDER TREATMENT FOR HYPERTENSION, GLYCOSURIA, AND OBESITY.

A COLORED WOMAN, FORTY-EIGHT YEARS OF AGE, AN EPILEPTIC SINCE CHILDHOOD, AND MILDLY MELANCHOLIC SINCE THE MENOPAUSE THREE YEARS AGO, WAS ADMITTED TO THE HOSPITAL SOME TWO MONTHS BEFORE THE CLINIC, COMPLAINING OF "WEAKNESS AND NERVOUSNESS." AND WAS FOUND TO BE SUFFERING FROM A CHRONIC ARTERIAL HYPERTENSION WITH OCCASIONAL VASCULAR CRISES, SLIGHT MYOCARDIAL INSUFFICIENCY, SOME RENAL INVOLVEMENT, GLYCOSURIA, AND OBESITY; ON THE FOURTH MORNING AFTER ADMISSION SHE AWOKE WITH RIGHT HEMIPARESIS, HEMIANESTHESIA, HEMIATAXIA, AND DYSARTHRIA, PHENOMENA THAT HAVE UNDERGONE CERTAIN CHANGES DURING THE MONTHS THAT HAVE ELAPSED SINCE THE TIME OF THE CEREBRAL INSULT.

The patient before you presents a congeries of syndromes of especial clinical interest. There is such a wealth of material in this single case that we may experience some difficulty in dealing with it in a satisfactory way in the short period of an hour. I shall ask the clinical clerk to give you a brief résumé of the history. In order to conserve our time I shall ask him to eliminate from his account most of the negative and perhaps some of the less important positive data in order that the essential phenomena may be presented to you without too great dilution.

STUDENT: The patient, Josephine S., a widow, is a colored cook and laundress, forty-eight years of age, who was admitted to the Johns Hopkins Hospital (Ward O) on September 30, 1920, complaining of "weakness" and of "nervousness."

The *family history* seems unimportant. In her own *past history* she reports several of the childhood diseases, also occasional sore throats, a fracture of the right arm at twelve, an attack of gastritis of six weeks' duration at eighteen, and an operation last year at this hospital for bursitis of the left elbow. There is no history of lues. There has been one pregnancy and the child is living and well.

Asked regarding her *present illness*, she states that at the onset of the menopause three years ago she became nervous and easily upset, crying frequently, and awaking in the morning with a feeling of dizziness and light-headedness. During the past three years she has noticed increased frequency of urination both during the day and at night, and she complains of "black specks" before her eyes, especially the right eye. She has been short of breath on exertion, and has noticed a little swelling of the ankles toward evening. Her appetite has been poor. She sleeps badly and worries much. She has suffered from hot flushes and from weakness. When asked for the cause to which she ascribes her nervousness, she stated that she thought it began with the separation from her daughter consequent upon the marriage of the latter.

On further inquiry into her nervous history it was found that she had been subject to "spells," which began at the age of nine and occurred monthly for years. She has had only two attacks, however, during the last two years, the last attack occurring eighteen months ago. She states that in some of these attacks she bit her tongue and once fell upon the stove and was burned.

DR. BARKER: What was her physical condition on admission?

STUDENT: The *status præsens* on admission, as dictated by the house officer, Dr. Reinoff, may be summarized as follows: Temperature, 97.6° F.; pulse, 92; respirations, 20; blood-pressure, 200 systolic, 90 diastolic.

Well-developed, obese, colored woman. Mental state clear except for depression. Pupillary reactions and ocular movements normal. Patient wears glasses. Eye-grounds show thickened arterioles and small patches of exudate in the right eye. No retinal hemorrhages. Hearing acute. All teeth have been removed; mouth otherwise negative. Neck and thyroid negative; no tremor.

Thorax rigid and somewhat barrel shaped. Lungs negative except for moderate emphysema. Heart somewhat enlarged to the left (12 cm.). Soft systolic murmur at the apex, not well trans-

mitted. Aortic second sound accentuated. No cardiac arrhythmia. Peripheral vessels (brachials and radials) somewhat thickened.

Abdomen negative. Slight pitting of the ankles on pressure. Deep reflexes present on both sides, but rather sluggish in the lower extremities. Babinski negative. Superficial reflexes normal. Pelvic examination negative.

Patient 30 pounds over calculated ideal weight (actual weight 167 pounds; height 5 feet, 5 inches). No evidences of hypophyscal disease.

DR. BARKER: Tell us, please, the results of the routine laboratory tests.

STUDENT: *Blood*: R. B. C., 4,448,000; hemoglobin, 78 per cent.; W. B. C., 8520. Several differential counts showed a reduction of the polymorphonuclear elements and a marked increase in the small mononuclears. The polymorphonuclears varied between 40 and 56 per cent. and the small mononuclears between 40 and 35 per cent. The eosinophils were only 1 per cent. The large mononuclears and transitionals were somewhat increased, one count being as high as 17 per cent. The Wassermann reaction in the blood was negative.

Urine.—Specific gravity 1020 on admission; considerable albumin; a little sugar; a few granular casts, and a few blood-cells. Subsequent examinations of the urine showed a tendency to fixation of the specific gravity between 1008 and 1013.

Renal Function Tests.—Phthalein output, 57 per cent. in two hours. Urea-N. in the blood, first examination, 27.7; on later examination, 13. Blood-sugar, on first examination, 0.21; on later examinations, after reduction of carbohydrate intake, 0.13 to 0.12.

DR. BARKER: The class has had, I believe, the opportunity of seeing this patient shortly after her admission. At that time Professor Palmer discussed the special dietetic problems that arose in this case from the coexistence of glycosuria and obesity, on the one hand, with chronic renal disease, on the other.

Was the carbohydrate tolerance tested here?

STUDENT: Yes; on carefully testing the carbohydrate tolerance, it was found that when she was taking 50 grams of protein and 60 grams of fat she could also ingest over 280 grams of carbohydrate without glycosuria. It has, therefore, been very easy to keep her sugar free. In order to reduce her weight, to throw but little burden upon the kidneys, and to control the glycosuria she has recently

been upon a diet containing about 1050 calories, and consisting of 60 grams of protein, 60 grams of fat, and 60 grams of carbohydrate.

DR. BARKER: Has she shown any tendency to acid intoxication?

STUDENT: No; the urine contains neither diacetic acid nor acetone.

DR. BARKER: On the fifth day after admission, that is, on October 4th, the patient, on waking in the morning, found that something strange had happened to her. Will you give us an account of what she described?

STUDENT: After she awoke that morning she found that she could not move her right side properly, that her speech was disturbed, that the vision of the right eye was dim, that she was a little deaf in the right ear, and that she had lost sensation on the right side of the body. Though she could make some movements with the right half of the body, she complained of being very weak on that side, and stated also that the right half of the body felt numb. Her mind was clear. She was puzzled by the situation.

DR. BARKER: Did she complain of any pain?

STUDENT: No; she was entirely free from pain and has had none since.

DR. BARKER: Was there any fever accompanying or following this attack?

STUDENT: No; her temperature was normal before and during the attack, and has been so ever since.

DR. BARKER: Was there any sphincter disturbance?

STUDENT: None whatever.

DR. BARKER: These discoveries reported by the patient are most interesting. Will you tell us what was found on physical examination that forenoon?

STUDENT: When tested for various movements the whole right side of the body was found to be weak. In the face, the weakness involved chiefly the lower facial domain, but not the upper facial. There was no eye-muscle paralysis, and no conjugate deviation of the eyes or the head. The movements of the left upper extremity were weakened throughout, and, when testing them, there were some clonic contractions of the muscles that flex and extend the forearm. On testing the movements of the right leg, all were found to be definitely weakened. The deep reflexes in the upper extremities were equal on the two sides. The deep reflexes in the lower extremities were absent or, at any rate, were not elicited. The abdominal re-

flexes were present. Plantar stimulation on the right caused no movement of the great toe, though there was a little spreading of the other toes. Plantar stimulation on the left yielded normal response. There was almost complete hemianesthesia for all modalities of sensation on the right half of the body; thus, there was total analgesia and total thermo-anesthesia on the right, and tactile sensation was lost everywhere on the right except in the right foot; there was also loss of the sense of position and of the sense of movement in the whole right side, except for coarser movements of the leg. There was marked dysarthria, but no aphasia. There was also hemi-ataxia on movement on the right side (finger-nose test, heel-knee test).

DR. BARKER: A most interesting syndrome! A syndrome that immediately gives the clue for the localization of the lesion to any one accustomed to thinking neurologically.

Did the phenomena that you have described persist, or have changes occurred since October 4th (about two months ago)?

STUDENT: Within five days the dysarthria had disappeared, the weakness of the right side of the body had become much less, though there was still some paresis, and the ataxia was less, but the sensory disturbances remained unchanged. By two weeks after the attack the muscular strength in the right side had largely returned and the sensory disturbances had become less marked; tactile sensation, also, had begun to return, and she could discriminate between cold and heat in many places; the postural sense had improved a little, but there was still some dulness of hearing in the right ear and a complaint of dimness of vision in the right eye. Four weeks after the attack there had been a little more return of sensation, but the hemiataxia remained unimproved.

During the past two weeks, however, a new symptom has developed; she has complained of a remarkable form of hyperesthesia when stimuli are applied anywhere on the right side. No matter what the stimulus, she complains of great discomfort, which she says is not pain, but a very disagreeable sensation that she cannot describe. She speaks of it sometimes as a burning, sometimes as a tingling, which, judging from her descriptions, seems to be very different from any ordinary paresthesia.

DR. BARKER: The evidence you have been accumulating is very significant. Are you sure that she has had no spontaneous pain in this right side?

STUDENT: Quite sure. The complaint is of a very disagreeable sensation which the patient says is nothing like pain. She asserts that she has had no real pain, whatever, and certainly there can have been no violent pains of any sort.

DR. BARKER: That is rather strange. With the other phenomena you have mentioned, I should have expected that she would complain of paroxysms of pain, or of persistent pain in the right side. Possibly, she may develop pain later. I hope not.

Have the eyes been carefully examined since the onset of these peculiar symptoms?

STUDENT: Yes; on November 4th one of the ophthalmologists, Dr. Alan Woods, made the following report: "Pupils normal; extra-ocular movements normal; some peripheral radial opacities in both lenses; moderate myopia; marked but moderate arteriosclerosis visible in both eyes; disks and fundi otherwise practically normal; concentric contraction of visual fields.

DR. BARKER: Here are the perimetric charts of the visual fields. Though the outlines are somewhat irregular, there is, in general, concentric contraction, and the contraction is about equal in the two eyes. No evidence of optic atrophy or of choked disk has been found.

Are there any other points regarding the case that you would like to mention?

STUDENT: During the past few days the patient has become more hypersensitive to stimuli of all sorts applied to the right side; even a camel's-hair brush applied to the skin calls forth that most disagreeable sensation of which she complains. The application of a cold test-tube calls forth a similar response. She can, however, now distinguish heat from cold.

The systolic blood-pressure has varied between 150 and 240 during her stay in the hospital; the diastolic, between 90 and 140 (Fig. 51). On one occasion, when she was depressed, tearful, and feared that she would not recover, she had a crisis of hypertension, the blood-pressure going to 240, but it soon fell again to 180. Albumin and casts are constantly present in the urine. The urine remains sugar free on the dietetic régime prescribed by Professor Palmer, and the blood-sugar is now 0.12.

DR. BARKER: Let us verify some of these neurological findings. First, let us test the sensation on the right side. When I apply this

camel's-hair brush, you notice her responses. She is evidently capable of paying close attention, and of giving discriminative replies to our questions. She says that when the camel's-hair brush is applied she feels nothing like ordinary touch, but has "that very disagree-

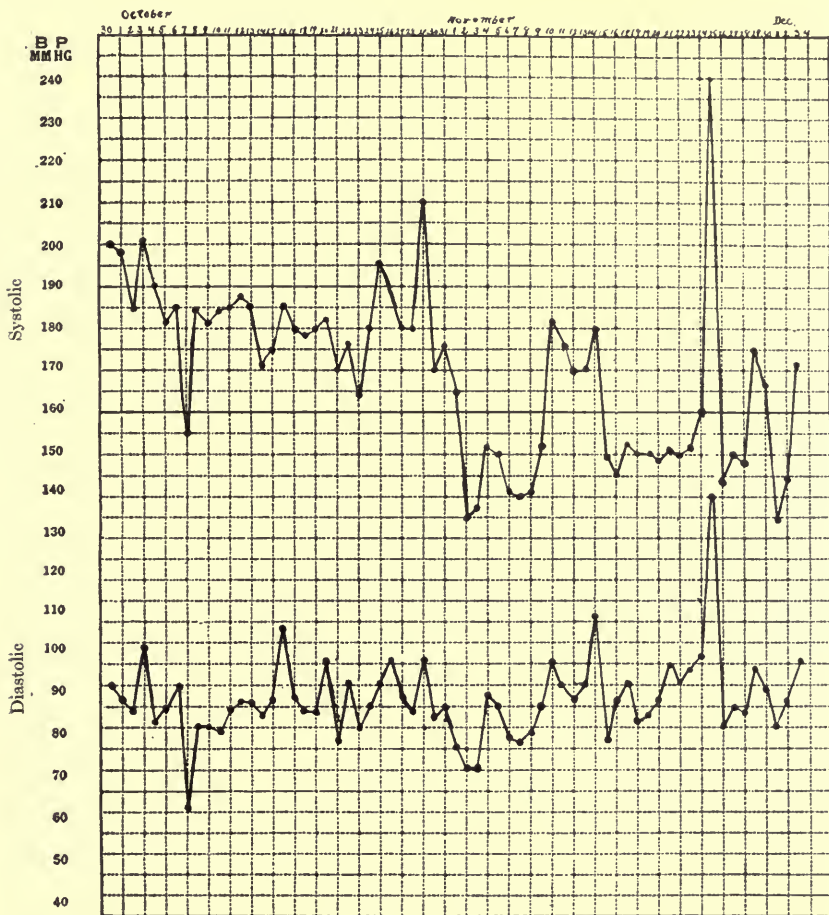


Fig. 51.—Blood-pressure chart of patient September 30th to December 3d. Note the hypertensive crisis on November 26th.

able sensation, which is not pain" and which she finds hard to describe. She says that "it runs through the whole right side." You notice also a remarkable motor response whenever the camel's-hair brush is applied. The face takes on an agonized expression, and the whole

body is thrown into contortion, as though the application were decidedly painful.

PATIENT: No, there is no pain; just that queer feeling.

DR. BARKER: Well, why do you wince so, if it isn't painful?

PATIENT (rather irritable): Well, because it's so very disagreeable.

DR. BARKER: I'm sorry to cause you even discomfort, but I wanted to make sure of just what you feel; at any rate as nearly sure as is possible.

PATIENT: Well, it isn't pain; it isn't anything like pain, but it is hard to bear all the same.

DR. BARKER: You see that she recognizes the hot test-tube and the cold test-tube as such, but evidently the thermal sensation is less prominent than the "queer, disagreeable sensation" that is also called forth by the application of a temperature stimulus. (To patient): Do you feel this pin-prick everywhere?

PATIENT: It gives me "that queer feeling," but does not feel like a pin-prick.

DR. BARKER: Does it not hurt you like the prick of a pin?

PATIENT: Not at all; only that queer feeling.

DR. BARKER: You see how definite she is about the absence of pain. Her postural sense is now much improved, though it takes a somewhat larger excursion than normal to permit her to say in which direction the toe, the knee, the hand, or the elbow is moved; still, all larger excursions are definitely recognized and their proper direction named.

Let us next try the vibratory sense. On applying this tuning-fork she feels the vibration everywhere in the bones and periosteum on the left side of the body, but on the right she feels no vibration at all, though she says that, when the tuning-fork is applied, she has again that mysterious "disagreeable sensation" that comes after the application of any form of sensory stimulus.

On the sensory side, then, she has still total analgesia, tactile hypo-esthesia, thermohypo-esthesia, partial bathyanesthesia, and total pallanesthesia, together with this peculiar hyperesthesia that consists of a most disagreeable sensation spreading through the right side and causing an agonized expression of the face and contortions of the body whenever a sensory stimulus of any sort is applied to the right half of the body.

Let us next test motility. The weakness on the right side is evidently very much less marked than it was. The grip on the right is, however, still a little less powerful than on the left, and the strength of the flexors and extensors of the knee and of the foot is a little diminished. On the whole, however, the muscles on the right side are quite strong now. Even the weakness of the lower facial on the right has largely disappeared. There is, then, still a slight hemiparesis dextra. It is interesting that there has been such marked regression of the hemiplegic disturbance as the present examination reveals.

We may next examine the reflexes. On testing the deep reflexes, you observe that the responses in the two arms are practically identical. With this heavy percussion hammer I can elicit both knee-jerks, but they are distinctly sluggish. The clinical clerk tells me that it has been difficult, if not impossible, to elicit them in the ward. One is never very surprised to find sluggish or absent knee-jerks in patients who have had glycosuria. It is quite common, as you know, to meet with loss of the deep reflexes in diabetes mellitus; the condition is sometimes spoken of as "diabetic pseudotabes" and is supposed to be due to a toxic-degenerative change occurring somewhere in the reflex arc.

The abdominal reflexes are present. Plantar stimulation yields plantar response of the great toes. There is certainly no positive Babinski sign here now on either side. On the left side there is a rather marked tickle response. You have noticed, too, that when I percuss the tendons on the right side or stimulate the skin to test the superficial reflexes on that side we get exactly the same response from the patient that we did when testing the sensation on the right; she complains of the same diffuse, disagreeable sensation and exhibits the same contortions. Even before the tendon is percussed the contortion appears, as though in anticipation of the disagreeable sensory response; whereas, on tapping the tendons on the left side, she behaves like any normal patient.

The tonus conditions on this right side are somewhat interesting. There is, as you see, no exaggeration, but rather a diminution of the deep reflexes on the right side. When I take hold of the right arm or of the right leg to flex the elbow or the knee, however, the limb is held rigid. I can forcibly bend either the upper or lower extremity and there seems to be just as much resistance in the agonists as in

the antagonists. I am inclined to think that this rigidity of the right upper and lower extremities on attempts passively to move them is a voluntary affair; she holds the limbs rigid in the hope of avoiding the calling forth of that disagreeable sensation of which she complains; this does not seem to be an actual disturbance of tonus. On direct command, as you see, she can relax the muscles controlling the movement of knee or elbow, and I can then make movements of flexion and extension without meeting with resistance. This is only for a moment or two, however, for the disagreeable sensation she experiences leads her again to contract rather forcibly all the muscles of the extremity. At first I thought we might be dealing with one of those peculiar rigidities that are due to amyostatic disturbance, that is, to a disturbance of the extrapyramidal motor innervations, but the explanation I have just given you seems to me to be more probable. I do not think we are dealing here with an amyostatic syndrome, in the sense of Strümpell, though it will be interesting to observe the patient from time to time with this particular point in mind.

Now for the co-ordination tests. With this finger-nose test you see definitely that there is a little ataxia in the right upper extremity. Though she touches her nose perfectly well with the tip of the forefinger of the left hand, when she tries to do so with the right hand she hits her upper lip first and then goes to the nose, or she touches the cheek just at the side of the nose before reaching the nose. This is not, however, a marked ataxia. It is not nearly so great a disturbance as one often sees in *tabes dorsalis*. In marked *tabes dorsalis* the patient, on attempting to touch his nose with the tip of his forefinger, may touch his shoulder or the top of his head instead.

You see, too, that she performs the heel-knee test fairly well on both sides, but there is a definite movement-ataxia on this right side, even though it is slight. The *hemiataxia dextra*, then, still persists, though it is of slight degree.

(To patient): Please let both of your arms lie perfectly quietly by your side.

(To class): As we have been making these tests my attention has been called to certain peculiar movements that are occurring here. I shall ask you to watch closely, during the next few minutes, the behavior of the two hands. Now you see what is happening. You notice some peculiar, slow movements of the fingers of the

right hand; there is spreading of the fingers, then flexion of some fingers, and extension of others. These peculiar, slow, worm-like movements are very characteristic of a certain disturbance of motility.

(To student): Do you know the name of this kind of movement disturbance?

STUDENT: I think it is athetosis.

DR. BARKER: Yes; these are typical athetoid movements. I wonder if you remember that full-page illustration of athetoid movements of the hand pictured in von Monakow's *Gehirnpathologie*. I wish we had a photograph of this hand. It is just as characteristic as von Monakow's illustration. But notice, please, in addition to these slow movements, certain other movements of this hand as a whole and of the fingers of the hand. Notice that, from time to time, she makes quick, jerky movements which have some of the elements of a voluntary movement in them, though they are purposeless. They are quite different from the athetoid movements, and they are a less prominent feature in this case than the athetosis. What kind of disturbance of motility is this?

STUDENT: Choreiform,

DR. BARKER: Yes; I should call this a choreiform, or choreatic, disturbance of motility. It is, indeed, interesting to observe this combination of athetotic with choreatic disturbances of motility in the right hand. Have these movements been noticeable before in this patient?

STUDENT: No; they had not been observed. I do not think they had occurred up to this time.

DR. BARKER: I think that very probable, and I feel sure that this syndrome, as a whole, will take on certain more definite characteristics than it has yet done as time elapses. One of the interesting features of this syndrome is its development through a period of time, and its persistence once it is established.

Do you know what this syndrome is called?

STUDENT: The thalamic syndrome.

DR. BARKER: Yes; it was designated the thalamic syndrome by Dejerine and Roussy, who wrote a very interesting article on the subject, published in the *Revue de neurologie*, vol. xiv, 1906. I shall pass the volume around in a moment, but, before doing so, let me translate to you Dejerine and Roussy's résumé of the thalamic syndrome. You will be exceedingly interested, I feel sure, with the close

correspondence with the picture before you in this patient. Let me translate freely: "In résumé we say that when one has before him a hemiplegia caused by a lesion of the thalamus, the exact topography of which will be stated presently, the patient shows a slight transitory and rapidly retrogressive motor hemiplegia, without epileptoid clonus and without Babinski sign. This hemiplegia is accompanied by disturbances of sensibility, both subjective and objective: subjectively, these consist of pains on the paralyzed side, which are lively and tenacious, not yielding to any treatment and constituting by themselves a real *impotence* (painful hemiplegia); objectively, they sometimes consist of a hypo-esthesia for sensations of touch, pain, and temperature; sometimes of hyperesthesia with dysesthesia, paresthesia, and topo-esthesia; finally, of persistent disturbances of the deep sensation, of loss of muscle sense, of astereognosis, and of hemiataxia. Often, also, choreo-athetiform movements appear. Hemianopsia may finally be met with in cases in which the lesion involves the posterior and inferior part of the thalamus."

I would refer you to this article also for the differential diagnosis of the thalamic syndrome from lesions of the midbrain, from cortical or subcortical lesions, and from hysteria, as time will not permit a further discussion of that side of the subject this morning.

The thalamic syndrome presented by our patient differs from the typical thalamic syndrome of Dejerine and Roussy in the absence of violent spontaneous pains on the paralyzed side. As I have said before, it will not be surprising if such pains develop later on, for the tendency of this syndrome is to become more pure as time elapses after the lesion.

You may ask, What has caused this lesion in the optic thalamus in its ventrolateral region? With the pronounced general atherosclerosis and arteriolar sclerosis presented by this patient, the first explanation that occurs to the mind as most probable is a vascular lesion, either cerebral hemorrhage or cerebral thrombosis, secondary to the atherosclerosis. Embolism would seem improbable in the absence of any mitral lesion. The slight myocardial insufficiency that existed when the patient entered had improved markedly before the thalamic lesion occurred.

We know that either a hemorrhage or an area of softening can destroy this posterior portion of the ventrolateral part of the thalamus,

lesions of which are concerned in the production of the thalamic syndrome. With a high blood-pressure, such as this patient has, one would think, first, of cerebral hemorrhage, causing destruction in this region; and hemorrhage may, in reality, have occurred. You may say, If so, why has there not been a febrile reaction since the insult? Well, it is common to have a little fever after a cerebral hemorrhage, probably owing to the absorption of a part of the blood. But if the hemorrhage were small it need not cause a febrile reaction. Thrombosis with encephalomalacia is, of course, more common perhaps with low blood-pressure than with high pressure; but we know that occasionally thrombosis does occur in association with hypertension owing to a local occlusive process ending in thrombus production. I do not think that it is always possible to decide, with certainty, between hemorrhage and occlusion.

You might ask, Since this patient has had epilepsy all her life, may there not have been a cerebral tumor that has given rise to this syndrome? I do not think it probable, for, in the first place, the epileptic attacks have been due to some cortical irritation rather than to irritation in the region of the basal ganglia; in the second place, the epilepsy has been slight, and there has been no attack for a year and a half; in the third place, there have been no other signs of cerebral tumor, and, in the fourth place, a tumor in the thalamus would have brought about a slow and progressively developing syndrome rather than a suddenly occurring syndrome such as we have observed in this patient. A gumma or a tubercle in the thalamus might be responsible for the production of a thalamic syndrome, but in this patient there is no history of lues, there have been no miscarriages, there is one living healthy child, the Wassermann reaction in the blood is negative (though the cerebrospinal fluid has not been examined), and there have been no evidences of a tuberculous infection in this patient; besides, tuberculosis is exceedingly uncommon in association with chronic arterial hypertension. On the whole, then, we can be sure, I think, that this thalamic lesion is of vascular origin, and has probably resulted either from a cerebral hemorrhage or from a cerebral thrombosis with encephalomalacia.

We know now, as I have said, the particular region of the thalamus that is most often involved when this syndrome is in evidence. Déjerine and Roussy in 1906 stated that a lesion of the thalamus involving the external nucleus in its posterolateral part and con-

cerning, besides, a part of the middle and medial nuclei, as well as a portion of the capsula interna, gives rise to a clinical picture known as the thalamic syndrome. In Roussy's large monograph on the thalamus, published in 1907, the evidence bearing upon the pathological anatomy is brought together.

I would call your attention also to an interesting paper by Henry Head and Gordon Holmes, published in *Brain*, 1911. These observers reviewed 10 cases in which the lesion had been confirmed by autopsy. They found that spontaneous pains were present in 8 cases; hemiataxia in 7, and involuntary movements in only 4. There was some degree of sensory loss in all the cases, but its degree varied from only slight disturbance of one or other modality of sensation to practically complete loss of all modalities. It would seem that the hemiparesis, when it exists, is due not to disease of the thalamus itself, but to a slight lesion of the capsula interna, which lies just lateral from the thalamus. The degree of hemiplegia depends upon the extent of this involvement of the capsula interna. A remarkable feature of the hemiplegia, or hemiparesis, is the absence of true rigidity and of the Babinski sign. The pyramidal tracts are, in reality, injured nevertheless; and it would look now as though integrity of the thalamus itself is necessary in association with pyramidal tract lesion to permit a positive Babinski phenomenon and the phenomena of true spasticity to appear.

You will recall that there was no hemianopsia in our patient. In some of the patients presenting the thalamic syndrome hemianopsia has been observed; in these patients the lesions involved the pulvinar of the thalamus, or the lateral geniculate body.

Partial deafness has frequently been observed in association with the thalamic syndrome, presumably due to involvement of the medial geniculate body, or its peduncle, in the lesion. It will be interesting to find out by otological examination whether the deafness in this case is dependent upon lesions in the ear or upon a central disturbance.

The hemiataxia of the thalamic syndrome may depend either upon the bathyanesthesia or, as seems more likely, upon the injury to the terminals of the cerebellothalamic neurons whose axons run through the brachia conjunctiva. It is known that these neurons exert a regulatory function upon voluntary movement.

The origin of the hemiathetosis and of the hemichorea has been

much discussed. English observers especially, accepting Hughlings Jackson's principle "that negative or destructive lesions cannot produce directly positive symptoms, or symptoms of overactivity," attribute the occurrence of hemichorea and hemiathetosis to the cutting off of inhibition or control. Centers whose activities are uncontrolled are, in all probability, responsible for the involuntary and spontaneous movements that accompany the thalamic syndrome. Hemichorea and hemiathetosis do not occur when the pyramidal tracts are seriously injured, hence they are absent in complete hemiplegia, or make their appearance only after the hemiplegia, or the hemiparesis that follows the acute lesion has begun to pass off. You have noticed that, in the present patient, no hemichorea or hemiathetosis has been observed in the ward, although it is now more than two months since the lesion occurred. Today, however, under the stimulus of this examination in the clinic, definite athetoid and choreiform movements have appeared. That is a very interesting fact. If this patient should have another attack of hemiplegia the athetosis and chorea would, in all probability, disappear. Violent athetosis of the arm has been permanently checked by excision of the arm center in the cerebral cortex (Horsley). It has been suggested, therefore, that the hemiathetosis and hemichorea that form a part of the thalamic syndrome may be due to removal of the inhibitory influence of a cerebello-rubro-thalamic mechanism upon certain motor systems, especially upon the motor area of the cerebral cortex.

The explanation of the hemianesthesia of the thalamic syndrome is comparatively easy. You will recall that the sensory neurons of the second order, the axons of which form the lemniscus medialis, terminate in end-arborizations in the ventrolateral nuclei of the thalamus. There are situated the cell bodies of thalamocortical neurons whose axons connect this region of the thalamus with the somesthetic area of the cerebral cortex. A lesion in the region of the ventrolateral nuclei of the thalamus could, therefore, destroy either the terminals of the fibers of the medial lemniscus, or the cell bodies and the beginnings of the axons of the thalamocortical neuron system. We must not, however, leave out of account the different modalities of sensation and their variable involvement in the thalamic syndrome. I think it very probable that the functions of deep sensibility (postural sense, movement sense) are mediated by the fibers

of the medial lemniscus, but it seems likely that pain sense, temperature sense, and possibly a part of the tactile sense are mediated by the upper continuations of Gower's tract, which, in some way or another, are relaid in the thalamus. We are not as yet sufficiently informed regarding the precise localization of the paths for these different modalities of sensation in the ventrolateral region of the thalamus. Certain it is that the paths are closely aggregated there, and a small lesion can involve the mechanisms mediating all the modalities of sensation. The extent of the destructive lesion will, however, determine in just how far each of the modalities (touch, pain, temperature, deep sensation) is involved. Refined pathological-histological studies of cases that have been carefully controlled clinically, and much delicate work upon the normal architectonics of the thalamus, will be required before we can safely, from the clinical symptoms, draw deductions regarding precise localization within the ventrolateral region of the thalamus.

Next, a word or two about the spontaneous pain that ordinarily occurs as a part of the thalamic syndrome, and especially, something with regard to this very peculiar and most disagreeable sensation that the patient experiences on the application of any sensory stimulus to the right half of her body. *This patient says that what she feels is not pain*; and I am much impressed with the discriminative power of this patient. I think it is certain that she does not feel pain; and I am beginning to wonder whether or not some of the so-called central pains of the thalamic syndrome may be an exaggeration of what this patient now feels, and perhaps not really pain in the sense in which we ordinarily use the word. Now what this patient experiences is evidently a most disagreeable "feeling-tone." In normal life disagreeable feeling-tones are associated with pain. An enormously exaggerated feeling-tone might, by some patients, in the absence of actual pain, be described as pain on account of the normal constant association of pain with negative feeling-tone. It is clear, I think then, that what this patient experiences is something in the nature of a pathological "affect." There is growing evidence that the thalamus is the site of the affective processes. If one analyzes the other cases of thalamic syndrome that have been recorded one gets many examples of increased negative feeling-tone. Gordon Holmes, writing of pain of central origin, states that, in the thalamic syndrome, "it is the tendency for stimuli of the unpleasant order to produce

more pain and discomfort on the affected side than in normal parts despite the diminution of sensibility that usually exists. Pain, whether produced by prick or pressure, scraping with the fingernails or any sharp object, extreme degrees of temperature (*i. e.*, below 15° C. and above 50° C.), all evoke a stronger reaction and give rise to more pain and discomfort than on the normal side of the body." He goes on to cite another remarkable fact, namely, that "a parallel overaction to pleasurable stimuli may be frequently obtained from the affected regions; mild degrees of warmth, for instance, may be more pleasant than on the normal side, and tickling, erotic, and other stimuli may excite a much stronger emotion from it." This excessive response to affective stimuli, despite a diminution of all of the ordinary forms of sensibility on the affected side, appears, as Holmes states, to be the most constant and most characteristic feature of thalamic disease.

The explanation for the pathological increase of affectivity now given is similar to that for the appearance of hemichorea and hemi-athetosis. It is assumed that the thalamic lesion causes an interruption of corticothalamic inhibitory fibers, as these pass from the capsula interna into the thalamus. There thus results a removal of the inhibition normally exerted by the cerebral cortex upon the thalamus. The organ of discriminative sensibility is thus cut off from the center of affectivity, and there is corresponding overactivity of the latter, which manifests itself by an exaggeration most often of negative, sometimes of positive, feeling-tone. It is possible, as Holmes suggests, that this pathological affectivity may, under these conditions, sometime occur in circumstances that are not recognized as naturally capable of producing it, in which event the affect would appear to be spontaneous and would be spoken of as spontaneous pain.

Before the end of this clinic I should like to arrange our diagnostic findings in some sort of order. The main points can, I think, be satisfactorily arranged under the following headings:

1. Atherosclerosis (general and arteriolar):

- (a) Chronic arterial hypertension, with blood-pressure of 180/90, with occasional vascular crises when the blood-pressure goes to 240/140.
- (b) Left ventricular hypertrophy, with slight cardiac dilatation and slight chronic circulatory insufficiency, as shown by the dyspnea and the edema.

- (c) Arteriolar nephropathy, with albuminuria, cylindruria, a tendency to azotemia, and arterial hypertension.
- (d) Arteriolar pancreatopathy, perhaps accounting for the glycosuria.
- (e) Cerebral arteriosclerosis (changes in the retinal vessels; vascular lesions in the posterior portion of the ventro-lateral region of the thalamus, giving rise to a thalamic syndrome—hemianesthesia dextra, hemiparesis dextra without spasticity and with negative Babinski, hemihyperaffectivity, hemiathetosis, hemichorea, and hemiataxia).

2. Epilepsy.

3. Obesity.

4. Mild melancholic state, probably partly a menopause neurosis, possibly partly secondary to cerebral atherosclerosis.

In addition to these main points in the diagnosis, a few minor points may be mentioned, namely:

5. Slight emphysema pulmonis.

6. Slight secondary anemia (hemoglobin 78 per cent.), with relative lymphocytosis (40 per cent.).

7. Refraction error (myopia with presbyopia).

The therapy for this patient should be comprehensively planned, and should be based upon the diagnosis outlined above.

The diet should be carefully directed with consideration of (1) the atherosclerosis with tendency to renal insufficiency, (2) the obesity, and (3) the glycosuria. The reduction of the obesity, the combating of the hyperglycemia, and the protection of the kidneys by dietetic measures should all react favorably upon the heart and help to prevent the tendency to myocardial insufficiency. The latter deserves especial consideration in a patient with this degree of hypertension. The heart should be carefully protected from overstrain, and the function of the heart muscle might be helped by judicious administration of digitalis preparations, especially when there is any tendency to dyspnea or to edema. The sodium chlorid in-take has already been reduced to a small amount. While the patient is in bed general massage might be of some advantage, but it is difficult to secure it in the public ward.

The epilepsy requires no treatment at present. There has not been an attack for a year and a half.

The mild melancholy state requires judicious handling. How much of it depends upon the menopause and how much upon the vascular condition in the cerebrum it is, as I have said, difficult to be sure. Besides attention to the somatic treatment, appropriate psychotherapy should be given to such a patient, in the details of which you are fully instructed by Professor Adolph Meyer and his associates in the Psychiatric Clinic. It should be pointed out to the patient that everything that is possible will be done to help her, and that in the meantime she must bear her ills as patiently as is possible for her to do.

Her refraction error has, I believe, already been adequately corrected by glasses.

The slight secondary anemia might be helped by the administration of iron, perhaps in the form of Basham's mixture or of Bland's pills.

Everything possible should be done to avoid the recurrence of vascular crises and the danger of further cerebral insult. The crisis observed in the hospital came out under a strong emotional stimulus; this gives a clue for a part of the psychotherapy.

Whether or not the administration of ovarian substance or of lutein tablets would be of any help here I do not know. Good results have been reported in the treatment of hypertension at the time of the menopause by such opotherapy. I think, however, that the arteriolar sclerosis has advanced to a fairly high grade in this patient, though undoubtedly the occurrence of vascular crises proves the sensitiveness of the vessels and their susceptibility to storms of hypertension of functional nature superimposed upon the fixed portion of the hypertension.

As to the treatment of the thalamic syndrome itself, I fear I have nothing very satisfactory to offer you. There will doubtless be a further retrogression of some of the symptoms, especially of the hemiparesis and of portions of the hemianesthesia. The hemiataxia is likely to persist and the hemichorea and hemiathetosis may increase as the hemiparesis passes off. I fear, too, that the affective reactions that result from stimuli applied to the right side of the body will increase rather than diminish, and that, later on, this patient may complain of severe spontaneous pain in the right side of the body. These pains are, usually, very recalcitrant to therapy, and this pathological affectivity is very resistant to pharmacotherapeutic

measures. Aspirin, or aspirin with codein, will sometimes be found to be of help. If they do not assuage, one might try pyramidon, or pyramidon with codein. Gordon Holmes recommends a mixture of sodium bromid, phenacetin, and tincture of gelsemium. The formula is given in an article in White and Jelliffe's *Modern Treatment of Nervous and Mental Diseases*, page 614. In very severe cases it may be necessary to give stronger remedies. I would remind you of Schlesinger's mixture that we use here for very severe pains, for example, in carcinoma of the spine. I think it would be worth while to try it in the spontaneous pains of the thalamic syndrome when they are too torturing.

In most severe pains two doses in the twenty-four hours will keep the patient easy. In painful cancer cases I often give 7 minims hypodermically at bedtime and 5 minims in the morning. Of course, one delays the administration of morphin in any form as long as possible; but when milder analgesics are inefficacious and the pain is atrocious, patients have the right to relief from it.

The general health of the patient should be maintained at the highest level possible, for this increases the morale of the patient and will help her to bear what she unavoidably must.

Some things can doubtless be done to protect the patient from external stimuli that call forth the pathological affective reaction. Many of these patients are very sensitive to cold on the anesthetic half of the body. Exposure to cold winds, to cold baths, and to sudden changes of temperature should, therefore, be avoided. Woolen underclothing should be worn the year round. Several of Gordon Holmes' patients wore warm gloves both summer and winter, as the hands could not bear cold. It goes without saying that emotional excitements and worry of all sorts should, as far as possible, be prevented.

You have had an unusual opportunity this morning to observe an excellent example of the thalamic syndrome in most of its manifestations. The syndrome is comparatively rare, though I suspect that it is present oftener than it is discovered. The resident physician, Dr. Mason, tells me that we have had 3 cases in the hospital during this year. I would advise you to be on the lookout for such cases when you go into practice for yourselves. After this morning's experience you are not likely to overlook them.

[*Subsequent History of the Case.*—The patient was discharged as

improved on the day of the clinic, December 7, 1920. She was advised to do no work for an indefinite time, and was given instructions as to diet. The Social Service Department was to keep her under observation.

The following note was made by Dr. V. R. Mason on the day of discharge: "Patient admitted with diabetes and hypertensive vascular disease, slight emphysema, and slight obesity. At 6 A. M. on October 4, 1920, without loss of consciousness, she became numb in right leg and arm. Combined with this there was slight disturbance of speech (dysarthria and slight difficulty in finding words). There was slight weakness of the whole right side, with slight weakness of the face. Hemianesthesia, almost complete, was present over the right side (not including the face), extending to the midline, but not crossing it. The vision was not definitely disturbed. Later, as sensation returned, the following were found:

"1. Touch impaired over right arm and leg.

"2. Pain impaired over right arm and leg.

"3. Heat and cold impaired over right arm and leg.

"4. Sense of position absent on right side.

"5. Astereognosis of right hand.

"6. Remarkable production of diffuse unpleasant sensation, radiating widely, causing patient to pull away when hot, cold, or painful stimuli are applied to right leg or arm; no spontaneous pain; slight hyperkinesis, consisting of slight choreatic or athetotic movements of hands; marked emotional response, that is, facial expression of pain; these changes begin just to right of midline.

"7. No hemianopsia.

"8. Slight hyperreflexia on the right.

"*Impression.*—Hemianesthesia with slight disturbance of touch, pain, and temperature; marked disturbance of deep sensibility; slight hemiparesis; peculiar emotional overresponse to summated liminal stimuli; typical thalamic syndrome."

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XXIV. EARLY BRAIN SYPHILIS

LUETIC MENINGITIS (IN THE FIRST YEAR OF THE DISEASE) WITH BILATERAL CHOKED DISK AND TRANSITORY PSYCHOSIS.

The patient before you is a Greek sailor, twenty-seven years old, who was for a few days on the surgical service, where he underwent an operation for removal of a dermoid cyst in the neck. He was discharged supposedly well. The next day he suffered from violent headache, and at the end of three days became delirious. He was then sent into the medical service of this hospital for study. I shall ask Mr. Ray to give you the history that has been obtained from his friends and in part, later on, from himself.

STUDENT: The patient, T. D., aged twenty-seven, is an unmarried Greek sailor, who has been fireman on a steamer. On admission to the hospital he was delirious, but his friends stated that he had suffered from "headache" and from "dimness of vision in the left eye." Under treatment in the hospital he became gradually more rational and a fairly full history has been obtained.

The family history seems to have no bearing upon the case.

In his past history nothing of importance was elicited except for the past year. In last October, however, he contracted gonorrhea, and in the following month a painful tumor appeared in the right groin; this was evidently a suppurating bubo, for the swelling was incised and drained. On December 20, 1919 he was again exposed to venereal infection, and on January 15, 1920 he noticed a sore on the penis. This sore did not entirely disappear until the following May. During March, 1920 an eruption appeared on his leg and his forearm, and later he noticed some papules upon his neck and forehead. On June 8, 1920 his ship arrived in Baltimore, where he was detained by the quarantine officer on account of the eruption. He was sent into the Marine Hospital for diagnosis and treatment. In that institution the diagnosis of syphilis was made, and he states that he had "seven injections into a vein" and "eight punctures in the back." He was discharged from the Marine Hospital apparently well on August 3, 1920.

He seems to have gone on very well until Labor Day, September 6th. On board his vessel he suffered from severe headache, and is said to have rushed up on deck stark naked, "feeling crazy" and crying out that he "could not bear the pain." He then, for the first time, noticed diminution of vision in his left eye, which has persisted since. From this time on he has had recurring headaches of variable severity.

Some time in the summer he noticed a swelling in his neck below the angle of the jaw on the right side. This swelling gradually increased in size, but was not tender.

In September there was a return of papules upon his arm, an outbreak of which the patient speaks of as his "second eruption."

On October 12, 1920 he applied to the Out-patient Department of the Johns Hopkin Hospital, stating that he desired to have the lump in the neck operated upon. He was referred for consultation to the surgical division, and was admitted to the surgical ward on

October 13th. The mass in the right neck was semifluctuant, and apparently encapsulated, though adherent to the skin. At operation, a cyst was found with sebaceous contents. The cavity was cureted and packed with gauze, and the patient was discharged from the surgical service on October 16th, apparently doing well. [Histological examination of the wall of the cyst in Dr. Bloodgood's laboratory indicated that it was of dermoid origin.]

On the day after discharge from the surgical service the patient again suffered from severe headache and had an attack of vomiting. Two days later his headache became much worse, and he is said to have shouted, to have cried out for from eight to ten hours, and to have rolled around on the floor, refusing to talk. By October 20th he had become outspokenly delirious, so disturbed that his landlord had him removed to this hospital. On admission the patient was semistuporous, though at first he could talk a little. He pointed to the occipital region and to the left temporal region of the head as the sites of his pain, although he stated that the head "ached all over." While the history was being taken the patient grew gradually less responsive, and finally ceased answering the questions of the interpreter. (He does not speak any English.)

A general physical examination was made and dictated by the house officer, Dr. Davis. It may be abstracted as follows: "Patient well nourished and well developed. Stuporous. Difficult to arouse. Respiration periodic. Skin dry and rough; a few small pustules visible on the back; pigmentation of earlier exanthemata visible on the forearms and legs. Epitrochlear glands palpable. Slight enlargement of the glands of the neck, axillæ, and groins. A little tenderness over the mastoids and over the antra. Slight divergent squint; slight ptosis on the right. Pupils, midway between dilatation and contraction, equal, regular in shape; they react to light directly and consensually.

"On ophthalmoscopic examination there is bilateral choked disk. The outlines of the disks are indistinct; the veins are greatly dilated; there are several fresh hemorrhages and areas of white exudate visible in the retina, especially along the vessels on the left. The changes are somewhat more marked in the left eye than in the right.

"Marked pyorrhea; considerable dental caries. Tonsils large and injected; slight pharyngitis. Neck a little rigid, but not definitely tender. Heart and lungs negative. Blood-pressure, 120

systolic, 70 diastolic. Pulse-rate 80; radial vessels palpable, but not much thickened. No arrhythmia. Abdomen negative.

"A number of venereal warts visible on the glans penis; no definite scar of the earlier chancre to be made out.

"Kernig's sign positive on the left, suggestive on the right. No abnormalities of the deep or superficial reflexes."

On account of the prevalence of epidemic encephalitis the house officer thought of this and of lues as possible explanations of the condition.

DR. BARKER: What laboratory tests were made on admission?

STUDENT: The blood, the urine, and the cerebrospinal fluid were examined.

Examination of the *blood* showed: Red blood-cells, 5,050,000; hemoglobin, 90 per cent.; white blood-cells, 12,000. The differential count showed: P. M. N., 90 per cent.; S. M., 8.6 per cent.; no eosinophils observed.

Three days later the blood examination revealed: Red blood-cells, 5,400,000; hemoglobin, 90 per cent.; white blood-cells, 6500. The differential count showed: P. M. N., 74 per cent.; P. M. E., 0.8 per cent.; S. M., 18 per cent.; L. M. and Tr., 7 per cent.

The Wassermann reaction of the blood-serum was positive.

Urine.—Specific gravity, 1025–1031. A trace of albumin was found on one occasion; sugar was absent; no casts were present. Urinary examination otherwise negative.

Cerebrospinal Fluid.—This was withdrawn for examination on October 20th. The fluid was not under increased pressure. Four hundred and two cells were present, and all of them were lymphocytes. The Wassermann reaction was positive in the fluid. The globulin was markedly increased, and the gold sol test showed a "paretic curve."

DR. BARKER: Did the physical signs change after admission to the hospital?

STUDENT: He was gone over carefully by Dr. Mason two days after admission. At this examination no ptosis was observable and, indeed, no eye-muscle paralysis of any sort. The bilateral choked disk persisted. There was a little weakness of the right side of the face. The deep reflexes in the arms could not be obtained. The patient remained a little dull, though he was less stuporous than on admission. There was no fever.

DR. BARKER: What treatment did the patient receive?

STUDENT: At first the patient was kept in bed and on a light diet. As soon as the report on the Wassermann examination was received, on October 22d, he was given an intravenous injection of 0.45 gm. of neodiarsenol. Within forty-eight hours the stupor disappeared entirely, the patient seemed rational, and became able, through the interpreter, to give a fairly clear history of his illness. He stated that he no longer had any headache. On October 24th he was given a second intravenous injection of 0.45 gm. of neodiarsenol.

DR. BARKER: Was there any violent reaction to these injections?

STUDENT: No. There was neither fever nor chill. The patient responded only by marked improvement in the symptoms.

DR. BARKER: Do the eye-grounds look the same now as on admission?

STUDENT: We can see but little if any change in the eye-grounds since he entered the hospital.

DR. BARKER: I had a look at his eye-grounds just before the clinic, and Dr. H. M. Thomas, who was with me, measured the swelling of the disk on each side and found it to measure approximately 5 diopters. That is a high grade of choked disk. I would advise some of the members of the fourth-year class to examine these eye-grounds in the ward. You will never see a more striking or typical example of bilateral choked disk. Be sure not to miss this opportunity. Be careful, please, not to tire the patient, however, when making your examinations.

I should like to test the reflexes and motility again now. There is no eye-muscle paralysis. The pupils are equal now and they react both to light and on accommodation. The right side of the face is still a little weak. You notice it especially when the patient tries to show his teeth. The left angle of the mouth is retracted more than the right. The tongue is protruded straight in the middle line. The grip of the right hand is approximately equal to that of the left. He is able to perform all ordinary movements of all four extremities. The abdominal muscles are strong. I find it difficult to elicit the deep reflexes on the right. There is a slight response when the biceps tendon is tapped, but the periosteal-radial and the triceps reflexes on the right are absent. All the deep reflexes are present, as you see, however, in the left arm.

The knee kicks are active and are equal on the two sides. There

is no patellar clonus and no ankle-clonus. Response to plantar stimulation is normal on both sides. The abdominal reflexes are present, but rather sluggish. Kernig's sign is still positive on both sides. Brudzinski's sign, however, is negative. You see that I can place his chin well down toward his sternum without difficulty. The patient is now alert; he looks comfortable, and he does not now complain of any pain.

To what part of the nervous system do the findings of this patient point?

STUDENT: To the central nervous system, and especially to the meninges.

DR. BARKER: Yes. Why do you think the meninges are involved?

STUDENT: On account of the positive Kernig sign and the high lymphocyte count in the cerebrospinal fluid.

DR. BARKER: Why has this patient a double choked disk?

STUDENT: There must be pressure of some sort upon the optic nerves or the optic paths.

DR. BARKER: Do you think that this pressure on the optic nerves is the result of a general increase of intracranial pressure or of some local pressure at the base of the skull?

STUDENT: It might be either.

DR. BARKER: What are the signs of general increased intracranial pressure?

STUDENT: Headache, dizziness, vomiting, bradycardia, choked disks, and psychic disturbances.

DR. BARKER: How many of these have been present in this patient?

STUDENT: He has had violent headache at times, occasional vomiting, choked disks, delirium, and abnormal behavior. There has been neither dizziness nor bradycardia.

DR. BARKER: Assuming that the choked disk in this case is not due to a general increase in intracranial pressure, but to a local process, where do you think this local process most likely to be?

STUDENT: There could be local pressure upon the optic chiasm or upon both optic nerves at the base of the skull.

DR. BARKER: Yes. Could it be at the base of the skull in the middle fossa or anterior to this? Which would you think the more likely?

STUDENT: In the middle fossa of the skull.

DR. BARKER: Yes. Local pressure in the anterior fossa could not cause choked disk. It would have to be in the middle fossa, for here only are the optic nerves and the optic chiasm accessible to pressure.

Are there any other localizing symptoms to be made out?

STUDENT: The weakness of the right side of the face might point to pressure also upon the facial nerve at the base of the skull on the right side.

DR. BARKER: Yes. And slight temporary ptosis was noticed on admission, though it has by now disappeared. What might that have pointed to?

STUDENT: Possibly to involvement of the oculomotor nerve also at the base of the skull.

DR. BARKER: Yes; though it is rather strange that there was only ptosis and no other eye-muscle paralysis. In any case, this was a slight and transitory phenomenon.

You are inclined, I think, to believe that some process has been going on at the base of the brain in the middle fossa of the skull, and perhaps, also, in the posterior fossa. Would you think this likely to be a diffuse process or a very circumscribed process?

STUDENT: I should think rather a diffuse process, either inflammatory or neoplastic.

DR. BARKER: Are there any indications of meningeal involvement?

STUDENT: Yes, decidedly. The positive Kernig sign and the marked increase in cells in the cerebrospinal fluid are two signs that point to the involvement of the meninges.

DR. BARKER: An involvement of the meninges at the base of the brain, that is, a *basal meningitis*, ought certainly to be considered here.

If we are dealing with a basal meningitis, what do you think is its etiology?

STUDENT: I think it is due to syphilis because the Wassermann is positive in both the blood and in the spinal fluid, because the globulin in the spinal fluid is greatly increased, and because the increased cells in the spinal fluid are lymphocytes. Besides, no bacteria were found in the smears.

DR. BARKER: What micro-organism is the cause of syphilis?

STUDENT: The *Treponema pallidum*.

DR. BARKER: Has this micro-organism ever been found in the cerebrospinal fluid in syphilitic meningitis?

STUDENT: I do not know.

DR. BARKER: The *Treponema pallidum* has been found, but only exceptionally in the cerebrospinal fluid in syphilitic meningitis. Fortunately, we do not have to depend upon the determination of the presence of the organism for the making of the diagnosis.

You will recall that one or two who saw the patient early thought that he might have lethargic encephalitis. Is it possible, do you think, that this meningitis could be a part of a lethargic encephalitis or meningo-encephalitis?

STUDENT: I suppose it could be, in spite of the fact that the man has syphilis. A man infected with syphilis might be the victim of lethargic encephalitis as a complication.

DR. BARKER: Yes. That is certainly true, and I have seen cases in which I thought that lethargic encephalitis might be superimposed upon an old syphilitic process. It would be very difficult to be sure, however. The causal micro-organism for lethargic encephalitis is still to be found, unless it should turn out, as I hope it may, that the micro-organism described by Strauss and his colleagues at the Mt. Sinai Hospital in New York is really the cause. A spinal fluid showing an increased lymphocyte count and increased globulin, but a negative Wassermann, is very characteristic of many of the cases of lethargic encephalitis in the present epidemic. But here we have, in addition, a positive Wassermann reaction in both the blood and spinal fluid. The man certainly has syphilis, and a syphilitic process in the brain and meninges could account for all the phenomena without the assumption of a complicating lethargic encephalitis. I am inclined to think that syphilis alone is responsible here. Does syphilis often cause a meningitis?

STUDENT: Yes. It is a very common cause, especially of basal gummatous meningitis. A convexity meningitis due to syphilis occasionally occurs, but is far less common.

DR. BARKER: Has the patient presented any signs of a convexity meningitis?

STUDENT: No. The signs have been those of a basal process rather than of a convexity process. He has had neither general nor local convulsive seizures.

DR. BARKER: When syphilis attacks the central nervous system

and especially the brain, isn't it common to have a luetic arteritis of the cerebral vessels?

STUDENT: Yes. That is very common, I believe.

DR. BARKER: What symptoms, or signs, would lead you to think of a cerebral arteritis rather than of a syphilitic meningitis?

STUDENT: In the vascular type of brain syphilis it is common to have a hemiplegia or an aphasia. The patient sometimes wakes up in the morning to find that he cannot speak or that he cannot move one side of his body.

DR. BARKER: Yes. The symptoms in this case point to the meningeal type of brain syphilis rather than to the vascular type of the disease. You must remember, however, that it is not uncommon to have mixtures of the two types due to simultaneous involvement of the meninges and of the arteries at the base.

But is it not very early in the disease for the brain to be involved in syphilis? You will recall that the patient noticed his chancre only last January, and he began to have symptoms referable to the brain as early as September and possibly earlier, though the history is somewhat vague. He says that when he was in the Marine Hospital in June he had eight lumbar punctures, which would suggest that nervous symptoms were present at that time (about six months after the appearance of the chancre).

STUDENT: We know now that syphilis of the central nervous system may occur very early in the disease. It is common in the first three years of the disease and not uncommon even in the first year, as in this case.

DR. BARKER: Yes. Since the observations of Naunyn, published about forty years ago, we have known that syphilis of the nervous system may occur quite early in the disease. Indeed, in Naunyn's analysis of 335 cases of syphilis of the nervous system, 48 per cent. were found to have occurred within the first three years of the disease. He asserted that from that time on the number of cases in which the nervous system was affected decreased from year to year. After ten years it was exceptional to find the central nervous system attacked as far as syphilitic meningitis and syphilitic arteritis are concerned. Of course, the parasymphilitic affections (tabes dorsalis and dementia paralytica) frequently do not make their appearance until ten years or more after the primary infection. Rumpf, too, long ago pointed out that syphilis of the nervous system may occur

early after the infection. In 9 out of 40 of his cases of cerebral syphilis the brain was attacked in the first year. Since these earlier observations of Naunyn and of Rumpf, all neurologists have become familiar with the tendency of syphilis to attack the meninges or the cerebral arteries early in the disease. It is known that the central nervous system may become involved even within six weeks after the primary lesion.

Much light has of late years been thrown upon this early cerebrospinal lues through the studies made upon the time of the generalization of the syphilitic infection.

Do you know how early *Treponema pallidum* leaves the primary lesion to reach other parts of the body?

STUDENT: I believe at the time the chancre appears.

DR. BARKER: Yes. It has been found that the *Treponema* is distributed throughout the body very early indeed after infection. Formerly, it was recommended to excise the chancre in the hope of preventing the generalization of the syphilitic process, but this has been proved to be futile.

The appearance of enlargement of the lymph-glands, especially of the retrocervical glands and of the epitrochlear glands, a few weeks after infection means the presence in those glands of the *Treponema pallidum*. The appearance of a secondary exanthem on the skin and of mucous patches in the mouth means a reaction of the skin and of the mucous membranes to the *Treponema pallidum* present in them. Syphilologists have now good reason to believe that at this stage the *Treponema* is distributed also to the viscera, to the walls of the arteries, and to the nervous tissues. It is remarkable, however, that in the viscera, in the arterial walls, in the meninges, and in the central nervous tissues the *Treponema* may remain quiescent or latent for a long period, causing no recognizable reaction either clinical or pathological-histological.

It is important to kill off the *Treponema* in the earliest stages of the disease. In the majority of cases syphilis could probably be completely cured by intensive antiluetic measures if they were instituted soon after the infection took place. The longer the time that elapses after infection before the institution of thorough treatment, the greater the danger of visceral, vascular, and nervous symptoms.

Do you think that there is any special strain of the *Treponema* involved in the infection of the central nervous system?

STUDENT: Some syphilologists have assumed that only special strains of the *Treponema pallidum* affect the central nervous system.

DR. BARKER: Yes. Some assert this and speak of a special *syphilis à virus nerveux*. What arguments have been adduced in favor of this?

STUDENT: I believe there are cases on record where several men, infected by the same prostitute, and at about the same time, have all later on developed syphilis of the nervous system.

DR. BARKER: Yes. Such instances have been reported. The consensus of opinion, however, among syphilologists and neurologists at present seems to be that there is no necessity of assuming a special strain of the *Treponema* responsible for neural syphilis. Further studies will be necessary, however, before the question can be considered decided. Now that we know that there are several strains of the pneumococcus, of the streptococcus, of the meningococcus, and of other organisms, it would not be surprising if we should find out later that there are also a number of different strains of *Treponema pallidum*, possessing somewhat different properties. Differences in disposition of the nervous system in different patients is, however, probably of greater significance than differences in the virus.

What do you think is most helpful in making a diagnosis of cerebrospinal syphilis?

STUDENT: Examination of the cerebrospinal fluid in a patient who presents symptoms referable to the central nervous system is the most helpful test.

DR. BARKER: Yes. The microscopical and biological examinations of the cerebrospinal fluid have proved to be most important aids in the diagnosis of cerebrospinal lues. The studies, especially by Ravaut, of pleocytosis of the cerebrospinal fluid in the secondary stage of syphilis revealed the frequency of changes in this fluid early in the disease, often when there were as yet no symptoms referable to the central nervous system. Of course, a pleocytosis or a lymphocytosis in the spinal fluid is not sufficient to prove the existence of cerebrospinal syphilis. A similar lymphocytosis occurs in poliomyelitis, in some cases of lethargic encephalitis, and in certain other organic diseases of the central nervous system.

The demonstration of an increase of globulin in the cerebrospinal fluid is also a very helpful diagnostic sign. The studies of Widal, Sicard, and Ravaut (1903) and those of Guillain and Parant

(1903) showed the importance of studying the globulin content of the cerebrospinal fluid in syphilis and in other diseases.

The Wassermann reaction is often negative in the cerebrospinal fluid in lues cerebrospinalis when only 0.2 c.c. of the fluid is used for the test; but if larger amounts of the fluid (0.4 to 0.8 c.c.) are used, a positive reaction is generally observable. Of course, in tabes dorsalis, and especially in dementia paralytica, the Wassermann reaction is commonly positive with a small amount of the fluid (0.2 c.c.).

Important as the examination of the cerebrospinal fluid is in establishing the diagnosis of lues cerebrospinalis, there are three peculiarities of the general symptomatology of the disease that I should like to emphasize.

One of these is the *extreme variability of the symptoms*. The clinical phenomena undergo the most marked fluctuation, the symptoms coming and going often within very short periods. This temporal oscillation of the symptoms in cerebrospinal syphilis has been noticed and commented upon by most writers on the disease.

A second peculiar feature, namely, the *multiplicity of the phenomena*, is also very characteristic of cerebrospinal lues. This is not surprising when we remember that syphilis may attack (1) the meninges, (2) the blood-vessels, especially the arteries, and also (3) the nervous tissues themselves. Different parts of the meninges may be simultaneously affected, as may the arteries that supply different portions of the brain or spinal cord. Attempts to localize the pathological processes of cerebrospinal syphilis necessitate, as a rule, the assumption of lesions in several often widely separated domains.

The third special feature to which I would refer is the fact that the syphilitic process shows a *predilection for certain special sites* (basal meninges, with involvement of the roots of the cerebral nerves; middle cerebral artery and its branches).

Some authors would add a fourth peculiarity, namely, the *tendency of the symptoms to disappear on intensive antiluetic treatment*. This is certainly true of many of the cases of cerebrospinal syphilis recognized and treated early. There is, perhaps, no more gratifying chapter in the history of medical therapy than that pertaining to the suitable treatment of these cases. Unfortunately, however, when the disease goes long unrecognized the secondary results of

vascular and even of gummatous lesions may be such as to be quite irreparable, and then the diagnosis of lues cerebrospinalis by the therapeutic test, or by what is known as diagnosis *ex juvantibus*, is not feasible.

The improvement in the condition of the patient before you soon after the first injection of neodiarsenol was almost magical. He has had so far only two injections, and you see how well he is today, compared with the description of his condition a few days ago. There is good reason to hope that this man may be freed completely of his syphilitic infection by a continuation of intensive anti-luetic therapy. In how far the optic neuritis may be overcome without residuals it is as yet too early to say. The choked disk, as you have heard, is very marked on both sides (at least 5 diopters). The vision in both eyes is impaired, that in the left eye being markedly impaired. There may be complete recovery later, but it is quite possible that some of the fibers have been destroyed and that some secondary optic atrophy will remain as a residual.

What treatment would you advise from now on for this patient?

STUDENT: I should think it would be well to continue the intensive intravenous arsenical therapy and also to give him injections of mercury, and perhaps, later on, some iodid of potassium.

DR. BARKER: Yes. He has responded very well to the treatment already begun, and this should be intensively continued.

Would you give him intraspinal therapy also?

STUDENT: If his symptoms do not clear up with intravenous therapy, it might be well to use the Swift-Ellis treatment or else salvarsanized serum intraspinaly.

DR. BARKER: Opinions have fluctuated (something like the symptoms of the disease) regarding the intraspinal treatment of cerebrospinal syphilis. Undoubtedly, accidents have followed intraspinal therapy in certain cases. I myself saw in one patient a paraplegia, and in another a paralysis of the bladder follow so quickly upon intraspinal therapy that a causal relationship could scarcely be denied.

The technic, however, of intraspinal therapy has of late been greatly improved and there is now much less danger than formerly. If a certain amount of cerebrospinal fluid be first removed, and then 30 or 40 c.c. more of the fluid be collected and mixed with some of the patient's own serum collected twenty-four hours after an intra-

venous injection of arsphenamin (salvarsanized and inactivated), and then allowed to flow back by gravity into the spinal canal, there would seem to be very little risk. There is being passed around an interesting article by Dr. J. A. Fordyce, of New York, giving the results of his experience with intraspinous therapy. He has had a large experience and is, I think, especially well qualified to pass judgment upon the method.

In early cases of cerebrospinal syphilis the Wassermann reaction can often be rendered permanently negative in both the blood and spinal fluid. The longer after the infection before the treatment is inaugurated, however, the more difficult you will find it to be to secure a permanently negative positive reaction in the cerebrospinal fluid. Even after prolonged intravenous therapy, and after thirty, sixty, or more intraspinous injections, though the cell count in the spinal fluid may be diminished and the globulin decreased, the Wassermann reaction often remains positive. And as long as the Wassermann reaction remains positive in the fluid the patient is not completely free from danger. Should the fluid become negative in all respects, it should still be examined every three months until it has remained so for at least a year. Unless it remain negative for this length of time on quarterly examination treatment should be continued.

Instead of arsenical intraspinous therapy Dr. Charles Byrnes has applied intraspinous therapy, with use of mercurialized serum. This method seems to have yielded very good results in a number of his cases.

In concluding this clinic let me draw your attention again to the importance of making a general diagnostic survey in every patient, no matter what his complaint may be. You will recall that this patient applied to the Out-patient Department of the hospital complaining of a swelling in his neck. You have seen more than once in your work that the thing the patient complains of is often far less important than something else that he harbors and pays but little attention to. Though he had had headaches and some impairment of vision in his left eye, what he regarded as important was the swelling in his neck. He was seen in the surgical division of the Out-patient Department and was sent into the surgical ward for operation upon the neck. The dermoid cyst was removed and the patient was discharged at the end of three days supposedly well. On return-

ing to his boarding house he began to have headaches, became very violent, and within three days was delirious and returned to the hospital, this time entering the medical service, where a general study was made, with discovery of the double choked disk, the Kernig sign, the positive Wassermann, and the pleocytosis in the cerebrospinal fluid!

I was very much impressed with the recommendation once made by Dr. Frank Billings at a Conference on Medical Education held in Chicago. He suggested that all patients entering a general hospital should be referred to a reception ward in which a general diagnostic study should be undertaken, and only after this study had been made and a complete diagnosis arrived at should the patient be referred to the different divisions for therapy. Dr. Billings' wide experience had convinced him of the frequency with which important conditions go entirely overlooked owing to the fact that diagnostic studies are often partial and incomplete, the attention of a surgeon or of a medical or surgical specialist being confined too exclusively to his own domain.

We should, at least whenever possible, study our patients as a whole. In every case a complete anamnesis and a general physical examination and psychical examination should be made, after which one can determine what laboratory tests, what x-ray tests, and what examinations by specialists are required in order that the drag-net shall be spread out sufficiently to enclose everything that is important for the diagnosis. If this method of procedure were systematically followed much benefit, I am sure, would accrue to patients entering the hospitals. In the patient before you the changes in the eye-grounds are so extensive that the eyesight is seriously threatened. How disastrous it might have been if the condition present had gone longer unrecognized! How very important for this patient the general diagnostic study has proved to be!

[*Subsequent History of the Case.*—On October 30th, four days after the clinic, a man who shared the patient's room died. The patient then became much frightened and so violent and noisy that it became necessary to remove him to the Phipps Psychiatric Clinic, where he was admitted on October 31st. He was then delirious and dis-oriented. There was no evidence of hallucinations, however, at any time.

After his transfer to the Psychiatric Department he had three

salvarsan injections, to which he reacted well and became more quiet. On November 18th he had an injection of salvarsan, after which he became resistant and sullen, talked very little, and could not be induced to allow any further treatment. He was, therefore, discharged on December 31st, but committed to Bay View as insane, chiefly because of lack of co-operation in treatment. His physical condition on his discharge was much the same as it had been on admission, except that Kernig's sign was negative and that the cells in the cerebrospinal fluid were reduced to 3, while the globulin was single plus.]

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XXV. CHRONIC DISSEMINATED MENINGOMYELITIS

A RANCHMAN OF THIRTY-TWO, COMPLAINING OF RECURRENT PAIN AND NUMBNESS IN THE LEFT LOWER EXTREMITIES, FOLLOWED BY WEAKNESS AND CLUMSINESS OF THE LEGS AND OTHER SIGNS POINTING TO A CHRONIC DISSEMINATED MENINGOMYELITIS, WITH CHIEF LOCALIZATION IN THE UPPER THORACIC PORTION OF THE SPINAL CORD; EXACERBATIONS AND REMISSIONS EXTENDING OVER THREE AND A HALF YEARS.

THE patient before you has during the last three and a half years presented symptoms and signs of a peculiar affection of the spinal cord. The difficulties of diagnosis have been great, the symptoms having suggested to some an inflammatory or degenerative process, and to others a neoplastic process. Last summer an exploratory laminectomy was done in the hope that something might be done by operation that would yield relief. For a time after the operation the patient did seem to be better, but another exacerbation of his symptoms has occurred and he has recently re-entered the medical service. I shall ask the clinical clerk, Mr. Zininger, to tell you the history of the patient.

STUDENT: The patient, Thomas T., is a Texas ranchman, single, aged thirty-two, who has been exhibiting disturbances of sensation and of motility since September, 1917 (about three and a half years ago).

The onset of the trouble was insidious. He began to have dull pain in the left hip and down the back of the thigh and calf; this pain he called "sciatica." He states that this dull aching pain would continue for three or four days; after this he would have an intermission for two or three weeks and then another attack of the pain. Pain of this sort recurred at intervals for more than a year, during which time he noticed that his legs gradually became "clumsy." Despite his symptoms, he entered the military service, joining an officers' training camp, but had to withdraw on account of disability. Though he could do much of the work, he found on several occasions that marching was very difficult. His symptoms, however, continued to be mild until May, 1918, when he enlisted for overseas service in the signal corps. Despite the recurring pain and the slight clumsiness of the legs he got on very well in this service.

In December, 1918 he suffered from an attack of influenza, and, after it, had severe pain in the left lower extremity constantly for a whole month. Besides suffering from pain he noticed, at this time, a certain amount of numbness in the left leg. In May, 1919 he ran a nail into his left foot. The wound became infected and was rather slow in healing, necessitating the use of a cane.

In August, 1919 the question of his discharge from the army came up, and though he had some symptoms, he was able to camouflage them sufficiently to be discharged from the army as "well." Returning to an out-of-door life, he was able to ride horseback until December, 1919; it then became too difficult to ride, for he found himself unable to use his left foot in the stirrup. In the autumn of the year 1919 he thought that his trouble must be rheumatic and took a course of hot baths at a health resort, but without much benefit.

In March, 1920 he injured his left ankle and, though there was a visible erosion of the skin over the ankle, he was surprised to find that he suffered no pain from the injury. In April, 1920 he observed he had a little difficulty in starting the flow of urine. By this time, too, the left leg had become very weak below the knee. In May, 1920 the right foot and leg became similarly involved. There was marked weakness and clumsiness that he could not explain. The numbness had gradually increased so as to be distributed over both lower extremities and the lower part of the trunk. He states also that he sometimes lost his feet in bed. At about this time he found that he could not walk except with the aid of crutches; and he observed that when he put his feet to the ground "the legs and abdominal muscles would go into spasms."

On June 24, 1920 he applied to the medical service of this hospital for study and treatment. At that time he was able to use the legs but little, and could not walk even with crutches. He complained of subjective numbness over the whole surface from the level of the xiphoid downward, stating that the skin felt everywhere "thick" and that his "toes felt different from what they did before." Besides losing his feet in bed, he could not tell whether or not they were covered unless he looked at them.

On physical examination there was partial spastic paraplegia of the lower extremities and spasticity of the abdominal muscles on palpation. He was somewhat tender over the upper thoracic

spine. There were no motor disturbances in the upper extremities or in the head and neck. Objective sensory disturbances at this time included, (1) loss of tactile sense below the level of the eighth thoracic segment, (2) very slight impairment of pain sense in the same area, and (3) some disturbance of deep sensation, shown by an inability to recognize the direction of passive movement of the toes, though gross changes in the position of the knees and hips were promptly recognized. The knee kicks and ankle-jerks were greatly exaggerated, though the deep reflexes of the upper extremities and in the head were normal. The abdominal reflexes were present and hyperactive. There was marked ankle-clonus and marked patellar clonus. The Babinski test was positive on both sides. The physical examination was otherwise negative, except for bilateral partial deafness (due to measles in childhood) and moderate hemorrhoids.

The Wassermann reaction in the blood-serum was negative.

Lumbar puncture was done and the cerebrospinal fluid was found to be clear and under normal pressure. There were 6 cells; the globulin test was negative; the gold curve was negative, and the Wassermann reaction in the fluid negative.

Roentgenograms of the cervical and thoracic regions of the spine showed no changes.

The existence of an intraspinal neoplasm being suspected, the patient was transferred to the surgical service for exploratory laminectomy. Before the operation air was injected into the subarachnoid space by lumbar puncture and an arachnoroentgenogram made. This was negative, except that there seemed to be more air at about the level of the fifth thoracic segment of the spinal cord than elsewhere along the canal.

The laminectomy was performed by Dr. Walter Dandy on July 6, 1920. An area between the third and sixth thoracic spinous processes was opened, and some 5 inches of the spinal cord were exposed. The dura was normal in appearance. No tumor was found. Opposite the third thoracic vertebra the spinal cord suddenly became reduced in size to about half the normal. At this level there were many adhesions which suggested the existence, earlier, of a meningomyelitis. These adhesions were freed and a catheter was passed downward without meeting obstruction.

DR. BARKER: How did the patient get along after operation?

STUDENT: He developed a mild cystitis and required catheteriza-

tion for a brief period. He soon improved, however, and became able to flex the left knee and to move the right foot slightly. He was discharged from the surgical service of the hospital on August 8, 1920.

DR. BARKER: Will you tell us of the course of the disease after he left the hospital up to the time of his present admission?

STUDENT: The patient continued to improve until the end of September, 1920, when he had a chill and high fever, which lasted a couple of days. The paralysis then became more marked and he again lost the power to stand. After this he again improved, however, and by the middle of December, 1920 felt much better, being able to walk some. About Christmas, 1920 he began to get worse again and his condition has progressively deteriorated until January, 1921.

At the end of the first week of January of this year a new symptom appeared. He noticed tingling in the fourth and fifth fingers of each hand and in a zone along the medial side of each arm up to the axilla, a zone that corresponds to the domain and distribution of the first thoracic nerve on each side. The patient has observed also some twitching of the right triceps muscle, especially on raising his arm or on placing his right hand on the top of his head.

He decided to return to the hospital for further study and treatment, entering the ward on February 26, 1921.

DR. BARKER: What was his condition at that time?

STUDENT: That was four days ago. He was re-examined by the medical house officer, Dr. Telinde, and by the resident physician, Dr. V. R. Mason. Aside from the neurological findings there was but little of interest. The tonsils and teeth were suspect and there were some hemorrhoids. There was still a little cystitis and an alkaline urine. The blood was normal. The blood-pressure was 100 systolic and 80 diastolic. The thoracic and abdominal viscera showed nothing abnormal.

DR. BARKER: Tell us please of his present neurological status.

STUDENT: The psyche is clear. Everything is normal in the domain of the cerebral nerves except for anisocoria, the right pupil being larger than the left. The left pupil was obliquely oval in shape. The pupils, however, reacted to light and accommodation, and the eye-grounds were perfectly normal. The eye-muscle movements and the movements of the face and jaws were normal. The motility of the neck, upper extremities, and upper trunk seemed to be entirely

normal. He had more power in the abdominal muscles than before, though there was still some weakness there. There was marked weakness in both lower extremities, the patient being unable to support his weight. The calves were smaller than normal, but were of equal volume on the two sides, the atrophy being apparently merely that of disuse. He could flex and extend both hips. He could also flex both knees, but the flexors of the right knee were weaker than those of the left. Flexion and extension of the ankles were markedly weakened. He could wiggle his toes a little, but the movements were much restricted. There was marked rigidity and hypertonicity of all the muscles in the lower extremities. On lifting the leg at the knee on either side the entire musculature of the lower extremity was thrown into clonic spasm. Patellar clonus and ankle-clonus were marked on both sides. The heel-knee test could not be performed on account of the rigidity and the weakness. The finger-nose test was well performed. There was no tremor of the fingers. No muscular twitchings were visible in any part of the body.

The kinesthetic sense was somewhat involved. The direction of the movements of the toes could not be recognized, though larger movements of the ankle, knee, and hip could be quickly recognized.

He was able to recognize light touch throughout the whole anesthetic area of the lower trunk and the lower extremities, but he stated that this touch gave a sensation of slightly different quality from that of normal parts, though it seemed difficult for him to describe clearly this difference. He seemed unable correctly to localize tactile sensations in the hypo-esthetic areas.

He could recognize the point of a pin in most places, though here and there he confused the head with the point, especially in the distal parts of the lower extremities.

The same was true of thermal sensation. He could distinguish the hot tube from the cold tube in most places, though here and there in the right lower extremity below the knee he was unable to discriminate between heat and cold, and there was quite a large area on the right anterior abdominal wall over which there was total thermanesthesia.

DR. BARKER: I have just been testing these various modalities of sensation and can corroborate what the clinical clerk has said. It is interesting that the patient asserts that painful stimuli make him feel a little worse in the otherwise hypesthetic areas than when

they are applied to the neck and face. There would seem to be a slight hyperesthesia for pain here. The response to painful stimuli seems, too, to be a little delayed, though it is somewhat intensified; perhaps it is the negative feeling tone that is somewhat increased.

STUDENT: He complains of a feeling of constriction in a band about the trunk.

DR. BARKER (to patient): Show us just where you have this feeling of a band about the waist.

PATIENT (pointing): Just here.

DR. BARKER: This band is about 4 inches wide and is situated just below the level of the umbilicus. Girdle sensations such as this are, as you know, common in *tabes dorsalis*.

STUDENT: The vibratory sense is less impaired now than on his previous admission, but he fails to recognize the vibrations in the neighborhood of the malleoli and the vibratory sense seems somewhat diminished throughout the lower extremities.

The upper level of the sensory disturbances corresponds to that of the sixth thoracic segment.

DR. BARKER: You have heard the neurological data that have been accumulated. They are epitomized in these two drawings prepared by the clinical clerk (Figs. 52, 53). Let us now discuss the localization of the lesions causing these disturbances and their probable nature.

When trying to localize lesions in the central nervous system we pay attention not only to the disturbed functions but also to the functions that are preserved. The disturbances of function give us the clues to the position of the diseased areas within the nervous system and the preserved functions give us clues to the structures that are still intact.

To disease of what part of the nervous system would you refer the objective findings and the symptoms of which this patient complains?

STUDENT: To the spinal cord, and especially to the upper thoracic portion of the cord.

DR. BARKER: Yes; the symptoms permit us to decide at once that the patient has a disease of the spinal cord, a *myelopathy*, and I agree with you that the predominant lesions must be in the upper portion of the thoracic cord; furthermore, they have been of long duration, three years and a half. You may, if you like, speak of a

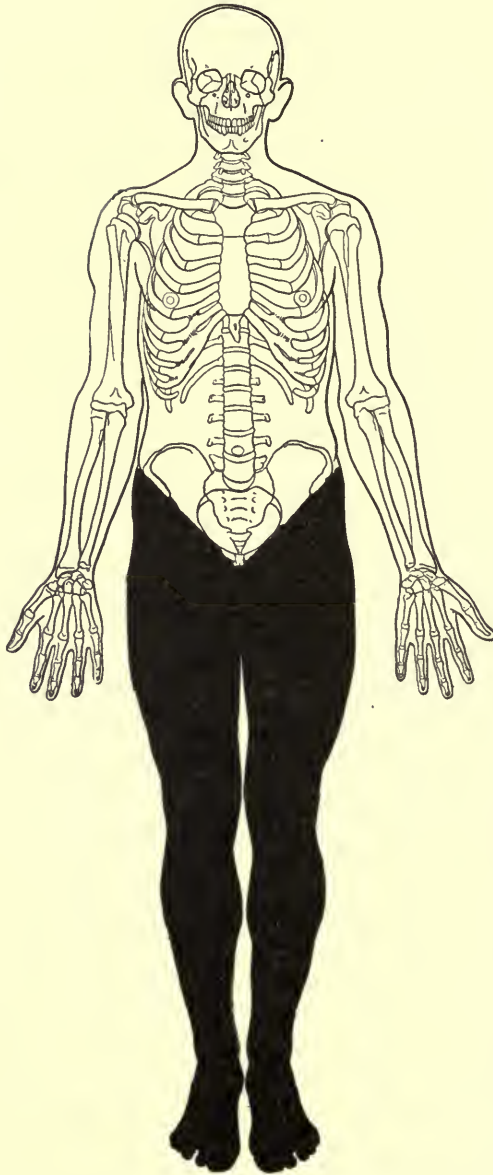


Fig. 52.—Chart of disturbances of motility and reflexes. Solid black represents area of spastic paraparesis with exaggerated tendon reflexes, loss of cremaster reflexes, and positive Babinski sign.

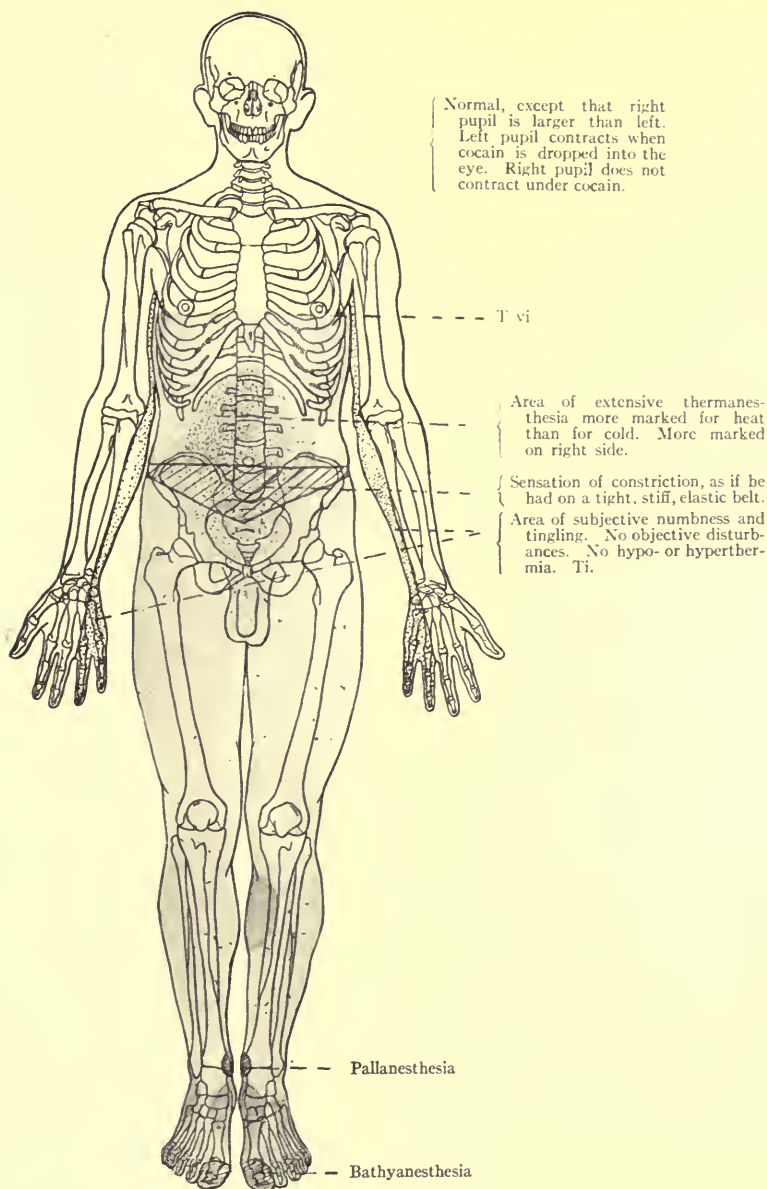


Fig. 53.—Sensory chart. Over whole area shaded in black patient complains of a peculiar “numb” and “dead” feeling, as if the skin were thick and dry. There is slight thermanesthesia over the whole area. There is some anesthesia to light touch, which becomes quite marked on the legs, amounting to almost complete anesthesia in spots on feet and calves. There is but little disturbance of pain sense objectively. The deeply shaded areas show almost complete anesthesia. Patient says he does not sweat over the shaded area.

myelopathia thoracalis chronica. That is merely a descriptive term, a kind of shorthand to summarize the locality of the lesions and their duration.

What is your idea about the sciatic pains that characterized the clinical picture in the beginning?

STUDENT: He might have had a complicating neuritis or root symptoms from pressure.

DR. BARKER: Yes; when pains like these in this patient appear and are followed later by definite signs of intramedullary change, one always suspects "root pains" and thinks of the possibility of meningeal irritation and compression of the nerve roots. There may have been a meningitis involving the roots of the lumbar and sacral nerves, especially since at the operation definite meningitic changes with adhesions were found in the upper thoracic cord.

To what lesions would you refer the sensory disturbances manifested by this patient?

STUDENT: The disturbance of discriminative sensibility (tactile localization, bathyesthesia) points to involvement of the posterior funiculi of the white matter of the spinal cord.

DR. BARKER: Yes. In what region of the posterior funiculi do you think the injury has occurred?

STUDENT: Since there are sensory disturbances all the way up to the level of the sixth thoracic segment, I should think it likely that an incomplete transverse lesion of the posterior funiculi at about this level of the thoracic cord could be responsible.

DR. BARKER: I think so too. But how could you account for the slight disturbance of pain and temperature sense?

STUDENT: I should think that these disturbances could be accounted for by injury to the ascending crossed paths in both lateral funiculi of the white matter.

DR. BARKER: Yes; that could account for them. The lesions, of whatever nature they are, must be slight if they be in the spinothalamic paths on each side, for there is only a little interference with the conduction of the impulses concerned in pain sensation and in temperature sense.

Could a lesion in the white matter at the same level account for the motor disturbances manifested by the patient?

STUDENT: Yes, I think so. Lesions of the pyramidal tract in each lateral funiculus of the white matter of the cord would account

for the spastic paraplegia, including the muscular weakness, the exaggerated deep reflexes, the patellar clonus and ankle-clonus, and the Babinski reflex on each side.

DR. BARKER: Why is it that he still has his abdominal reflexes?

STUDENT: I do not know. They often disappear in pyramidal tract lesions.

DR. BARKER: Yes, that is so. But the paraplegia is not complete here, and there can be only incomplete severance of the paths of the pyramidal tracts. It would seem as though the fibers permitting the preservation of the abdominal reflexes have escaped. I understand that the cremaster reflexes have disappeared.

STUDENT: Yes, we could not get them, though we have tried repeatedly.

DR. BARKER: They are absent now. Is there any evidence of involvement of the spinocerebellar paths?

STUDENT: Marked clumsiness of the left foot was an early symptom, and later on there was clumsiness of the right foot. This ataxia was probably not wholly due to weakness, but was due partly to the bathyanesthesia and perhaps partly to interruption of the spinocerebellar paths.

DR. BARKER: It would not be surprising if both the dorsal and ventral spinocerebellar paths had been involved in this patient, for they lie upon the margin of the lateral funiculus, and we have seen that there is evidence that both the more deeply situated pyramidal tract and the more superficial spinothalamic tracts have been involved. Moreover, there were meningeal adhesions at the level of this principal lesion, and the whole cord, when viewed at the operation performed by Dr. Dandy, was reduced in size.

After the operation the patient improved for a time and then got worse again. Indeed, exacerbations and remissions have been a prominent feature in his case. About two months ago he began to have paresthesias on the medial surface of each of the upper extremities. To what level do these symptoms point?

STUDENT: To the first thoracic segment on each side.

DR. BARKER: Yes: it looks as though this segment were also involved in the pathological process, though the symptoms are subjective, not objective, as yet.

How do you explain the pupillary findings?

STUDENT: Do you mean the anisocoria and the irregular shape of the left pupil?

DR. BARKER: Yes.

STUDENT: Ordinarily, I should think of a midbrain lesion, but there are no other eye-muscle disturbances and the pupils react well to light and on accommodation.

DR. BARKER: Could a lesion in the spinal cord account for the pupillary symptoms?

STUDENT: Some pupillary fibers do descend into the spinal cord and run out through the first thoracic segment to the cervical sympathetic. We believe that the first thoracic segment is somewhat affected in this patient on account of the paresthesias in the upper extremities of which he complains.

DR. BARKER: Yes, one must keep these facts in mind, but if the dilated pupil in the right eye were due to sympathetic irritation one would expect to find other phenomena of sympathetic irritation present on that side, namely, exophthalmos and widened lid slit, but these are not present. It would be rash, I think, to speak too positively about the localization of the lesions responsible for the pupillary symptoms in this patient, but I think it is possible that they are really of midbrain origin rather than of spinal-cord origin.

Is there anything pointing to marked involvement of the gray matter of the spinal cord in this patient?

STUDENT: The anterior horn cells would seem to be everywhere intact, for there are no signs of lower motor neuron lesions. There is no marked atrophy and no reaction of degeneration in any of the muscles, nor is there any fibrillary twitching.

DR. BARKER: How do you explain the weakness of the detrusor of the urinary bladder and the weakness of the intestines? this patient has had both retention of urine and retention of feces.

STUDENT: They might be due to lesions of the splanchnic motor-cell column in the lateral horns of the gray matter.

DR. BARKER: Could they be due to lesions in the white matter?

STUDENT: I should think so, for these lateral-horn motor cells of the visceral system must be innervated by paths of supraspinal origin, just as the anterior horn cells are innervated by the pyramidal tract fibers.

DR. BARKER: Everything points then to an involvement of the white matter rather than of the gray matter of the spinal cord. The

white matter of the dorsal funiculi and of the lateral funiculi have suffered on each side. Possibly the white matter of the anterior funiculi has suffered also, though it is difficult to judge of this. It would be surprising, with such extensive changes in the white matter, not to have some changes in the gray matter, too, but certainly none of the marks that permit us to recognize such changes are observable. We must conclude that the lesions are those of a leukomyelopathy rather than those of a poliomyelopathy; moreover, these lesions of the white matter, though predominantly located in the upper portion of the thoracic cord, have probably involved also other foci of the white matter lower down in the cord, and there may possibly have been slight lesions also in the midbrain accounting for the pupillary symptoms. The meninges have certainly been involved in the upper thoracic region and possibly also in the lumbosacral region. We are dealing, therefore, with a chronic disseminated meningoleukomyelopathy.

Now let us turn to an even more difficult part of our task, namely, the consideration of the *nature* of the lesion responsible for this patient's symptoms and signs.

Do you think we are dealing with a disturbance of circulatory origin, of toxic degenerative origin, of inflammatory origin, or of neoplastic origin?

STUDENT: I think that neoplasm can be ruled out on account of the findings at the exploratory laminectomy. Dr. Dandy stated that no tumor was present and that the cord was smaller in size than normal at the level of the principal lesion.

DR. BARKER: I do not think it is surprising that an extramedullary tumor was thought of before the operation last July. The absence of fever and the slowly progressive course made the existence of extramedullary tumor easily conceivable. Intercostal neuralgias are quite common in association with extramedullary tumors, but in this patient the severe pain was probably due to an associated meningitis of low grade.

That we are dealing here with a genuine myelitis or meningomyelitis I feel very certain. It does not seem possible to me that we have, in the first place, dealt with a myelomalacia from thrombosis of the vessels, followed by an inflammatory process later. The whole history of the case, including the onset and the course of the malady, is against it. A consideration of all the facts makes one think of a

disseminated myelitis, chiefly a leukomyelitis, involving predominantly the white matter of the posterior and lateral funiculi. The principal lesion is undoubtedly in the upper portion of the thoracic cord, but that there are disseminated focal lesions, in addition, I have no doubt. The meningeal involvement has, apparently, been of low grade.

Now what could be the etiology of such a chronic disseminated meningomyelitis with its chief focus in the upper thoracic cord but with other foci elsewhere?

STUDENT: It is certainly not of syphilitic origin, because of the negative Wassermann reaction in the blood and of the wholly negative findings in the cerebrospinal fluid.

DR. BARKER: Yes; we can, I believe, rule out both a syphilitic and a tuberculous origin for this meningomyelitis. We have not, however, the data that will permit us to decide with certainty upon the precise etiology. It is possible that we are dealing with a chronic recurrent infection of the nervous tissues. Clinical pictures such as this do occur in atypical forms of infection with the virus of the Heine-Medin disease (*Flexneria noguchii*) and also in atypical forms of infection with the virus of encephalitis lethargica. Both these diseases have, as you know, been prevalent. We must remember, however, that this patient had his first symptoms in December, 1917. That is at a date before encephalitis and encephalomyelitis of the epidemic form were recognized in this country, though about the time when the disease was first recognized in Austria. I think it probable, however, that isolated cases of the disease were occurring in America at the time of onset of this patient's trouble, and it is quite possible that his malady is of this origin. Nevertheless, when we have not the data that permit us definitely to decide upon the etiology, it is best to keep our minds open. The pupillary disturbances in the case are in favor of an infection with the virus of encephalitis.

In connection with this clinic I should like you to read the article on "Myelitis," by Henneberg, in Lewandowsky's *Handbuch der Neurologie*; and also the article by Taylor and Buzzard in Allbutt and Rolleston's *System of Medicine*; you will find in them excellent epitomes of the whole subject. You will also be interested in reading an article by Dr. B. Sachs, of New York, on *Infectious Forms of Myelitis*, and one by Dr. W. G. Spiller, of Philadelphia, on a

case presenting a small myelitic lesion. I have written on the board a few other references, which you may find helpful.

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XXVI. HYSTERICAL MANIFESTATIONS IN AN IMBECILE

A FEEBLE-MINDED MARRIED WOMAN, JEALOUS OF HER HUSBAND, MANIFESTING CONVULSIVE SEIZURES, CONCENTRIC CONTRACTION OF THE VISUAL FIELDS, ANOSMIA, AGEUSIA, HYPOACUSIA, ASTASIA-ABASIA, AND INCOERCIBLE VOMITING WITH ANURIA.

We have today an interesting case of a kind that I am not often able to present to you.

Our patient, Mrs. Sarah M., is a married woman, thirty years old, who entered Ward G of the Johns Hopkins Hospital ten days ago, complaining of "headache, constipation, dizziness, and loss of appetite."

Her *previous history* contains several important points. She has had measles, pertussis, pneumonia at five, and malaria at fifteen. During most of her life she has suffered from occasional headaches.

Her eyesight, she asserts, has always been rather poor. Until she was five years old she was subject to convulsions, but she has had none since that time until after the onset of her present illness. About two years ago she underwent an extensive pelvic operation, when one ovary, half the other, both tubes, and the vermiform appendix were removed. Observe that though this was an extensive operation, it was not a complete gonadectomy. Menstruation has continued since the operation. She has been married ten years and has had one child, born the third year after her marriage; it died from some infantile disorder when thirteen months old. In other respects her past history is negative.

The patient's *present illness* began four years ago, in the summer of 1914, with frequent headaches, which were most severe in the morning, became better toward midday, and increased again in the evening. The pain began, she says, in the top of her head, and then radiated toward the occiput and both temporal regions. About three weeks ago the headache became continuous, and here in the hospital she complains of incessant pain in the head. (To patient): Have you much headache now?

PATIENT: Yes.

DR. BARKER: About a month after the onset of her headache she began to have "dizzy spells"; these came on when she got up in the morning, but improved toward the middle of the day, and disappeared altogether in the afternoon. When these attacks were at their worst she says she was dizzy, even when lying down, and felt as if she were being "spun round." In October, 1916 the dizziness became continuous, so that she could not walk without assistance. If she attempted to walk alone she would fall backward. When does she say she began first to fall?

STUDENT: In the autumn of 1916.

DR. BARKER: Did she always fall backward?

STUDENT: She says always.

DR. BARKER: Shortly after the appearance of the vertigo she began to suffer from constipation, and states that she did not have a movement of the bowels for a week. Previously they had always acted normally. She consulted a physician, who gave her an enema. Note the presence of this tendency to fecal retention. Was there any retention of urine?

STUDENT: There was later on.

DR. BARKER: The patient was sent to a hospital, where she was treated for two months, with some relief of the constipation. Since then, however, she has never had a normal movement. Cathartics "are of no use" and she has constant recourse to enemata.

In August, 1915 she felt a peculiar "hot flush," diffused "all over her body." About ten minutes later she experienced a tingling sensation in her left hand, radiating up her left arm, spreading across her chest to her right arm, and then to her head, whence it extended over the rest of her body. The tingling sensation was followed by a clonic convulsion, accompanied, it is said, by loss of consciousness. Does she remember the convulsion?

STUDENT: No.

DR. BARKER: There was no loss of sphincter control in this attack or in subsequent seizures. She never injured herself or those around her. Did she bite her tongue?

STUDENT: No; never.

DR. BARKER: She says that the doctor did not tell her the nature of these seizures. About a year after the first of them she had a second, of a similar character. On this occasion she went to bed as soon as she felt the flush, and the convulsion came on after she was in bed. In March, 1916, she had two more attacks of the same kind.

Last October, for no assignable reason, she began to vomit after eating. For two weeks all food and liquids nauseated her and she continued to vomit after every meal. The amount of vomited material was not large and contained only the food eaten at the previous meal. There was never any blood in it. Note this regular vomiting associated with nausea after meals. About three days before the vomiting ceased she went through a period when she did not void any urine at all for two and a half days. She was sent to a hospital where she was given medicine, after which she was able to urinate. She says that when she vomited in the hospital the vomitus was expelled for a distance of from 4 to 6 feet, underneath the middle of the next bed. The projection of the vomited material seems to have been more marked than is seen even in the "projectile vomiting" of cerebral neoplasm. It would be interesting to get a report from those who actually saw it, as to whether there was any voluntary effort in the projection. She has continued to have attacks of vomiting, preceded by nausea, every two or three weeks up to the present

time. They always occur after meals, and when the vomiting is over she feels relieved.

About three weeks ago she noticed that her hearing was impaired, especially in the left ear, and that she had lost all sense of taste and smell. This is an important point. Since the beginning of her illness she has had to have new eye-glasses about once a year, but she was able to read without fatigue until about three months ago, when she noticed that her sight was becoming much worse. Just before she entered the hospital she had new glasses, which she says do not suit her. At present she cannot read for more than a few minutes at a time without fatigue and pain in the eyes.

When the patient was admitted to the hospital, ten days ago, she had not voided any urine the day before, and did not do so until the day after, making two days of complete failure to void. She does not urinate now without abdominal pain. She asserts that after every meal now she has pain in her stomach, radiating into her back and down the right side of her abdomen.

Physical examination shows a large, well-nourished woman. Her eyes react normally to light and on accommodation, but the extra-ocular movements are apparently coarsely inco-ordinate. If she is asked to look at the examiner's finger, she will roll her eyes in every direction, but will insist that she sees the finger. (To patient): Please look at my finger. This finger. Suppose you sit up a minute. It will be easier for you. Can you find my finger now? I think you can all observe the remarkable motions of her eyeballs when she is told to follow the movement of my finger. You perceive that at first she makes no attempt to follow it, but, after a little persuasion, she does so. There is, sometimes, a marked loss of parallelism of the eyeballs as though there were temporary spasm. There seems to be also a disturbance of the attention which I would have you notice. She hears a request that she look at any object and responds to it, but she responds very slowly, and in the pause intervening between the question and her response there is evidently abnormal innervation of the eye muscles. When she looks straight forward there is no nystagmus, though there is repeated winking; with deflection of her attention from time to time there is a corresponding change in the position of the eyeballs. There seems to be no actual paralysis of the eye muscles, and there is no conjugate deviation of the head and eyes.

The nose and throat are negative. The teeth are in bad condition (caries; gingivitis; dead teeth), and there is a wide space between the medial and the lateral incisors in the upper jaw. That is rather interesting. Wide spacing of the teeth is always worth paying attention to, especially if you suspect anything wrong with the pituitary gland. You notice also that the upper median incisors are somewhat notched (though they do not suggest the typical Hutchinsonian notching), and that they are quite large in comparison with the lateral incisors, which are relatively small. This may mean nothing, but such a conformation is suggestive of status lymphaticus. From the number of dead teeth it is likely that x-ray examination will demonstrate that she has some periapical granulomata.

She hears very well with the right ear, but apparently not at all with the left. The exact tests of her hearing by one of our otologists will be reported later.

Examination of the trunk reveals no marked abnormalities. There is no general glandular enlargement. The chest and abdomen are negative. The vascular system is negative. The blood-pressure is not increased.

In the extremities the reflexes are all present and are essentially normal, according to the reports of the several physical examinations that have been made in the ward. There is a rather peculiar broadening of the finger-tips; not true clubbing, but a suggestion of quadri-laterality. (To patient): Will you let me see your hands? Her hands are not especially large. The soft parts are not overabundant, though the rugæ are, perhaps, a little more marked than normal. The thenar and hypothenar eminences are normal. She does not bite her finger-nails, as do so many neuropaths and psychopaths. Like the finger-tips, the tips of the toes are also slightly quadri-lateral.

It is important to be very sure about the reflexes in such a case as this; let us test them again now. The ankle-jerks and the knee-jerks, as you see, are normal. All the deep reflexes in the upper extremity of each side can be elicited; they are equal on the two sides. Coming to the superficial reflexes, I should like to make especially sure that the Babinski sign is negative. You see that, on plantar stimulation, there is a normal plantar reflex, both on the right and on the left. In differentiating functional from organic disease of the nervous system the testing of the abdominal reflexes is also very

important. This patient's abdominal reflexes are quite active. She has a well-marked dermatographia.

(To patient): Please try to sit up in bed without using your hands. She says she cannot do so on account of weakness. This statement would be important if the abdominal reflexes were not present. For in one organic disease, namely, multiple sclerosis, which is often confused with functional nervous disease, the first signs are often weakness of the abdominal muscles, on the one hand, and loss of the abdominal reflexes, on the other. In multiple sclerosis, in my experience, it is rare to find normal abdominal reflexes.

This patient is said to be markedly ataxic. When told to touch her nose with her finger she has, in the ward, touched her forehead or her cheek, and when asked to run the heel of one foot down the shin of the other leg she has been unable to do it. If this ataxia is genuine, we must try to determine some organic cause for it. (To patient): Please touch my finger with your forefinger. You see the attempt and the extreme error she makes. But the interesting point is that the error is not the error of the ordinary ataxic. If you watched her closely when she was making the attempt, you must have seen that her eyes were turned in the direction opposite from my finger, so that the explanation of her pointing error just now is obvious (she was looking at the window on her left, while my finger was on her right). (To patient): Please touch your nose with your forefinger. What is the trouble? Can't you find your nose?

PATIENT: I don't know why I can't find it.

DR. BARKER: You saw the wide error that she made. She says she does not know why she cannot find her nose. The ataxias due to posterior funicular lesions of the spinal cord are well known to you, but here we are dealing with an error on attempt to perform a co-ordinated movement that has, in my opinion, nothing to do with degeneration of the posterior funiculi.

Now let us try the heel-knee test. (To patient): I would like you to place your right heel on your left knee, and then run the heel smoothly down the front of your shin.

PATIENT: I can't do it.

DR. BARKER: Have you any idea why you cannot do it. She says that since she has had these "spells" she has not been able to hold her leg in that position. (To patient): Now let me lift your leg up. Could you hold it in that position?

PATIENT: It will drop down.

DR. BARKER: I let go of her leg. It did drop, but I would have you notice how it dropped. (To patient): Now we may try the other foot. Let me bend your knee so that we can raise it as high as possible. What do you think will happen if I let go?

PATIENT: It will drop down.

DR. BARKER: Did you notice the way in which it "dropped"? It was lowered slowly and with deliberate purpose to the surface of the bed. You will also notice the ease with which the leg was extended upward after the suggestion as to bending it. (To patient): Now let us try your arms. You are pretty strong in your arms, are you not?

PATIENT: No; I am not at all strong in my arms.

DR. BARKER: Let me raise your left arm. Could you hold it up if you wanted to do so?

PATIENT: No; I could not. No matter what you told me. I could not do it.

DR. BARKER: Suppose you try holding the right arm up. (Support was here surreptitiously withdrawn from left arm.) You notice that when her attention was directed to her right arm her left arm dropped soon after I released it, *but not until after there had been a preliminary maintenance of the elevated extremity bent at nearly a right angle.*

STUDENT: In the ward it has been observed that when the patient is standing erect with the eyes closed she falls backward; but the resident physician, Dr. Bloomfield, thinks that if she were allowed to fall she would be able to save herself from injury. It has also been noticed that if, while eating her dinner, she is told suddenly, in an off-hand manner, to brush crumbs from her mouth, she does so without difficulty or hesitation.

Sensory examination has revealed no objective loss of the sensations of touch, heat, and cold. Tests made with the point of a pin and the head of a pin, however, revealed transient areas of analgesia over both forearms; on the next day these areas had normal sensation. There has been marked analgesia to pin-pricks over the whole tongue. (To patient): Can you tell me the difference between the point and the head of a pin if I touch you with them.

PATIENT: It would depend upon how deep you pricked me.

DR. BARKER: We will try pricking the left leg first. (To patient):

Close your eyes, please. Now was that the head or the point of the pin?

PATIENT: I did not feel anything at all.

DR. BARKER: I tried, as you saw, the effect of stimulation with both the head and the point, but she asserts that she has no perception whether what touches her is sharp or blunt. On deep pricking, she says "it does not feel very sharp." Now I will try stimulation of the right leg. (To patient): Have I touched you at all?

PATIENT: Now I feel it sharp.

DR. BARKER: Very sharp?

PATIENT: It did not touch me at all this time.

DR. BARKER: Now let us try the arms. Please keep your eyes closed. Now tell me whether you feel something sharp or something dull on the left arm?

PATIENT: I don't feel anything at all.

DR. BARKER: She asserts that she feels nothing in either arm. So at present there is almost complete tactile analgesia in the skin of the extremities. When I test over the face with the head of a pin she says she does not feel it, but when I use the point she says she feels something dull. The analgesia, therefore, is not complete on the face, but there is hypo-algesia even there.

Let us test the sensibility for heat and cold. (To patient): Please close your eyes and then tell me whether what is touching you now is hot or cold.

PATIENT: I can't tell yet.

DR. BARKER: Tell me whether what I am using now is warm or cool?

PATIENT: Cool.

DR. BARKER: She feels something "cool" on the right side, but she has thermal anesthesia on the left side. You require a very simple apparatus to make this test, for if you have nothing else at hand you can always breathe or blow on the part. Close to the patient's skin the breath gives a sensation of warmth; blown from a little distance it causes a cool sensation. I shall test the right leg in this manner. (To patient): Does this feel warm or cool? (Breathing on right leg.)

PATIENT: Warm.

DR. BARKER (blowing): How about this?

PATIENT: I did not feel anything at all.

DR. BARKER: She is said to have complete loss of taste and smell. Let us test her nose and her tongue. (To patient): Is this a pleasant odor or a disagreeable one?

PATIENT: I don't smell anything at all.

DR. BARKER: I have tested her with spirits of camphor and tincture of valerian, and she cannot distinguish between them. (To student): How many taste modalities are there?

STUDENT: Four: sweet, sour, salt, and bitter.

DR. BARKER: Yes. They are easily tested by applying to the tongue solutions of sugar, vinegar, salt, and quinin. This patient has apparently anesthesia for all taste stimuli. (To student): What is the technical term for taste anesthesia?

STUDENT: Ageusia.

DR. BARKER: And for olfactory anesthesia?

STUDENT: Anosmia.

DR. BARKER: Examination of the eyes with the ophthalmoscope shows that the fundi are normal. Perimetric examination of the visual fields, which is very important in a case like this, shows a marked uniform constriction. It is a case of genuine "tubular vision," a very characteristic finding. Tubular vision or extreme concentric contraction of the visual fields may occur either in organic or functional nervous disease. The normal person can perceive—that is, can take in and arrange—many things at once, whether these are sensations, memories, or more complicated mental states, such as emotions or abstract ideas. This comprehensiveness of perception is characteristic of the normal field of consciousness. The hysterical mind, on the other hand, can take in much less. The multiple sensory impressions are there; they reach the "subconscious mind," but they are not assimilated to the whole system that we call "personal consciousness." There is contraction of the field of consciousness. A normal person, besides seeing the object fixed by him on the retina, is conscious also of objects at the periphery; an hysterical patient very often is not. But such tubular vision is sometimes a part of a double hemianopsia from organic lesions of the occipital cortex, with preservation of central vision; or, sometimes, it may be due to a retinitis pigmentosa which has not injured the maculæ. We shall have to consider these several possibilities later, when we try to arrive at diagnostic conclusions regarding the patient before us.

Now let us test the patient's hearing with tuning-forks. Only

the vibration of a tuning-fork of high pitch is heard by air conduction with the left ear; but the vibrations of all forks are heard by air conduction with the right ear. On testing bone conduction with the tuning-forks the patient says she hears nothing on either side, though air conduction, as we have seen, is good. That is an interesting and rather characteristic anomaly. From the tests of bone conduction alone one would think that the cochlea was functionless, although we know, of course, that it must be able to function, for the patient can hear by air conduction and she could not do so if there were labyrinthine deafness. To the relative unilateral hypoacusia on the right side I shall return later; I shall also discuss the vestibular function later.

The patient has no difficulty in speaking; there is not the slightest slurring of the speech. She also understands all that is said to her in simple language. I may say to you, however, in her presence, that her telencephalic powers, especially those of her cerebral cortex, are greatly below those of a normal person of thirty. The cognitive functions are markedly deficient and the affective-conative reactions are infantile in character. These facts must be borne in mind when we come to pass final judgment on the nature of the case.

A number of laboratory tests and *x*-ray examinations have been made. The blood examination is negative. There are 4,872,000 R. B. C. and 7800 W. B. C. The hemoglobin is 85 per cent. (Sahli). The differential count is practically normal. The Wassermann test in the blood is negative. Examinations of the urine and of the stools are negative. After a test-meal the stomach contents showed normal acidity. The cerebrospinal fluid was tested in Richmond and was reported normal. *x*-Ray examination of the head was essentially negative, though the sella turcica is rather small.

She has a slight struma and a slight tachycardia; there is probably a slight hyperthyroidism.

(To patient): How do you explain the fact that you cannot walk?

PATIENT: I can walk if I hold on to something.

DR. BARKER: What happens if you don't hold on to something?

PATIENT: I fall down.

DR. BARKER: Which way do you fall?

PATIENT: I fall backward. I just can't stand up.

DR. BARKER (To student): What is the technical term for inability to stand?

STUDENT: Astasia.

DR. BARKER: And for inability to walk?

STUDENT: Abasia.

DR. BARKER: Yes, this patient exhibits both symptoms; she has, then, astasia-abasia, an interesting form of loss of co-ordinative power, which we must discuss later.

(To patient): Do you feel that you are a sick woman?

PATIENT: No, I don't feel sick.

DR. BARKER: But you feel sick when you vomit, don't you?

PATIENT: Yes; I do then.

DR. BARKER: But not now?

PATIENT: No.

DR. BARKER: Do you feel sad, blue, depressed, gloomy?

PATIENT: You are bound to feel that way when you can't get well.

DR. BARKER: What makes you think you can't get well?

PATIENT: The doctors "turned me down"; they told me they could not cure me.

DR. BARKER: Suppose you found out that a part of your condition was curable, would you be glad or sorry?

PATIENT: Glad, of course.

DR. BARKER: Why did you get sick? That is what we want to find out.

PATIENT: No one has ever told me that.

DR. BARKER: Do people tell you that you ought not to consider your health? Are people good to you?

PATIENT: I don't feel that people are good to me when I am all the time sick.

DR. BARKER: You mean that they don't sympathize with you? How about your family? Have they treated you badly?

PATIENT: They get out of patience with me sometimes and say that if they were in my place they would "cut out doctors."

DR. BARKER: But you need doctors when you are sick, don't you?

PATIENT: Yes; or I would not have stuck to them all this time.

DR. BARKER: Is your husband living?

PATIENT: Yes.

DR. BARKER: Have you any children?

PATIENT: I had one child. It died about seven years ago.

DR. BARKER: Have you been pregnant since?

PATIENT: No.

DR. BARKER: How long have you been sick?

PATIENT: Off and on for about four years.

DR. BARKER: Have you had any worry on your mind? (To class): I would have you notice how accessible and responsive this patient is. There is a great difference between her type and the schizophrenic or dementia præcox type of patient.

(To patient): Have you had any special worry?

PATIENT: I lost my brother about a year ago.

DR. BARKER: And that was a great grief to you. Have you had anything else to trouble you?

PATIENT: My bad health worries me, of course.

DR. BARKER: Are you and your husband perfectly happy?

PATIENT: Sometimes we are and sometimes not.

DR. BARKER: Has he seemed to drift away from you on account of your illness?

PATIENT: No; not on that account.

DR. BARKER: Was there any drifting apart before you were ill? But perhaps you would rather tell me about that at some other time when we are alone.

I should like to see you try to walk a little. Suppose you let them move you out, and then come back in a dressing gown and try, so that I may see what you can do.

(Patient removed.)

I may avail myself of this opportunity, while we are waiting for the patient to come back, to go into her case a little more fully in its emotional and social aspects. Before the patient came to Baltimore she had been seen by more than one physician and she has been seen by several since she entered the hospital. Thus, among others, Dr. Hall of the psychiatric clinic has seen her and talked with her. It seems that her case is an interesting one from the standpoint of social maladjustment. She has, or thinks she has, a definite cause for mental distress and worry, which is of a kind that is often responsible for functional nervous states, though in her case we are not sure as yet that it is an important causative element. She thinks that her husband is far too deeply interested in another woman, and she is greatly troubled in regard to his fidelity to her. A short time before she entered the hospital she and her husband had a definite marital conflict. She asserts that he is indifferent and that this irritates her. How far back her suspicion of infidelity goes, or

how well founded it is, we have as yet not discovered. In nervous patients suspicions of this character are, of course, sometimes well founded; sometimes they are not.

Here is the patient again. Now we shall have an opportunity to see how she walks. (To patient): Walk with me, please, a little, and let me see how you get along. You observe the clumsiness of her attempts and her tendency to cling for support. I have shown you, before, cerebellar inco-ordinates in whom the lack of co-ordination was due to neoplasm or to degenerative lesions, and the kind of inco-ordination manifested by them was, you will recall, quite different from what it is here. (To patient): Don't you think you could walk by yourself?

PATIENT: I am afraid I shall fall.

DR. BARKER: But suppose I promise not to let you fall.

PATIENT: I can't walk by myself. I know I shall fall.

DR. BARKER: When she tries to stand alone she falls backward. As she walks with my arm supporting her I can perceive a strong repulsion. It is something more than the effect of gravity. There is, I think, a voluntary thrust backward. If the support be momentarily withdrawn there is a strong attempt at recovery, as if she intended to save herself from falling. She walked better with Dr. Sprunt when he brought her in than she does with me. I shall let him take her out. But before she goes I want to say to her that I feel sure that many of her symptoms can be relieved. She will, in my opinion, "get well" of what she regards as her main troubles and be able to use her muscles properly; she will also, I believe, become able to smell, to taste, to hear, and to see quite well again after a time. These functional troubles of which she complains are, I am confident, entirely "curable"; and it is for us to work out together the problem of getting her well again. (Patient removed.)

You may be surprised that I can honestly attempt to reassure the patient in the terms I used just now. Later on you will understand why I desire to make use of this occasion to give the patient a positive suggestion that her symptoms will yield to treatment.

(To student): Has any intensive examination of the cochlear and vestibular functions been made in this patient by a specialist?

STUDENT: Yes. She was examined carefully by Dr. Shelton Watkins of Professor Crowe's department. His report is as follows: "In the left ear only the tuning-fork of highest pitch is heard on air

conduction, and on bone conduction the patient says she hears nothing when any of the tuning-forks are applied. In the right ear the vibrations of all forks are heard on air conduction, but on bone conduction no sounds are heard with any fork. Fork C (256) is heard for five seconds on air conduction. On testing for the vestibular functions, no spontaneous nystagmus is made out except on extreme lateral deflection of the eyes. On irrigating the left ear for forty seconds with cold water there was nystagmus to the right and falling to the left and backward. On similar irrigation of the right ear there was nystagmus to the left and falling to the right. Impression: Vestibular apparatus intact. Results of hearing tests contradictory and unreliable, for the patient says she can hear on air conduction, but that she hears nothing on bone conduction!"

DR. BARKER: Now let us summarize our findings in the patient who has just left the room. She is a feeble-minded married woman of thirty, who is jealous of her husband, and has recently told him that she will take to the law unless he gives up "the other woman." As a child she had convulsions; she was wilful, often throwing herself on the floor and screaming in order to get what she wanted. She has suffered no physical traumata, but two years ago had an extensive surgical operation at which the vermiform appendix, both Fallopian tubes, one ovary, and part of the other were removed. Her present illness began four years ago with headache and pains in the head. A month later she began to have dizzy spells during which she could not walk without assistance. Since 1916 the vertigo and the inability to walk have been constant. In August, 1915 she had a convulsive seizure; in September, 1916, a second; in October, 1916, two more, and in March, 1917, three more, all preceded by an aura, and associated, it is asserted, with loss of consciousness; but none of them caused any injury to the person and in none of them did biting of the tongue or loss of sphincter control occur. Most, if not all, of the attacks followed emotional upsets. In October, 1916 there was a period of nausea and persistent vomiting after meals lasting two weeks and remarkably projectile in character; this incoercible vomiting was associated with anuria for nearly two days. Since then there has been recurrence of nausea and vomiting every two or three weeks, chronic constipation, and some pain in the epigastrium after ingestion of food. Shortly before entering the hospital she had another period when she voided no urine for

two days, and after that voided only with a bowel movement or when catheterized. Her temperature, pulse-rate, respiratory rate, and blood-pressure have been normal throughout her illness. Our physical examinations have revealed (1) normal nutrition despite the history of nausea, vomiting, and epigastralgia; (2) normal thorax and abdomen except residuals of pelvic operation; (3) marked and peculiar disturbances of co-ordination of eye muscle movements, and of movements of the trunk and extremities with pronounced astasia-abasia; (4) normal deep and superficial reflexes; (5) areas of transitory cutaneous analgesia, but no loss of deep sensibility, concentric contraction of visual fields with normal eye-grounds, anosmia, ageusia, and hypoacusia, and (6) normal vestibular reactions. Laboratory tests of the blood, stomach contents, feces, and urine have been negative, and roentgenograms of the skull have revealed no abnormalities other than a rather small sella turcica. (To student): To what part of the body do most of the symptoms of this patient refer?

STUDENT: To the central nervous system.

DR. BARKER: Do you think that they are due to what we call "organic" or to what we call "functional" disease of the central nervous system?

STUDENT: I think we should make very sure that organic disease is not present before we decide that we are dealing with a functional disorder.

DR. BARKER: That is a very safe rule to follow, and I hope that every member of the class will always observe it. I would emphasize, too, the importance of remembering that in many cases the signs both of an organic disease and of a functional disorder are simultaneously present.

Well; what organic diseases are suggested by the symptoms this woman presents? What diseases ought we to consider as possibly existent?

STUDENT: On account of the headache, vertigo, projectile vomiting, and marked disturbance of co-ordination I think that brain tumor should be thought of as a possible explanation of the patient's symptoms.

DR. BARKER: Yes; I agree with you. The symptoms you mention are, indeed, strongly suggestive of intracranial tumor. To what region do such disturbances point?

STUDENT: I should think to the posterior fossa of the skull; either the cerebellum or its connections, or the cerebellopontile angle may be involved.

DR. BARKER: That is a plausible surmise. Let us analyze it a little. Cerebellar tumors do cause remarkable disturbances of coordination at times and this cerebellar ataxia is often accompanied by projectile vomiting, headache, severe vertigo, and adiadochokinesis; the tumor sometimes compresses the nerves at the base of the skull and may even cause anosmia by compression of the olfactory lobes. What is strongly against the diagnosis of cerebellar tumor, however, in this patient?

STUDENT: The absence of choked disks.

DR. BARKER: Yes; bilateral and outspoken choked disk is present very early in patients suffering from cerebellar tumor, in probably 90 per cent. of the cases; and there is not the least sign of choked disk here; the eye-grounds are negative. A small tumor in the tegmentum of the midbrain involving the red nucleus and the brachium conjunctivum may, however, cause cerebellar ataxia and yet not cause choked disk. But even the ataxia in this case is not typically cerebellar. There is marked disturbance of station and of gait, but it is very different from typical cerebellar titubation.

Again, it is hard to reconcile the implications of a tumor of the cerebellopontile angle (acusticus tumor; trigeminus tumor) with the symptoms in our patient. The patient complains, it is true, of both deafness and vertigo, but Dr. Watkins' report shows us that her reports on her hearing are utterly unreliable, or perhaps I had better say very misleading, for she asserts that on bone conduction she hears nothing, whereas on air conduction she hears everything in one ear and high-pitched sounds in the other ear. The vestibular apparatus, as tested by Bárány's methods, appears to be normal. We can then rule out an acusticus tumor especially, also because the typical chronology of the development of symptoms is lacking. Nor is there anything pointing to disturbance of function in the domain of the N. trigeminus; there is no dysmnesia, no anesthesia of the face, and the corneal reflexes are present. We may, therefore, with some confidence, I think, rule out tumor of the cerebellopontile angle.

Besides tumor of the brain, what organic diseases should we rule out?

STUDENT: On account of the loss of smell and taste and the impairment of vision and hearing, a chronic inflammatory process at the base of the skull, say a basilar meningitis due to tuberculosis or to syphilis, might be thought of.

DR. BARKER: Yes. But this process has been going on for four years! There is no fever. The Wassermann test of the blood is negative. And an examination of the cerebrospinal fluid, made in Richmond, was reported negative. Do you think of still other organic diseases that we ought to consider?

STUDENT: Perhaps multiple sclerosis.

DR. BARKER: Yes. In a patient like this whose symptoms include disturbances of vision and inco-ordination one should always think of the possible presence of diseases that cause multiple lesions in the central nervous system. Of such diseases, three especially should be remembered. I mean (1) multiple sclerosis, (2) cerebrospinal lues, and (3) non-suppurative encephalitis or encephalomyelitis. We have already ruled out lues. As to multiple sclerosis, I think we can rule it out also, for there is no optic atrophy, no nystagmus, and no loss of abdominal reflexes. One can never, perhaps, be absolutely sure, but the evidence here is strongly against the existence of multiple sclerosis. And as to encephalitis, the clinical course of the disease in our patient does not correspond to it; there is no real paralysis of the eye muscles, there has been no somnolence and no fever, the cerebrospinal fluid is normal, and the patient's symptoms are of four years' duration; moreover, encephalitis has not been epidemic since the early nineties.¹

Before we fall back upon a diagnosis of a functional disorder let us recall that this patient is mentally defective and that she has had convulsive seizures. Her exact status in the imbecile scale has yet to be determined, but she has had wit enough, as you have heard, to contract a marriage, though not enough to refrain from being jealous of her husband. She had convulsions in childhood up to her fifth year. In 1915 she had a convulsive seizure and since then has had six more. Does she suffer from true epilepsy, or can we satisfactorily explain these seizures in some other way? In favor of the diagnosis of epilepsy is the aura that precedes each attack, the assertion that the convulsions are associated with unconsciousness, and the fact that

¹The reader will note that this clinic was held in April, 1917, before the recent outbreak of encephalitis following the late epidemic of influenza.

the patient is mentally subnormal, since we know that many imbeciles, even those of high class, also suffer from epilepsy. On the other hand, the convulsive seizures have, in most instances at least, followed emotional upsets; the patient has never bitten her tongue in an attack, nor has she lost control of the sphincters during a seizure. Unfortunately, we have had no opportunity to observe one of these "convulsions" ourselves. We should like to observe (1) the exact duration of an attack, (2) the precise degree of disturbance of consciousness that accompanies it, and (3) the order and nature of the disturbances of motility, and the behavior of the reflexes during an attack. We know how closely the convulsive crises in hysteria may resemble an epileptic seizure. And yet, if we observe closely, we can, as a rule, easily distinguish the one from the other. Hysterical crises are less stereotyped in character than epileptic seizures; they vary much in different patients and in the same patient on different occasions. A hysterical convulsive crisis nearly always follows some emotional situation (marital conflict; opposition to desire; fright; chagrin). The initial cry so common in epilepsy is lacking; if the patient falls she does not hurt herself; there is no biting of the tongue and no involuntary passage of urine or feces. Consciousness is not really lost in the hysterical crisis; one can nearly always elicit some sign of sensation and of awareness if one goes about it in the right way. The jerking movements are of larger excursion and less regular than are the clonic contractions of epilepsy. If there be screaming, sobbing, or irregular thrashing about in the attack, one may be more sure that he is dealing not with epilepsy, but with hysteria. The muscular contractions in a hysterical convulsive crisis often correspond to movements that accompany strong emotions (anger, erotism, joy, pain, etc.). Moreover, a hysterical attack, as a rule, lasts much longer than an epileptic seizure, but, unlike the latter, it can often be arrested by a strong psychic influence exerted by a physician or other intelligent bystander.

Whether or not the convulsive attacks in this patient have been hysterical rather than epileptic, she presents a number of other symptoms that are, undoubtedly, I believe, due to hysteria. Among these the most striking are (1) the astasia-abasia, (2) the complaints of loss of smell, taste, and hearing, (3) the attacks of incoercible vomiting with anuria, and (4) the concentric contraction of the visual fields.

Since the descriptions of Charcot and Richer, of Weir Mitchell,

of Jaccoud, and of Blocq neurologists have been familiar with the peculiar form of co-ordinative disability that prevents standing (*astasia*) and walking (*abasia*). Different forms of *astasia-abasia* are met with in the functional neuroses. The form that you have just had the opportunity of observing is one of the most interesting. The patient really has a fear that she cannot stand or walk; she believes that if she attempt either she will fall. Hence a very good name for this form and one that has already been applied to it is "staso-basophobia." There is no genuine cerebellar ataxia here due to lesions of the cerebellar paths. The patient is rather a victim of her pathological ideas and fears.

Total or partial losses of the senses of smell, sight, taste, and hearing are very common in hysteria and every clinician of large experience has met with instances of hysterical anosmia, hysterical amblyopia, hysterical ageusia, and hysterical hypoacusia. In these cases careful testing usually reveals diminution rather than complete loss of sensation. Sometimes there is unilateral loss rather than bilateral.

Attacks of incoercible vomiting with anuria are by no means infrequently met with among hystericals. Charcot called special attention to such attacks, and they have been a prominent feature in the patient we have had under examination today. The suppression of the urinary secretion in these patients seems to be due mainly to the loss of water from the body through vomiting; but there may be, in addition, an inhibition of the renal secretion of central origin. One must make sure when a hysterical patient does not void whether the bladder is full or empty. For failure to void need not necessarily be due to suppression of the urinary secretion (anuria); sometimes, in hystericals, it is due to retention of the urine through spasm. When the latter condition exists, catheterization should be avoided or the patient will be likely to develop a catheter-habit; left to itself, retention from spasm will generally disappear in a day or two.

Contraction of the visual fields with resulting tubular vision is also a common finding on the perimetric examination of hystericals. When a hysterical hemi-anesthesia exists, the visual field on the side of the anesthesia is often more contracted than the other. The contraction of the field often grows under examination. It is interesting that the hysterical patient with contracted fields, unlike patients whose fields are contracted from a bilateral hemianopsia or from

retinitis pigmentosa, behaves ordinarily as though the visual fields were not restricted, which shows that he really values for orientation the impressions on the parts of the retina that on campimetric determinations seem to be anesthetic. It would be interesting in our patient to make an especial examination of the color fields also, for their behavior in hystericals is often just inverse to that in lesions of the optic nerve. In the latter the fields for green and red go first, those for yellow and blue later, whereas in the hysterical the limits of the field for blue may be more restricted than the field for red.

In the usual type of hysteria the patient, when she meets with one of the conflicts of married life, gives way to tears and reproaches. But there is another type of patient, of which we had an example here not long ago, who reacts under the same conditions in an entirely different manner. As you saw, this patient was very willing to answer questions, and the manifestations of her subconscious self, as thus revealed, were simple and even crude in type. This is partly due to the nature of the case, which belongs to the type that Jelliffe describes as anxious "to be constantly in the limelight for the purpose of attracting attention or to invite pity." It is also partly due to the fact that she belongs to the uneducated and uncultivated class. But in this particular instance there is also, I am sure, a rather high grade of mental defect. Under the circumstances, if she were a woman whose antecedents were those of good breeding and of careful training in self-control, her subconscious self would find expression in far more subtle and complex ways. You may observe this same difference in the manifestation of grief. In those who are well-bred and habitually self-controlled the presence of strangers and of outsiders exercises a restraining influence, whereas in those belonging to what in the old world are called "the lower classes," the presence of observers, especially in numbers, seems to excite noisy and unrestrained expression of feeling.

Hysteria in all its manifestations is a subject that has held great interest for the medical profession ever since there were physicians at all. The ancient writers believed the malady to be associated with derangement of the uterus and its appendages, in fact, as Ormerod says, "they held the frankly material view that hysteria was due to the wanderings of the womb round the body, like those of a lion round its cage." Each succeeding century witnessed endeavors by physicians to discover the distinctive characteristics of hysterical

disorders and to lay the foundation of a rational therapy in connection with them. So numerous and so diverse were the theories advanced that when we look over the literature of the subject we feel inclined to agree with the English surgeon, George Tate, who published *A Treatise on the Hysterical Affections* in the early part of the last century, in which he described hysteria as

"An ignis Fatuus that bewitches
And leads men into pools and ditches."

It is only within the last half century that any great advance has been made toward a real knowledge of the condition, and a survey of everything that has been worked out in regard to it during that time will lead many to agree with Jelliffe who says that hysteria is less a clinical entity than a *cohors morborum*.

Modern theories in regard to hysteria date from the studies of Charcot and his school. The chief psychological element in these theories, dissociated personality, received its first great impulse from Charcot himself, but it was elaborated by Janet, and later on, by Freud. For Charcot hysteria was a psychosis, but he regarded it too much in the light of an indivisible entity, where the more modern psychologists see a *cohors morborum*, the cases having little really in common, except a tendency to emotional reactions of a similar character. To Janet, who was Charcot's pupil, we owe the idea of the part played by the subconscious self, a view that looms large in the psychotherapy of today.

Janet believes that there exists a region below the normal personal consciousness; this is ordinarily called "the subconscious." In this region ideas may exist in a sort of "twilight state," in which the individual has no clear perception of their existence and may not even recognize their existence at all. For Janet hysteria is a form of mental hypotension, characterized by the contraction of the field of personal consciousness, and by a tendency to the dissociation and emancipation of certain systems of ideas and of functions, which, by their synthesis, constitute the unified personality. To Janet the hysteric and the hypnotic states are identical, being based upon the common factor of suggestibility.

Freud's theory, developed some years later, is that in certain persons, in whom there usually exists a constitutional basis, some emotion, in most cases of a sexual nature, arises during the infantile

period and is suppressed, because it is thought to be wrong, or shameful, or disgusting. Therefore it remains buried in the region of the subconscious. These impressions do not, as a rule, lead to a definite neurosis up to the time of puberty. According to the Freudian theory, the suppressed instinct is perfectly normal; but it is suppressed because the patient refuses to "face" it. In some instances the emotion is simply one of fear or anger. The suppressed emotion then, according to the Freudian school, becomes later *converted* in the hysterical into a physical symptom. In the psychasthenic, on the other hand, the suppressed emotion, instead of remaining quiet in the subconscious region, becomes attached to some perfectly harmless phobia or obsession, the content of which, in itself, is not enough to account for the disturbed state of the patient. In other words, the hysteric suffers from the *conversion* of an emotion into a physical symptom, while the psychasthenic suffers from the *transfer* of an emotion from a real and painful experience to some other experience to which the patient would normally be indifferent. This is an interesting theory; although proof of it has not yet been worked out, it is a good working hypothesis.

W. A. White has said in this connection: "The character of the psychogenic traumata that produce hysteria is their large content of painful *affect*. A painful affect, fully reacted to at the time, may produce no harm, but if, for any reason, reaction fails, the feelings become repressed and the possibility of dissociation is created. Failure of reaction may be due to failure of conditions that make effective reaction possible, such as the loss of a husband, father, or friend by death."

Charcot's, Janet's, and Freud's are the three main theories that have attempted to explain hysteria to us. Other theories are variants of these and two of them should not be passed over without mention.

Thus, Babinski and others of his school consider that hysterical patients are those whose ills are brought into existence by the power of suggestion, and their "cure" can be effected through the power of persuasion. Suggestion, used in this sense, implies the effort by one mind to make another mind accept or realize an idea that is manifestly unreasonable, whereas in persuasion the idea utilized is reasonable, or at least not in opposition to good sense. This doctrine is known as "pithiatisme."

Then there is the so-called "biological hypothesis" of hysteria, of which Dubois and his followers, especially Schnyder, are the expo-

nents. According to their doctrine hysteria is the persistence in adult life of a childish type of reaction to the facts of existence. It is a mode of reaction in persons of a naïve, simple, and elementary mentality; a mentality lacking in development and deficient in judgment and critique. Such a mentality, when placed in an environment to which it finds difficulty in adapting itself, develops the hysterical reaction. This view would agree very well with the phenomena studied in our patient today.

All these theories are in agreement upon one point, namely, that the hysteric is the victim of false ideas; but there is much difference of opinion as to how far these ideas influence the response. There is no doubt, however, that the emotional reactions of hysterical patients are abnormal and that the emotional symptoms displayed are out of all proportion to the stimuli that call them forth.

Whether the Freudian theory be accepted wholly, partially, or not at all, the Freudian system of treatment of hysteria has much to recommend it, especially when there is not too much mental defect. Inasmuch as the emotions, whatever their cause, are buried in the subconscious self, it becomes necessary to "dig them up" before they can be removed from the patient's mind. Freud does this by analyzing the patient's mind and getting at the suppressed emotion and bringing it into the region of clear consciousness. This is done, directly, by gaining the patient's confidence and inducing her to speak freely; and, indirectly, by the analysis of dreams and the use of association tests, such as those devised by Jung and Riklin. When the suppressed emotion at the root of the patient's condition is ascertained, she is led to face it and to realize that the experience is one that might happen to anyone; she is taught to view the situation as a conflict, developed by our race between nature and social life, for society has built walls around itself for its protection. When this point in the analysis has been reached the patient, the psycho-analysts assure us, usually gets well. This is what Freud calls "treatment by catharsis," a term derived from the old Greek idea of tragedy. In psycho-analysis *the diagnosis is also the cure*, or, to express this in a different way, one gets back to the suppressed emotion by psycho-analysis, and when the suppressed experience has been brought to light and resolutely faced the patient gets well.

Of course, treatment of hysteria by the Freudian method requires, on the part of the physician, a considerable expenditure of time and

effort, which patients of moderate means cannot always afford. Moreover, the patient must be more or less intelligent and interesting to make a doctor willing to undertake this long method of cure. But the symptoms of hysterical patients can often be relieved by comparatively simple methods of psychotherapy; merely for the relief of symptoms, it really does not matter what methods are employed, so long as the physician gains the confidence of the patient and is able to inspire her with the idea that he can make her well.

Janet recommends hypnotism, and in his hands it has been a very successful method of treatment. I think that this patient might be relieved of her present symptoms by being hypnotized; but, on the other hand, the symptoms might later return or they might be replaced by others of a different character. Sometimes the driving out of one "devil" is succeeded by the entering in of seven other "devils" worse than the first! It is interesting, by the way, to think that a good many of the old cases of "possession by devils" were, in reality, examples of the hysterical psychoneurosis. Dr. Hugh W. White, of Yencheng, China, has told me of remarkable observations he has made of demonism among the Chinese. I hope he will publish his records some time. Meyer Solomon's remarks in this connection show a great deal of insight. In speaking of the Freudian conception of the subconscious self he says:

"This conception, then, postulates an inner hidden, contriving, or ingenious personality, or other self, allied to the concepts of demonstrated demoniacal possession. . . . Beneath these unconscious thoughts the real and living personality on the floor below is fighting bravely for survival and of a means, or an opportunity, for expression. . . . And how does he make himself known in this manner? It is in hidden form, in disguise, in mask, in remote bodily disturbances, in breaches of conduct—in the psychopathological acts of everyday life (as well as in other ways). And so we find that this little fellow, really the little, or even still, the big devil down below, fights vigorously for freedom. And all of this goes on without the owner of the little fellow knowing a blessed word about it all. Only by little tricks, by sleight-of-hand work, by peculiar manipulations, does this hidden and repressed personality throw faint shadows of his form upon the screen. These are the psychopathological acts of every-day life of which Freud speaks."

In making a decision as to any special method of treatment to

be employed in any particular case, the patient's mental caliber is a matter for consideration. One must sympathize with Babinski, who remarks that, "For imbeciles and weak-minded types hypnosis may be profitable. Re-education for such is a waste of time."

Dubois and Dejerine, as well as many physicians in this country, have been in the habit of treating their hysterical and psychoneurotic patients by methods of isolation and psychotherapy, the method that Weir Mitchell made famous in this country as the "rest cure." The first thing to be done (as it would be in this case) is to isolate the patient. Take her away from everybody who knows her, put her in a room by herself, preferably a small one, and allow her to see no one but her nurse and her doctor. At the Salpêtrière the difficulties of isolating a public ward patient are overcome by putting curtains around the bed. I got my own first stimulus to apply the simpler forms of psychotherapy by watching Dejerine at work in 1904. Visitors are forbidden, no letters are allowed, and the patient is placed upon a so-called Dubois diet. This diet consists of $2\frac{1}{2}$ ounces of milk every two hours for the first day, the quantity of milk being gradually increased, until on the sixth day the patient is taking about 3 quarts of milk. Then an ordinary diet, suited in calories to the patient's needs, is given, the patient being required to eat regardless of choice. Every day she is visited by some one of the physicians on the staff, and receives continued positive assurances that her ailments are curable, and that if she will do as she is told she will get well. Symptoms are ignored as much as possible. The patient is given massage three times a week, and her attention is centered, as much as possible, on getting back to her normal weight (by increase or decrease). The object of this system, of course, is that no suggestions but those of the right sort shall reach the patient's mind. The origin and nature of her nervous and mental symptoms may, however, be explained to her, and, if it seem desirable, the nature and relationship of emotional conflicts may be discussed. After an interval, the length of which varies in different persons, the patient is allowed up in a chair, and later is required to exercise in the open air. It is assumed that she can do what she thinks she cannot do, and in most cases she can be led to do it. It is very seldom that hysterical symptoms last long under such treatment, though they sometimes do so, especially in cases where the patient has been operated upon for a hysterical contracture. I have such a patient

at present who has had an operation upon the shoulder. It happens, occasionally, that one of the very best surgeons or orthopedists may be misled into thinking that a hysterical manifestation is due to organic disease of a joint or muscle. Indeed, it was a great surgeon, Brodie, who was the first to call attention to the hysterical joint, which has since gone by the name of "Brodie's joint." Patients of this kind can, and often do, deceive the very elect. Some of the best surgeons in the country have been led to operate upon an hysterical joint when definite symptoms, ordinarily indicating operation, have persisted.

Isolation, attention to genuine pathological local conditions, improvement of the general nutrition, good nursing—all these points, together with psychotherapy and re-education, will often restore the psychoneurotic patient to health. How much inferiority of the cerebral cortex enters into the particular case before us today must be worked out while she is under observation. I think it would be well if she were transferred, at least for a time, to the psychiatric clinic for a thorough-going analysis of the mental state.

I am glad that I have been able to show you a good case of major hysteria. It used to be spoken of as a very common condition, but, while it is true that certain forms of psychoneurosis are quite common, major hysteria of this type is not one of them. The wonderful passionate attitudes, described by Charcot, are seldom seen, but, as it happens, we have had 2 or 3 such cases even in this hospital.

And before concluding this clinic, which I fear has already lasted longer than our allotted hour, I want to tell you of an interesting case of the sort which I studied here last year. The patient was a woman of refinement and means, who was in the private ward. She entered the hospital on account of what were supposed to be epileptic attacks. During the attacks, which came on in the early morning, she appeared to be almost asleep and would remain in that condition, unless she were aroused, for fifteen minutes to half an hour. At first we were afraid that she might have a brain tumor with true epilepsy, but, fortunately, Dr. Sprunt saw her during a prolonged seizure, of which she had no memory afterward. It was a sort of twilight state, in which certain of the movements suggested an epileptic attack, but other movements of erotic origin revealed their true nature. When she came out of the attack she did not feel badly physically, though she sometimes wept, because she still had an occasional attack despite

the fact that she had been in a hospital in a distant city for several weeks and hoped that she was getting well. Dr. Meyer and Dr. Thomas saw her in consultation, and we all felt justified in assuring her that she did not have a brain tumor, and that we believed she could get well. After careful psycho-analysis, in which we were greatly helped by Dr. Moore of the Psychiatric Clinic, we got at a very interesting background to her condition. She was a devout Catholic and she had married a Presbyterian. Before their marriage she and her husband had agreed that, if they had children, the boys should be brought up in the father's religion and the girls in that of their mother. She confessed, however, that, at the time she made the agreement, she did not believe her husband would hold her to it. But the husband was not only a Presbyterian, but a Scotchman, with the tenacity of his race and his creed. He intended to live up to the contract and he expected her to do the same. Shortly before she became ill the matter became of immediate importance, for the time had arrived for the religious instruction of the oldest boy. In this case there was all the material for a genuine marital conflict. But the wife was a woman of education and refinement, and had a very sensitive nature; the ordinary methods employed in such marital contentions, such as re-primations and tears, were repugnant to her. The psychiatrist thought that her mental condition probably influenced the subconscious self to believe that anything was better than to lose the soul of her boy, and that these attacks of illness were the result of subconscious suggestion, the underlying idea being that they would arouse her husband's compassion and cause him to fear the influence of opposition to her wishes upon her health. I do not know whether this explanation is a correct one or not, but it was the one given to the patient and it did seem to do her a great deal of good. She is now much better.¹

I feel sure that such reactions to suppressed emotions do occur, though, of course, at the bottom there is the hysterical temperament and at the basis of the hysterical temperament, in my opinion, there must be some form of congenital deficiency, an abnormal *Anlage*. I cannot help but believe that the hysterical patient is born a potential hysterical, and even the theories and doctrines of the Freudian

¹The patient referred to did very well for some months after leaving the hospital, but, later on, again went into trance-like states, and in one of them developed a lobar pneumonia from which she died. Unfortunately, an autopsy could not be obtained.

school, to my thinking, favor this view. Freud and his followers refer the symptoms of hysteria back to traumatism, especially traumatism of a sexual nature, which they trace back to the infantile period of life. I think that, to explain hysterical conditions, we should go farther back still, to a special *Anlage* of the brain. For the kind of trauma that Freud has in mind must occur in the lives of a great many people, but only relatively few respond with hysterical manifestations. If we grant the existence of infantile sexual trauma, as understood by the Freudian school, I think we must also grant the existence of an abnormality on the embryologic side, a pathological *Anlage*; and this, in my opinion, is probably much more important than the infantile stimulus upon which Freudians lay so much stress. And, if I am right, the hysterical is never really cured, but will always be likely, in certain circumstances, to make an hysterical response to certain emotional stimuli.

[*Subsequent History of the Case.*—The patient was transferred to the psychiatric department on April 27th. On entrance there, her intelligence was tested and found, by the Binet test, to correspond to that of a child of seven years. Her attitude was extremely resistant, and only the most indirect form of suggestion could be employed. The moment she realized that an effort was being made to influence her, she opposed it. Close observation gave the impression that there was a certain deliberate intention to deceive. Her taste and smell were tested when she entered the psychiatric ward by the same means employed at the clinic, and with the same results, but it was decided to try some further tests. One of her meals was salted excessively and she was watched while eating it. She ate about half and then refused the remainder, saying that she was not hungry. Her next meal was also similarly salted, and when it was brought to her she declined to eat it, saying "I can't taste it, of course, but I think there is something wrong with it and I would like another tray." A third meal, which was not salted, she also refused, with the same excuse. After that she forgot, or appeared to forget, about the matter. During the three weeks she was in the psychiatric ward she never had a normal movement of the bowels, but her stools, after enemata, showed no signs of mucus. She frequently insisted upon her inability to urinate, but it was never found necessary to use a catheter.

Some attempt was made further to investigate her relations with her husband. She admitted that she had quarreled with him several

times on account of another woman who boarded in the same house with them. On one occasion she had insisted that her husband should order this woman out of the house, and, after his refusal to do so, she had a convulsive seizure. She asserted, however, that she did not accuse her husband of infidelity. All that she complained of, she said, was that "he ought not to go round with that other woman so much."

She gave a history of hallucinations, which began, she said, with the impression of a light that followed her across the room and vanished when she opened the door. She said that just after her brother's death, which she seemed to have felt acutely, she constantly heard voices (generally her brother's voice) calling her, just as she was falling asleep or just as she woke up. Whether these were true visual and auditory hallucinations or the so-called hypnagogic hallucinations or pseudo-hallucinations of Baillarger is a little difficult to decide.

She improved a good deal under treatment by means of occupation, training, etc., and her gait was much better when she worked daily in the gymnasium. If she were not noticed she would do quite a little sewing, though she stated in the beginning that she could not, and would not, sew. Her whole attitude was that of an obstinate, undisciplined child of seven.

She complained a great deal of her eyes; nevertheless she wrote a great many letters, in one of which she must have expressed a wish to get away from the hospital, for when she had been in the psychiatric ward three weeks, her physician came up from Richmond and insisted on taking her back with him immediately. She was discharged, therefore, at the end of the third week. The assistant physician in charge of her in the psychiatric ward had a little conversation with the patient's own doctor, who expressed surprise at the impression she had given in regard to her husband. In his own intercourse with the husband, he said, the man had seemed to be kind to his wife and solicitous in regard to her health. He had never suspected the existence of any trouble between them until the night before the patient left Richmond for Baltimore, when her brother had made some complaints of the husband's conduct. In the psychiatric department it was regarded as unfortunate that, with the exception of the brief conversation with the doctor from Richmond, the authorities had no account of the patient's illness except from herself. The consensus of opinion was, however, that intracranial tumor, epilepsy, and dementia præcox could be ruled

out and that the case was one of hysterical manifestations in an imbecile.]

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XXVII. MULTIPLE NEUROFIBROMATA WITH COMPRESSION OF THE SPINAL CORD

A FARMER OF FORTY-EIGHT, SUFFERING FROM VON RECKLINGHAUSEN'S DISEASE, IN WHICH, IN ADDITION TO PIGMENTATION OF THE SKIN, TUMORS OF THE SKIN, AND OF THE NERVES, THERE WERE PAINS, ANESTHESIAS, PARESTHESIAS, ATAXIA, SPHINCTER DISTURBANCES, EXAGGERATION OF THE DEEP REFLEXES, AND A POSITIVE BABINSKI SIGN, THE LOCALIZING SIGNS POINTING TO ORGANIC LESIONS, PROBABLY COMPRESSION OF THE CERVICAL PORTION OF THE SPINAL CORD BY AN INTRASPINAL NEUROFIBROMA.

THE patient before you today, a white farmer, forty-eight years of age, presents a rather complex neurological syndrome, which merits analysis and discussion as regards the site of the lesions and their nature. I shall ask the clinical clerk, Mr. Sadler, to give you an epitome of the history of the patient and of the physical findings.

STUDENT: The patient, William K., is a white farmer, forty-eight years of age, who was admitted to Ward F of the Johns Hopkins Hospital (service of Professor Thayer) about eight days ago, complaining of "numbness, weakness, and pain in the neck and shoulders" since December, 1918. He had been under treatment earlier in the Church Home and Infirmary and in the Out-patient Department of the Johns Hopkins Hospital. He was also a patient in the stationary clinic of the hospital in March, 1920. I shall, therefore, give a composite history including the data derived from these several sources.

The patient states that when chopping wood in December, 1918, he suddenly had a very severe pain in the back of his head and neck. The pain was so severe that he says he was, for a time, totally incapacitated, but it "let up" gradually. Since then he has suffered, intermittently, from sharp pains behind both ears and in the back of the neck. In April, 1919 he noticed a feeling of numbness in the right hand, particularly in the third and fourth fingers, and a similar numbness in the right foot, referable chiefly to the lateral border of the foot. Later on he noticed, also, numbness in the left hand and in the left foot, and occasionally cramp-like pains in both legs.

There seems to have been a rather steady progression of the sensory changes in the patient from the beginning until the present

time. These sensory changes now involve the whole body below the neck, being limited above by the lower border of the mandible in front and the mastoid region behind. The patient states that it has become impossible for him to button his clothing, and as the numbness has progressed, he has ceased to be able to recognize objects placed in his hands. In addition to the numbness of the limbs and trunk there has been some tingling in the hands and feet, and a peculiar itching sensation, especially in the shoulders. At times he has had a sense of constriction about the chest, the abdomen, and the legs. He has grown progressively weaker, so that now he is practically disabled.

As his symptoms progressed he noticed some difficulty in walking. His legs, he says, "would interfere with one another," and he could not tell what he was walking on. His gait gradually grew more and more unsteady, the unsteadiness being more marked in the dark than during daylight. He observed, too, that on trying to drive a nail, or to chop wood, he was unable to hit the same place twice. When in this hospital in March, 1920, the sensory disturbances and the ataxia were suspected to be due to cerebrospinal lues, notwithstanding the fact that the Wassermann reaction in both the blood and the cerebrospinal fluid were negative. It seems that while in the hospital he received three injections of nearsphenamin, and later on, between April and July, was given eleven more of these injections, and potassium iodid was administered internally. No improvement followed this intensive antiluetic therapy. Instead, the nervous symptoms steadily progressed.

The patient states that during the past two months the pains have become ever more severe. They now begin in the back of the neck and behind the ears and radiate downward into the shoulders. These pains are worse in the morning and pass off during the day. He asserts that the pains are accentuated by throwing the head back, and that he can secure some relief by bending the head forward and hunching up his shoulders. Recently the persistent itching, which he says he feels under the skin of the neck and the shoulders, has been very troublesome.

During the past three years he has had to rise two or three times at night to pass urine, and the amount of urine passed has been increased. At times he has had involuntary passage of urine, and, on two occasions, involuntary stools. He has naturally become

anxious and depressed about his condition, and he has entered the hospital again in the hope of securing some relief.

His family history is negative, except that his father died of paralysis and one uncle of tuberculosis.

As to his own past history, he states that he had an attack of pneumonia at the age of nine, and that he suffered from measles and mumps in childhood and, later, from occasional sore throat. He denies venereal infection. Some seven years ago a nasal polyp was removed from his nose. Otherwise his past history is negative except for the fact that his right ankle has always been weak, so that he has had some difficulty in using his right foot.

On admission to the hospital a week ago the first *physical examination* was made by the house officer, Dr. Telinde, a summary of which is as follows:

"Temperature, normal; pulse-rate, 100; respiration rate, 20; blood-pressure, 120 systolic, 75 diastolic. Well nourished. Small areas of pigmentation visible over the skin, two of them of the size of a dime on the back part of the thigh. A small, firm nodule the size of a pea is visible in the middle of the forehead, and a few sessile fibromata can be seen on the skin of the back; a few minute, scarlet telangiomata are scattered over the skin. Beneath the skin of the left forearm there is a small, firm, movable tumor, measuring 1 by 3 cm. in size. Over the medial epicondyle of the left humerus there is a similar tumor the size of a lima bean, and another just above it. Beneath the skin near the upper portion of the right sternocleidomastoid muscle is another fibroid nodule, and there is still another upon the medial surface of the lower part of the right thigh.

"On the left side of the skull, in the frontoparietal region, is a boss-like eminence. Eye-grounds, pupils, and eye muscles are normal; no protrusio bulborum. Moderate pyorrhea. No struma. Heart and lungs negative. Slight thickening of peripheral arteries; brachials tortuous. Abdomen negative. Genitals negative. Rectal sphincter somewhat relaxed. Prostate not enlarged. Patient's mentality normal, except for some irritability during the present illness.

"On walking there is some uncertainty and staggering. The patient walks with a broad base; slaps the floor with his feet, and says he feels as though he were walking on cotton. He walks much better with the eyes open than when they are closed.

"Romberg definitely positive. Muscular tonus generally in-

creased. Atrophy of the right calf and of the anterior tibial muscles on the right. The right calf is 2 cm. smaller in circumference than the left. There is definite ataxia on movement of the upper extremities, well shown on trying to perform the finger-to-finger and the finger-to-nose test. There is less ataxia in the lower extremities as shown by the knee-heel test. No signs of motor irritation.

"On testing sensation, there is hypesthesia throughout the neck, trunk, and upper and lower extremities. This is somewhat more marked in the distal portions of all four extremities than elsewhere. Deep sensation as regards the large joints does not seem to be involved, though movements of the great toe on each side are not recognized except when the excursions are large. The patient does not recognize the direction of passive movements of the fingers in the two hands. There is no analgesia, but there is loss of the vibratory sense over all of the bones of the body except those of the skull. The patient fails to recognize familiar objects placed in his hand. He states that for some time he has himself observed that he cannot recognize the things he touches unless his eyes are open. No disturbances in the domain of the cerebral nerves. The abdominal reflexes and cremasteric reflexes are absent. Babinski positive in the right foot; equivocal in the left. Deep reflexes exaggerated. Pupils active."

DR. BARKER: What laboratory tests were made?

STUDENT: The blood, the urine, and the cerebrospinal fluid were examined.

Blood examination: Red blood-cells, 4,616,000; hemoglobin, 82 per cent.; white blood-cells, 5680. Differential count: Polymorphonuclear neutrophils, 62 per cent.; polymorphonuclear eosinophils, 1 per cent.; small mononuclears, 28 per cent.

Urine: Specific gravity, 1018; chemical reactions normal in all respects; microscopic examination negative; phthalein output 50 per cent. for the first hour.

The *Wassermann reaction* in the blood has been continuously negative since the patient first came under observation, although many tests have been made.

Lumbar puncture was done on November 9, 1920. There were only four cells; the *Wassermann reaction* was negative and the globulin tests were negative. Several lumbar punctures were made in Department L while the patient was under observation in the

Out-patient Department; they were always entirely negative. There is, however, a report of one examination of the cerebrospinal fluid made on December 10, 1920, in the laboratory of the Phipps Clinic, in which the Wassermann reaction in the spinal fluid was doubtful with single quantity; the test was repeated with double and quadruple quantities, and said then to be positive. There was a negative gold curve, but there was some increase of globulin both with the Ross-Jones test and the Pandy test.

DR. BARKER: Though this single finding is of real interest, I should not be inclined, considering the whole history in this case, to lay much stress upon it as indicating a luetic infection. Long periods of tests of both blood and cerebrospinal fluid have been quite negative for the Wassermann reaction, for globulin test, and for cell count. Moreover, under intensive antiluetic therapy, this patient's symptoms have steadily progressed; there was no amelioration whatever. If the therapeutic test be worth anything, it is against the existence of lues in this case. The patient is married and has had a healthy child. His wife has had no miscarriages. The patient states positively that he has never suffered from any venereal infection. Though the symptoms referable to the spinal cord and the somewhat tender boss on the left side of the skull might suggest lues, the symptoms can, I think, be fully explained without the assumption that a luetic infection has existed. Though it must be admitted that the positive findings in this one cerebrospinal fluid test are a little disturbing, I should be inclined to think them of no significance, unless other tests later on compel us to the conclusion that a lues really exists in this patient. It is well that the confusion resulting from a single report of this sort should come up for discussion in this case. For though we undoubtedly overlook lues sometimes, by accepting, too easily, single or multiple negative tests, there are occasions, like the present one, when we might be unnecessarily influenced by a single suggestively positive test.

Though, on the purely clinical grounds mentioned, syphilis can, I believe, be ruled out in this patient, I desire to call your attention to the fact that positive Wassermann reactions do sometimes occur in patients suffering from tumors of the central nervous system in the entire absence of a luetic infection. Vincent in 1912 reported several cases of tumors of the central nervous system in which a positive Wassermann reaction was obtained in the cerebrospinal

fluid, although the subjects were manifestly not syphilitic. He asserted that these spinal fluids yielding the positive Wassermann reaction had certain other special characters that would often permit one to prophesy in advance that the Wassermann reaction would be positive. These special characters included: (1) a yellow color to the fluid; (2) the presence of albumin; (3) sometimes the presence of fibrin; (4) sometimes the presence of complement; and (5) the absence of an increased cell count. Vincent pointed out that heating the spinal fluid to 56 degrees for a half-hour would diminish the strength of the Wassermann reaction in these fluids or abolish it altogether.

In 1920 F. Stern contributed an article on positive Wassermann reactions in non-luetic diseases of the brain. In this article there is a full review of the whole literature on this subject and a number of cases are cited.¹

Have any *x*-rays been made in this patient?

STUDENT: A roentgenogram of the cervical spine was made. There were no signs of arthritis or of cervical rib. The spine looked normal. I neglected to state that the examination of the feces of the patient was negative.

DR. BARKER: What were these subcutaneous tumors thought to be?

STUDENT: Lipomata, fibromata, neurofibromata, and gummata were all thought of. One of the tumors was removed from the subcutaneous tissue and was sent to the laboratory of surgical pathology for histological study. It was about the size of the end of one's little finger, and was found, on histological examination, to be composed of whorls of cells of spindle-shaped type (fibroblast type), with much eosin-staining, intercellular substance. Dr. Bloodgood stated that the tumor was not sarcoma, but was a "fibroma arising from a nerve sheath."

DR. BARKER: I think we could have prophesied what would be found on histological examination. When you find subcutaneous, firm masses, such as you see in this patient, in association with these

¹Since giving this clinic I have received an article by G. Guillain, of Paris, who reports finding a positive Wassermann reaction in a patient with pressure upon the cervical cord from a neurofibroma. This positive reaction disappeared, however, when the cerebrospinal fluid was heated for fifteen minutes at 56° C. The Wassermann reaction in the blood of his patient was entirely negative. Guillain concludes that syphilis could be entirely ruled out.

little tumors of the skin itself, and associated with these areas of pigmentation, you can be very sure that you are dealing with a more or less generalized fibromatosis of the peripheral nerves, that is to say, with von Recklinghausen's disease.

Let us now examine the nervous functions of this patient ourselves. But first let me point out that there is no difficulty in demonstrating to you the four types of phenomena so often met with in von Recklinghausen's disease. They include, you will recall, (1) tumors of the skin; (2) tumors of the nerves; (3) pigmentations of the skin, and (4) functional disturbances of the nervous system.

The tumors of the skin in this patient are relatively few in number, at least in contrast with the thousands of tumors sometimes seen in the skin of patients suffering from this disease. Here on the forehead, however, you see a firm sessile nodule the size of a pea, the skin over it being smooth, glistening, and tightly stretched. On the back, in the region of the lumbar spine, is a pedunculated, shrunken tumor covered by wrinkled skin. This type of tumor is very common in von Recklinghausen's disease. Here you see a few other minute fibromata in the skin, some of them sessile, some of them pedunculated. In addition, note these minute scarlet hemangiomas scattered over the skin of the patient. These little hemangiomas are not infrequently present, along with the fibromata of the skin, in von Recklinghausen's disease.

The subcutaneous tumors on the peripheral nerves are also easily demonstrable in this patient. This scar on the forearm represents the point from which the tumor was removed for histological examination. Here, above the medial condyle of the left humerus, is the small elongated tumor to which the student reporting the case has already referred. It is easily movable from side to side, but not in the longitudinal direction.

This nodule in front of the upper part of the sternocleidomastoid muscle is visible, I think, from a distance, though it is not very large. I can feel, too, the nodule on the medial surface of the right thigh in its lower third. These small tumors are not lobulated as lipomata are. After you have once become acquainted with von Recklinghausen's disease I think you will have no difficulty in recognizing the fact that these tumors are situated upon subcutaneous nerves, and that they are fibromatous in nature.

There is some localized pigmentation of the skin in this patient.

Here you see one or two larger patches of a brownish color, and scattered over the back and trunk generally are some minute brownish-black spots. On the back of the neck there is a brown area of pigmentation about $\frac{1}{2}$ cm. in diameter, covered also with hair. Hairy moles of this sort are not uncommon in association with the other phenomena of von Recklinghausen's disease.

I can feel no nodules in the abdomen in this patient. Some of the staff will remember the case of a child I showed at one of these clinics some years ago, in which there were multiple nodules palpable in the abdomen, probably situated upon the sympathetic nerves in the mesentery.

The disturbances of nervous function are of peculiar interest in this patient. One of the astonishing things in von Recklinghausen's disease in most cases is the relatively slight disturbance of nervous function observable, despite the enormous number of fibromata that may exist in the course of the various peripheral nerves. In some instances, however, marked disturbances of nervous function appear, and one has to try to explain these less common cases. The patient before us presents a marked disturbance of sensibility of the skin below the head. There is, as you see, tactile hypesthesia from the level of the mandible down to the feet. This diminution of tactile sensibility is less marked this morning than it has been in the ward. It appears to be variable. There is no marked analgesia or thermanesthesia. There is, however, complete loss of vibratory sense in all the bones of the body except those of the head; and there is, as you see, some loss of deep sensation, for when I move the great toes, and make even larger excursions, the patient is unable to recognize either the movement itself or its direction. We have, therefore, bilateral diminution of tactile sensibility and of deep sensibility below the head, without much disturbance, if there be any, of pain or temperature sense. This is a peculiar dissociation of sensibility, just the opposite of what one sees, you will recall, in syringomyelia, in which there is loss of pain and temperature sense with retention of tactile sensibility and of deep sensation.

This patient also shows marked ataxia. He presents a definite Romberg sign, and, as you see, when he attempts to touch the end of his nose with the forefinger of either hand with the eyes shut, he misses the mark, touching his forehead, his temple, or his chin, rather than the goal aimed at. In the lower extremities the ataxia

is somewhat less marked, though the knee-heel test is not quite accurately performed; and when he runs his heel down the front of his shin there is a good deal of deviation from a straight line.

As far as motility is concerned, you see that he has, in addition to his general muscular weakness, a definite wasting of the right leg below the knee, with weakness of both flexion and extension of the foot at the ankle. There is, perhaps, a little hypertonicity of the muscles, and the deep reflexes in the arms and in the legs are definitely exaggerated. On the right side there is a positive Babinski sign; on the left side this is not elicitable at present. In contrast with these marked neurological disturbances below the head (and to them must be added the sphincter disturbances which you will recall in his history, namely, incontinence of urine and feces) there seem to be no disturbances in the domain of the cerebral nerves, nor are there any symptoms referable to lesions within the brain itself.

How can we explain these remarkable disturbances of function (sensibility, motility, co-ordination, tonicity, reflexes, sphincters) in this man's body below his head?

STUDENT: The wasting of the right leg below the knee is an old affair, but I can get no history of poliomyelitis. The electrical reactions of the muscles have not yet been tested. The positive Babinski reaction indicates a definite disturbance of function in the pyramidal tract. There must, therefore, be a lesion within the central nervous system rather than in the peripheral nerves to account for the injury to the pyramidal tract. The disturbances of sensibility, involving the whole trunk and all four extremities, but leaving the head undisturbed, suggest the possibility of some lesion in the spinal cord high up.

DR. BARKER: Yes; I think the deductions that you have made are reasonable. Supposing that we assume a lesion of the cervical portion of the spinal cord as accounting for the phenomena (say with the exception of the atrophy of the right leg below the knee), what parts of the cervical cord must be injured?

STUDENT: The disturbances of touch and of deep sensibility, together with the inco-ordination, would suggest injury to the long sensory paths of the posterior funiculi (columns of Goll and Burdach). The slight pyramidal tract disturbance would point to injury of the lateral funiculus.

DR. BARKER: Yes; it would seem to me that the symptoms here point to posterolateral involvement with integrity of the gray matter

and also of Gower's tracts, in which are situated the upper continuations of the fibers conducting impulses of pain and temperature sense. In other words, an incomplete transverse lesion of the upper cervical spinal cord, injuring the posterior funiculi on both sides and, to a less extent, the lateral funiculus, especially on the right side, would account for the tactile hypesthesia, the bathyanesthesia, the exaggerated deep reflexes, the positive Babinski, the sphincter disturbances, and the inco-ordination.

Now it is exceedingly interesting that the cervical nerve roots within the spinal canal are a site of predilection for the development of neurofibromata, and a number of cases of compression of the cord in this region by such tumors have been reported in the literature. In this article by Peter Bassoe and Frank Nuzum, published in the *Journal of Nervous and Mental Diseases* (1915), you will see on page 788 a figure showing tumor growth in the cervical nerve roots at the level of the fifth cervical segment, with invasion of the spinal cord in the region of the posterior horn. Even more striking are the illustrations that accompany this article by Preble and Hektoen, published in the *American Journal of the Medical Sciences* (1901); on pages 14, 15, and 16 of the article you will see how the spinal cord has been compressed by a neurofibroma that had developed upon the fourth right cervical nerve. The transverse sections of the cord above and below the lesions show the secondary degenerations in the posterior and in the lateral funiculi. Evidently the lesion of the cord must have been severer in this case of Preble and Hektoen's than that in our patient can be.

As early as 1903 our professor of neurology, Dr. H. M. Thomas, called our attention to the occurrence of paralysis and muscular atrophy of the arms and legs in neurofibromatosis. You will find his article on this subject in the *Bulletin of the Johns Hopkins Hospital* for that year.

Though the condition is rare, compression of the spinal cord by intraspinal neurofibromata has been reported by still other observers (Schlesinger, 1898; Spillmann and Étienne, 1898; Haushalter, 1900; Cestan, 1900; Henneberg and Koch, 1902; Lion and Gasne, 1904; Peusquens, 1910; Hunt and Woolsey, 1910; Guibal, 1910; Schlesinger, 1911; Coyon and Barré, 1914; Guillain, 1921). Christin and Naville (1920) review some 20 cases of central neurofibromatosis recorded in the literature and add 4 cases observed by themselves.

Just how many lesions inaccessible to palpation there are upon the nerves in our patient no one can form any adequate guess. At autopsy upon cases of this sort there are often to be found upon internal nerves a large number of tumors that were entirely unsuspected during life. It is even possible that this atrophy of the right leg, below the knee, in our patient may depend upon neurofibromata somewhere in the course of the peripheral nerves innervating them.

Though we are probably right in assuming as the cause of the nervous disturbances in our patient a compression lesion of the spinal cord in the cervical region due to an intraspinal fibroma upon one or more of the cervical nerves, certain other conditions might perhaps be thought of as explaining these neural disturbances. Could you mention one or two?

STUDENT: I thought of the possibility of a funicular myelitis such as we see in pernicious anemia.

DR. BARKER: Yes; the involvement of the posterior funiculi and of the lateral funiculi such as we see in this case would naturally call to mind the conditions that are met with in the ataxic paraplegia of anemic patients. This man, however, has no anemia. Moreover, the fairly sharp limitation of the sensory disturbances at the junction of the head with the neck, the wide distribution of the tactile hyperesthesia, and the absence of a history of the parasthetic phenomena in the hands and feet that are so characteristic of anemic funicular myelitis, are all against the diagnosis of an anemic or a diffuse toxic degenerative process in the posterolateral funiculi, it would seem to me, and are in favor of that of an incomplete transverse lesion in the upper cervical spinal cord due to pressure.

What other possible explanation have you thought of for the nervous symptoms and signs?

STUDENT: We know that in von Recklinghausen's disease there are often a large number of tumors upon the nerve roots, especially upon the posterior roots within the spinal canal. A very wide distribution of such lesions within the spinal canal could, perhaps, account for the functional disturbances.

DR. BARKER: You are right, of course, in thinking of that possibility, and no one dare assert, with certainty, that many tumors do not exist within the spinal canal of this patient. It is scarcely conceivable, however, it seems to me, that such an even and diffuse involvement of tactile sensibility throughout the whole of the trunk

and the four extremities could be due to simultaneous involvement of practically all the posterior roots. It is much easier to conceive of a pressure-effect upon the posterior funiculi in the cervical region as responsible for these wide-spread disturbances of the tactile sense. In any case we are certain that there is some spinal cord involvement in addition to any involvement of the nerve roots, for otherwise we could not account for the Babinski phenomenon. The sphincter disturbances, too, are more common in association with medullary lesions than in association with lesions of the roots of the peripheral nerves.

The evidence, then, would seem to me to favor the view that we are dealing with a compression myelitis in the upper cervical region, dependent upon the existence of one or more neurofibromata upon the cervical nerves within the spinal canal.

What can we do to help this patient? His life as it is is a burden to him, and he is totally incapacitated for work.

STUDENT: If the diagnosis of compression myelitis in the cervical region be correct, he might be benefited by surgical therapy.

DR. BARKER: I think it would be well worth a trial. Removal of the neurofibromata causing the pressure in the cervical region might go far to relieve the functional disturbances, though it is not likely that there would be a complete restoration of the functions of the cord.

It is, of course, true that even if it were found possible to remove a compressing fibroma from the situation mentioned, the patient might develop later on other fibromata that would cause additional disturbances. That risk would, however, have to be taken. Many of these patients go through life without central neural disturbances, and it is quite possible that, if we could relieve him of his present disability, he would get on, at any rate for a long time, fairly well.

After he has been observed for a while longer in the ward the whole matter can be placed before the patient frankly, and he can make his decision as to whether or not he will submit himself to surgical therapy. Should he do so, I shall be glad to report to you later the results.

[*Subsequent History of the Case.*—The patient refused an exploratory operation for the purpose of determining whether there was, or was not, a tumor pressing on the cervical portion of the spinal cord, preferring to have the intraspinous injections of salvarsanized serum

continued. On January 17th, after he had been in the hospital about a week, he was given 0.4 gram of diarsenol intravenously, and on the following day the serum from 50 c.c. of his blood, drawn after the intravenous injection, was injected intraspinaly. He had severe pain about his cervical region afterward, but no other reaction. In view of the fact that he had manifested no improvement under intensive diarsenol therapy, and that the treatment by intraspinal injection is not devoid of danger, the idea of further antiluetic treatment was abandoned. The patient continued to decline to be operated upon and was discharged on January 25th, with directions to return if his symptoms increased.

The patient was re-admitted on September 27th, entering the surgical service with a view to operation. The findings were about the same as those on his previous admission, except that there was an increase in all the symptoms. After examination by Dr. Thomas, Dr. Dandy, and all the surgical staff it was decided that he was suffering from some atypical neurological condition, probably some organic degenerative disease of the central nervous system, and that operation was not indicated. The patient was discharged "untreated" on November 11th, ten months after his first admission.]

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DISEASES OF METABOLISM

XXVIII. ENDOGENOUS AND EXOGENOUS OBESITY WITH MULTIGLANDULAR ENDOCRINOPATHY

A WOMAN OF FIFTY-TWO, WEIGHING 432 POUNDS, SUFFERING ALSO FROM CHRONIC ARTHRITIS AND BEGINNING CIRCULATORY INSUFFICIENCY. DISCUSSION OF THE DIAGNOSIS AND TREATMENT OF OBESITY.

THE calculated ideal weight of the patient to be presented to you today is 143 pounds. Her actual weight, on admission, was 432 pounds, or 289 pounds in excess of her ideal weight. I think I have before cited to you Ebstein's classification of the stages of obesity. He describes (1) the enviable or majestic stage; (2) the comical stage, and (3) the pitiable stage. When we see the patient, and learn of her present discomforts, you will agree with me that she has already entered upon the "pitiable stage" of this malady. The patient, like many of the obese, is very sensitive about her overweight. I shall ask the clinical clerk, Miss B., to tell you the main points in the history before the patient is brought in.

STUDENT: The patient, Hilda D., is a single white woman, fifty-two years of age, who entered the hospital recently complaining that she was "losing ground," that she was "becoming excessively stout," and that she had "trouble with her feet."

On inquiring into the family history we find that she has four sisters, all of whom are stout, one of them being almost as heavy as the patient. She has only one brother, who is tall and thin. On her father's side, the family were all of large frame; they were heavy people, but she says they were not "fat." It was her mother's family that showed a marked tendency to obesity. No definite history of the occurrence in the family of acromegaly or of gigantism could be made out.

The habits of the patient would account for some exogenous obesity. She has always eaten three large meals a day, and has been very fond of meat, of candy, and of ice-cream. To quote her

own expression: "My appetite is fine. I like good food and plenty of it." She has had her full quota of sleep—eight or ten hours each night and an hour every afternoon. Though she has done her own housework, and worked for a time as an assistant in a shop, she has taken but little physical exercise.

In childhood she had the usual exanthemata and frequently suffered from tonsillitis, and later from quinsy. At the age of sixteen she had an attack of what was called "malaria." In her teens, too, she had her first attack of acute rheumatic fever with polyarthritis, and later on in early life had two subsequent severe attacks of acute rheumatism. Fortunately, the rheumatic fever does not seem to have been complicated by endocarditis.

As a young girl she suffered from sick headaches, which, from her description, sound like attacks of ordinary migraine. In later life she had a different kind of headache, which will be referred to later on. For many years she has noticed that she got out of breath easily and that her pulse became accelerated on slight exertion; but of late the dyspnea and tachycardia have become much more marked. She has always had excellent digestion.

She menstruated first at the age of twelve, but her menstruation has always been very irregular and the flow scanty. Throughout her adult life she has had many periods of amenorrhea lasting from several months to as long as two years at a time. Seven years ago her menstruation ceased (at the age of forty-five), and there has been no return of menstrual flow until two months ago, when she had what appeared to be an ordinary menstrual period.

DR. BARKER: When bleeding from the uterus reappears after menstruation has apparently ceased for some time, what suspicion is aroused in your mind?

STUDENT: Malignancy.

DR. BARKER: Yes; it will be necessary in this case to make sure whether or not any malignant growth is developing in the cervix or body of the uterus. Will this be easy to do?

STUDENT: Bimanual palpation of the uterus would be practically impossible in this patient on account of the obesity.

DR. BARKER: Yes; I doubt very much if anything could be made out by the ordinary method of examination. It is possible that by means of examination with a speculum or by curetment decision can be arrived at. Has she any other urogenital symptoms?

STUDENT: She has had no pain. She arises two or three times at night to pass urine. Otherwise the urogenital history is negative.

The patient says that she was a nervous child. In later years, however, she has had no marked nervous symptoms except the severe headaches that began three or four years ago. Each headache was preceded by dimness of vision for about half an hour. She would notice this dimness of vision in the shop, where she could not tell stripes from plaids. The headaches became so severe that she was compelled to stop work two years ago, since when this variety of headache has ceased. She stated that the headache was deep in the head through the temple. Of late she has had some frontal headache on waking in the morning; but this seems to be quite different from the severe headaches that compelled her to stop work, and also, from the sick headaches of her childhood.

DR. BARKER: What does this history of headache suggest to you?

STUDENT: The headaches in childhood seem to me to have been due to migraine. The severe headaches of three or four years ago, preceded by dimness of vision, make one suspect a brain tumor or, possibly, increased blood-pressure.

DR. BARKER: In what region would you suspect the tumor to exist if there were one?

STUDENT: On account of the dimness of vision preceding the headaches, the recurrent amenorrhea, and the obesity I would think of the hypophysis.

DR. BARKER: Yes; a tumor of the hypophysis with intermittent swelling in it might compress the optic chiasm and cause disturbances of vision. Could you make out whether or not she had a bitemporal hemianopsia at that time?

STUDENT: The patient simply mentions "dimness of vision." From her description there does not seem to have been limitation of the temporal fields, though I cannot be sure.

DR. BARKER: What else could cause bitemporal hemianopsia besides a tumor or swelling of the hypophysis?

STUDENT: I do not know.

DR. BARKER: Well, an internal hydrocephalus, I suppose, might do it through the pressure of fluid in the floor of the third ventricle. It would be rather uncommon, however, to have such a temporary and transitory hemianopsia in hydrocephalus.

Why did the patient come to the hospital?

STUDENT: Of late she has become so short of breath on slight exertion that she can scarcely walk at all. She has had pains in her ankles, which she attributes to the old rheumatism. She felt that she was "losing ground," was becoming "stouter," and feared permanent invalidism. She applied to the hospital in the hope that something might be done to help her.

DR. BARKER: Would you give us a brief account of the development of her obesity?

STUDENT: It is difficult to procure precise dates and weights. The patient says that she weighed 90 pounds at nine years of age, which would be about 30 pounds above the average weight for that age. She asserts that she was not markedly fat until she was twelve years old, but what her weight was then she does not know. At the age of seventeen she thinks she weighed about 200 pounds, and as her life advanced she suddenly grew heavier. Some twelve years ago (in 1908) she dieted for eight months and lost some 65 pounds in weight during that period.

DR. BARKER: Many of these patients form good resolutions about diet and exercise, and act upon them for a time, but it takes a great deal of will-power to maintain the restrictions. In excessive obesity it is seldom possible for the patient to succeed with a reduction cure without close supervision, encouragement, and, in reality, command from her physician. Even in the best circumstances of supervision successful reduction may be difficult.

Has the patient suffered much from painful joints of late?

STUDENT: She says that her ankles bother her a good deal and that her knees are a little stiff and that they creak.

DR. BARKER: It is very common to see a villous arthropathy or a static arthropathy develop in the joints of the lower extremities in the obese. We shall have to try to determine how much of her arthropathy is due to strain and how much, if any, is due to infection, or to intoxication.

You state that she has become very short of breath of late?

STUDENT: Yes; she now has dyspnea on the slightest exertion; indeed, when lying quietly in bed she is quite short of breath.

DR. BARKER: Patients with pronounced obesity are prone, sooner or later, to develop myocardial insufficiency. It is no wonder that they do. There is often fatty infiltration of the heart muscle itself; the intrathoracic space is encroached upon by the shoving

up of the diaphragm by the abdominal fat; arterial hypertension and arteriosclerosis often develop in these patients and throw additional strain upon the heart muscle; the strain of pumping blood through 270 pounds of extra adipose tissue is no small addition to the work of the heart; and, if the heart muscle has been injured by infection at any time, it is very likely to give way relatively early in these patients. You will recall that this patient had three attacks of rheumatic fever in earlier life. Though she does not seem to have had a rheumatic endocarditis, it is quite possible that her myocardium was more or less injured during these attacks. But we are anticipating a little. Will you tell us of the physical examination made on this patient when she was admitted to the hospital?

STUDENT: On admission a note on her physical condition was dictated by Dr. Felty: "Temperature normal; pulse-rate, 100; respirations, 24; the blood-pressure, 140 systolic, 64 diastolic. Height, 5 feet, 6 inches; calculated ideal weight, 143 pounds; actual weight, 432 pounds; excess of weight, 289 pounds. Masses of panniculus over the entire body; subcutaneous fat firm and diffuse, not painful; fat especially abundant proximalward in the extremities, but very abundant also on the trunk, and especially in and upon the abdomen and about the hips. The skin of the abdomen, especially that below the umbilicus, is tough and thick and resembles pig's skin; the fat hanging down in folds has caused some irritation; the skin is reddened and brawny from the friction.

"The patient is mentally alert and does not look ill except for the evident shortness of breath even while at rest.

"The head is large; the neck very short; marked double chin; hair rather oily; lid slits narrow; eyelids a little puffy; pupils equal and react to light and on accommodation; slight conjunctivitis; extraocular movements normal; visual fields, roughly tested, normal. Eye-grounds negative.

"Slight pyorrhea alveolaris; several suspicious teeth to be investigated. No-glandular enlargement. Thyroid isthmus difficult to palpate.

"Thoracic examination difficult on account of obesity: possibly some emphysema. Dimensions of heart cannot be determined by percussion. Soft systolic murmur audible at the pulmonic area."

DR. BARKER: It would, of course, be useless to attempt delimitation of the heart area by percussion in a woman as obese as this one. How could you determine the exact size of the heart?

STUDENT: About the only way would be by means of the teleroentgenogram.

DR. BARKER: Yes; roentgenological examination would, despite the obesity, give one a very good idea of the size of this patient's heart. You would have to keep in mind, however, that the diaphragm is shoved up and that the heart would be placed in a more transverse position than normal. You could, however, measure the total area of the heart surface in the teleroentgenogram and get an approximate idea of the degree of enlargement in that way. You could tell, too, by the general configuration of the heart in the x-ray plate whether or not the left side was enlarged disproportionately to the right.

STUDENT: An electrocardiogram has been taken. A normal mechanism is reported, with left ventricular preponderance.

DR. BARKER: What else was made out at the general physical examination? Please continue the report of Dr. Felty's examination.

STUDENT: "Marked lumbar lordosis; double hallux valgus; tendency to talipes varus. Movement of the ankle-joint painful. On passive movements of the knees creaking could be felt. Hands relatively small; fingers tapering; no tremor of the fingers. Tendon reflexes and superficial reflexes normal.

"The distribution of the hair on the body is interesting. The hair of the head is soft in texture, abundant, grows a little low on the forehead, and rather far forward on the temples. Axillary and pubic hair scanty; in contrast with this, a marked growth of hair on the chin; indeed, the patient has had a beard and has been compelled to shave for several years. A little pitting on pressure on the legs above the ankles and on the skin of the abdomen."

DR. BARKER: We will now have the patient brought in in order to verify some of these findings. (Patient brought in.)

(To patient): We shall keep you only a little while in the clinic. I want our students to be familiar with this kind of trouble and to learn how to deal with it.

(To class): You note that the patient breathes rather rapidly, and with some difficulty, though she is lying quietly on her back. As I hold up the right upper extremity you will observe the relatively small hands and tapering fingers and the marked increase in circumference of the extremity in the proximalward direction. The measurement around the middle of the biceps is 18 inches. The rugæ on the backs of the knuckles are more marked than normal.

The lunulæ do not show at the bases of the nails. There is nothing suggesting acromegaly about these hands, but, rather, they suggest a hypohypophysism. The soft parts on the backs of the hands are a little increased, but not nearly so much as one would expect in marked



Fig. 54.—Anterior view of patient with extreme obesity.

Fig. 55.—Lateral view of the same patient.

hypothyroidism. Her eyes are not prominent and the lid slits, as you see, are narrow. This would suggest hypo- rather than hyperthyroidism, despite the tachycardia which I interpret as due to the circulatory insufficiency.

You note that the skull is fairly large, but the acra of the head are not particularly prominent (Figs. 54, 55). The chin is a little turned up; there is a very marked double chin and a huge collar of fat about the short, thick neck. The bimalar distance is rather wide. There is a little spacing of the upper incisor teeth. Note these huge masses of fat beneath the scapulae. The condition of the abdomen, however, is the most striking feature. Besides the large amount of fat in the abdominal wall there must be a great deal of fat in the omentum and in the retroperitoneal areas in this patient. There are enormous masses of fat about the hips and thighs. You notice that the fat hangs in folds above the knees. As we pass distalward in the lower extremities, however, the fat is relatively rapidly reduced in amount and the feet are not especially large. You observe the double hallux valgus. Notice, too, these varicose veins in the flanks and on the lateral surface of the thigh. They have not caused any pain, however, and have never been thrombosed. These knee-joints creak a little as I flex the leg upon the thigh. Note how scanty the hirci are here; there is a similar scantiness of the crines pubis. There is a little hypertrichosis of the forearm and just a little below the knee, but none elsewhere on the body. The skin is, for the most part, rather dry. She tells me, however, that she has some sweating of the face and neck, especially when she is a little nervous. She is sensitive to cold rather than to heat—a little suggestive of hypothyroidism. (Patient removed.)

DR. BARKER: What laboratory tests have been made upon this patient?

STUDENT: The blood, urine, and feces have been examined and the basal metabolism has been tested.

She has 5,370,000 red blood-corpuscles; hemoglobin, 100 per cent.; white blood-corpuscles, 10,000. In the differential count there were 76 per cent. polymorphonuclears and 19 per cent. small mononuclears. The Wassermann reaction was negative.

The urine had a specific gravity of 1020 and contained no albumin, no sugar, and no casts. An occasional white blood-corpuscle was seen. Examination of the feces was negative.

The basal metabolism was examined by Dr. John T. King, Jr., who found it 18 per cent. above the average for the patient's age and sex. It seems, however, that the patient had been taking 3 grains of thyroid substance for several days before the basal metabo-

lism was tested. Allowing for this, Dr. King thought that her basal metabolism was probably within normal limits.

DR. BARKER: Has any test been made of her carbohydrate tolerance?

STUDENT: Yes; she was given 100 grams of glucose, and the blood-sugar was followed afterward. It went as high as 0.328 and yet no glycosuria occurred. At 7.30 A. M., half an hour before the glucose was ingested, her blood-sugar was 0.143; at 8.30 A. M. it was 0.247; at 9 A. M., 0.328, and at 10 A. M., 0.200.



Fig. 56.—Lateral roentgenogram of foot.

DR. BARKER: That is a very interesting observation. See what a remarkable hyperglycemia can temporarily occur in this patient without glycosuria. The threshold of her kidneys for glucose excretion is obviously very high. In most patients the mobilization of this amount of glucose into the blood would be accompanied by glycosuria. The findings in this patient in this regard are so exceptional that I think the test should be repeated later on.

What *x*-ray examinations have been made?

STUDENT: Roentgenograms of the left ankle have been made as well as one of the skull.

DR. BARKER: Let us place them on the illuminating frame and examine them. The findings in this ankle are interesting. You note a number of exostoses at the lower end of the tibia as well as at the lower end of the fibula. They are soft and feathery; they make one think a little of a luetic process, but the Wassermann reaction in this patient is quite negative and there is no history of



Fig. 57.—Dorsoplantar roentgenogram of foot.

lues. One could think also of some bony change dependent upon a diseased hypophysis. These bony outgrowths do not look like those we see ordinarily in hypertrophic osteo-arthritis, nor are they in the position usual for chronic infectious arthritis. Here is a very marked spur on the os calcis.

In this roentgenogram of the skull (lateral view) we shall be interested, of course, in examining the sella. You notice that the sella as a whole is large, and it is, I think, disproportionately large for the size of the skull. In spite of the relatively large size of this

sella, it is also relatively shallow. However, its bony outlines are fairly well preserved. This sella, therefore, is somewhat suspect, though I should not have been surprised to have seen much greater changes than those that are visible. On looking at the calvarium one does not see any impressions that suggest increased tension within the skull. I do not believe that there can have been, therefore, any marked hydrocephalus in this case. The sphenoidal sinus is clear. The frontal sinuses are not unusually large.

Have any other examinations been made of this patient?

STUDENT: Dr. W. W. Palmer and Dr. T. B. Fitcher have both examined her; they were both interested in the metabolic and endocrine aspects of the case.

DR. BARKER: This patient presents a good opportunity for the study of a remarkable case of obesity from the endocrine side and from the metabolic side. Certain other examinations will doubtless be made here too. We should, for example, like to have a report from the consulting dentist on the condition of the gums and of the dead teeth; one from the nose and throat department, on account of the history of recurring tonsillitis and quinsy and the three attacks of rheumatic fever; one from the eye department, including the results of an exact delimitation of the visual fields, to be sure that there is no encroachment upon either of the fields for form or color, and one from the gynecological department with regard to possible malignancy of the uterus. For our records, too, it will be desirable to have careful photographs made of the body as a whole—an anterior view, a posterior view, and a lateral view. These will register the exact distribution of the fat at present; and after treatment it will be interesting to compare, later on, the distribution of the fat with what we now see.

Has the patient taken off any weight since entering the hospital?

STUDENT: Yes; she has taken off 29 pounds already.

DR. BARKER: That is a very rapid reduction in weight. I suspect that a part of this loss of weight is represented by loss of water rather than of fat. The patient was suffering from beginning myocardial insufficiency when she entered the hospital, and doubtless the improvement of the function of the heart muscle has helped her to eliminate a certain amount of excess of water.

STUDENT: There is another factor that I should mention. The patient has been ingesting very large quantities of common salt.

Before coming to the hospital she had taken an ordinary salt-cellarful of salt with her food at each meal. Since she entered the hospital the amount of salt has been reduced to a normal intake.

DR. BARKER: That is, certainly, an important point. A reduction of the salt intake would favor the elimination of fluid in this case. What diet has she taken?

STUDENT: In the first place 1000 calories, with marked relative reduction of carbohydrates and fats. During the past two days she has received only 750 calories.

DR. BARKER: In a patient as heavy as this one, with the tissues in a state of pre-edema, a marked reduction in weight usually occurs during the first week or two of treatment, consisting of rest, support of the heart muscle, and restriction of the food and the fluid intake. After this first period, however, it is unsafe, in my opinion, to take fat off with great rapidity. Of course, the patient may be reduced much more rapidly and safely when under close supervision in a hospital or sanitarium than when at home without close supervision. I shall return to the treatment a little later.

The endocrine conditions in this patient are particularly interesting. The case illustrates very well how difficult it is to fit the pictures we see in practice into the rigid frames of theory. We are now all thoroughly familiar with certain classical endocrine syndromes (acromegaly and gigantism; hypophyseal dystrophia adiposa-genitalis; Graves' disease; myxedema; tetany; status thymicolymphaticus; the several suprarenal syndromes, including Addison's disease, pseudohermaphroditism, pubertas præcox and hirsutismus with virilismus; eunuchism and eunuchoidism, etc.). But the endocrine glands are closely linked up into a chain of hormonopoietic glands, and even in the classical endocrine syndromes it is common to have some hints of involvement of glands other than the principal one involved. In the so-called multiglandular syndromes we meet with instances in which two, three, or more of the glands are markedly involved, it being often difficult to feel sure, perhaps, that one is more involved than another.

In the patient that has been before us we saw certain signs that are very suggestive of disturbance of hypophyseal function. The remarkable obesity, with the peculiar distribution of the fat, the relatively small hands and feet with tapering fingers, the spacing of the upper medial incisors, the recurring amenorrhœa, and the

configuration of the sella in the roentgenogram—all suggest a disturbance of the hypophysis. The increased carbohydrate tolerance points in the same direction, indeed, toward a hypohypophysism.

In many cases of hypophyseal obesity there is genital dystrophy and a failure of the secondary sex character to develop; or there may be a faulty development of the external genitals, and in later life a retrogression of certain of the secondary sex characters. In this patient the hirci and the crines are scanty, suggesting a hypogenitalism possibly indirectly of hypophyseal origin. On the other hand, this patient menstruated as early as the twelfth year, and she has grown a heavy beard for the last ten years; these signs, in turn, point to a hypergenitalism, secondary perhaps to disturbance of the function of the cortex of the suprarenal gland. Women that grow beards are apt to be somewhat sthenic and to show a masculine tendency in both the somatic and the psychic spheres. Both the hypophysis and the cortex of the suprarenal have been supposed to influence the secondary sex characters through the intermediation of the gonads, but the conditions that exist must be very complex, and our present view of them is probably altogether too simple to explain the clinical phenomena that we meet with. One might say in this case, for instance, that a hypohypophysism had been responsible for the hypogenitalism that caused the scanty hirci and scanty crines, whereas a hyperinterrenalism (overactivity of the function of the cortex of suprarenal) was responsible for the hypergenitalism that caused the growth of the beard and the rather sthenic type of patient. I think you will see, however, that such an explanation is far from satisfactory, for it is difficult to see how a hypogenitalism and a hypergenitalism could coexist in the same patient, unless perhaps they occurred at different times in the life history of the individual. Even with the aid of the latter hypothesis it is difficult for me to conceive of a satisfactory explanation of the hypotrichosis in some areas and of the hypertrichosis in others. It may be, of course, that a neural regulatory factor as well as a chemical regulatory factor will have to be considered here. But, with this additional intermediate factor assumed, an adequate explanation would not seem easy to secure. I draw your attention to such discrepancies and disharmonies of actual clinical pictures with current theories in order to warn you against making "cock-sure" diagnoses in these cases; I would rather encourage you to record carefully your observa-

tions of facts and to keep those sharply separated from any speculative interpretation of the facts that you may make based upon current theories.

If the thyroid functions are involved in this patient it is on the side of hypothyroidism rather than on the side of hyperthyroidism. There would seem to be no especial evidence available warranting us to implicate the parathyroid glands or the thymus in the production of this syndrome.

To sum up the diagnosis in this patient, as far as our study has gone, we are justified, I believe, in concluding that she has:

1. An obesity, probably partly endogenous, partly exogenous in origin.

2. An endocrinopathy, probably multiglandular, due to disturbances of the functions of the hypophysis, of the cortex of the suprarenal glands, of the gonads, and possibly to a slight degree of the thyroid.

3. A chronic circulatory insufficiency of slight grade, with enlargement of the left heart, slight arterial hypertension; in the main, we deal on the circulatory side with an obesity cardiopathy.

4. A chronic arthritis, including villous arthritis of the knees, and possibly also a slight toxic-infectious arthritis of the ankles. The exostoses on the os calcis and on the lower end of the tibiæ and fibulæ belong here.

5. An oral sepsis.

6. A chronic tonsillitis.

How would you plan the therapy for this patient?

STUDENT: I think she should have a carefully planned reduction cure to be carried out over a long period, preferably in the hospital, under close supervision.

DR. BARKER: Yes, if anything of importance is to be accomplished for this patient, the therapy will have to be comprehensively planned and most carefully conducted. As the hour is nearly up a brief outline only of the therapy can be given.

In the first place, as in every reduction cure, attention should be paid to the function of the myocardium. Despite the obesity I always begin the reduction cure in a very obese person by keeping the patient in bed for a short time, at the beginning making an especial effort to ensure good heart-muscle function. Thus, I often give the patient, at first, a Karell diet; that is, 4 ounces of milk every

two hours in the daytime (or 28 ounces per day) for six days, allowing during this period no other liquid and no other solids. If the patient has great thirst, a little cracked ice is permitted. A small dose of saline is given early each morning, but only enough to give one free movement, not enough to cause violent purgation. A course of digitalis should be given during the period of rest and milk diet. I use, as a rule, the powdered leaf in pill form, giving 2 grains three times a day for the first three or four days, and afterward a smaller dose, three times a day, for a longer period. After six days the patient is placed upon a diet containing 880, or 1000 calories, the diet consisting chiefly of protein (avoiding extractives), but containing also 5 per cent. vegetables, including leafy green vegetables in abundance, a little milk, and some fruit. This ensures an abundance of protein, of vitamins, and of salts, and the patient gets enough carbohydrate to prevent the development of acidosis. The fat necessary for the patient is derived from his own tissues.

As soon as the heart muscle is well compensated the patient begins to perform certain exercises in bed. A very good system of such exercises has been worked out. A patient can be taught to exercise regularly while lying quietly in bed. After the muscles have been toned up in this way the patient is allowed to get up gradually, and then to take gradually increased exercise, until he is walking at least one hour in the forenoon and one hour in the afternoon regularly every day. In a patient like the one before you some weeks might be required in working up to this schedule of exercise.

During the first few weeks several pounds per week may safely be removed from the patient, but after that I think it is better to go more slowly, and to be content with taking off about a pound per week. I have seen patients suffer disaster from too rapid reduction of weight. Great caution and discretion should be used in the rapidity of reduction. That is why the patient should be constantly under supervision during a reduction cure. Of course, in the mild cases of obesity such strict precautions are less necessary, but when a patient has reached the pitiable stage or even the comical stage of obesity one cannot be too careful in the method of procedure.

The following diet list (a modification of Umber's list) gives a "skeleton diet" of 880 calories, and also a list of foods that can be used to supplement the diet at the discretion of the physician:

DIET FOR REDUCING WEIGHT (AFTER UMBER; MODIFIED)

The following "skeleton diet" amounts to about 880 calories, containing 93.7 gm. protein; this may be supplemented according to the needs of the particular patient by an "accessory diet," consisting of given portions of foods, each "accessory portion" corresponding to a food value of 100 calories.

Skeleton Diet (= 880 Calories)

Morning: 1 cup (250 c.c.) coffee or tea, with 1 tablespoonful (15 c.c.) milk; 1 small slice (50 gm.) brown bread, or $\frac{1}{2}$ slice (30 gm.) white bread

Forenoon: 1 small orange or 1 small apple, or similar amount of other fresh fruit.

Noon: 2 slices (250 gm.) roast meat; 2 portions (200 gm.) green vegetables boiled in salt water; a little fruit.

Afternoon: $\frac{1}{2}$ cup (125 c.c.) coffee, with 1 tablespoonful (15 c.c.) milk.

Evening: 1 slice (100 gm.) meat, or a little chicken or fish; 1 portion (100 gm.) green vegetables; $\frac{1}{2}$ slice brown bread (25 gm.); 1 cup tea (if desired). At bedtime a little raw fruit.

Accessory Diet. (Each portion = 100 Calories)

80 gm. roast beef; 200 gm. oysters; 40 gm. white bread, graham bread, or rye bread; 20 gm. zwieback; 12 $\frac{1}{2}$ gm. butter; 20 gm. Swiss cheese; 25 gm. sugar; 100 gm. potatoes; 30 gm. rice, peas, beans, or buckwheat; 20 gm. flour; 200 gm. apples; 150 gm. apple sauce; 500 gm. cranberries; 150 gm. milk; 150 gm. wine; 30 gm. brandy or whisky.

Accessory Diet of Filling Foods of Low Caloric Value

100 gm. cooked asparagus	=	43	calories
"	"	green beans	= 20 "
"	"	green peas	= 108 "
"	"	tomatoes	= 20 "
"	"	spinach	= 52 "
"	"	turnips	= 40 "

You will find other valuable hints regarding diet in von Noorden's monograph on obesity (English translation), and in the excellent article by Dr. W. W. Palmer in Nelson's *Loose Leaf System*. You will be interested, too, in looking over the collective review of reduction cures made in Matthes' article in vol. xiii of the *Ergebnisse der innere Medizin*.

In the Gynecological Clinic here Dr. Kelly has several times removed large masses of fat from the abdomen by excision (lipectomy), and this is now a not uncommon surgical procedure.

I have had no experience with injections of colloidal solutions of palladium (leptynol). Kaufmann and Gorn have reported good results, however, by the use of this method. Injections of from 50 to 100 mg. of the colloidal palladium are made from 1 to 2 cm. deep

into the fat of the abdomen once or twice a week. Further experience of the use of this remedy will be necessary before passing judgment upon it.

With most patients the régime I have outlined above, which consists in (1) maintaining the strength of the heart muscle; (2) a suitable diet; (3) suitable exercise under close medical control, and (4) encouragement, will be found to be sufficient. There are some patients, however, who, despite this régime, still do not lose weight. In such cases it is worth while to try endocrine therapy.

The administration of thyroid gland or of thyroxin (Kendall) will frequently accelerate the metabolism and in nearly all cases will lead to a reduction in weight. Under the closest medical supervision the use of thyroid is, undoubtedly, sometimes advantageous. I cannot warn you, however, too strongly against the indiscriminate use of this remedy; and I never allow a patient to take it except when under close supervision. Much harm has been done by patients who have treated themselves with thyroid extract; and even in the hands of physicians thyroid extract is a remedy that is not devoid of danger.

In hypophyseal obesity the administration of extract of the anterior lobe of the hypophysis, or of full gland, is sometimes of real help. In some cases good effects are obtained in the treatment by the combination of hypophyseal substance with thyroid substance. As far as possible I like to avoid the use of more than one endocrine substance at a time, for I fear always a return to the old polypharmacy or "shot-gun prescription." Sometimes, it is true, endocrine substances of different sources may be advantageously combined, but I fear that there is, just now, a tendency to overdo multiglandular therapy. We know as yet really so little about the glands of internal secretion and the effects of the substances they contain upon the bodily processes that their use is, to a large extent, empirical. We shall find out more quickly about their effects by using them separately and noting carefully the results than by using mixtures, in which state we can only guess the results due to any one of the components.

E. Grafe has recently (1920) urged the adoption of very strict diets before resorting to endocrine therapy. He begins with a reduction to 50 per cent. of the maintenance requirement with a maximum of 1500 c.c. of fluid. He reduces the protein, the fat, and the salt

to small amounts. In some cases he allows only 25 per cent. of the maintenance requirement and only 1000 c.c. of fluid.

In the patient you have seen today at least three dangers must be kept in mind: (1) that of malignant growth of the uterus; (2) that of hypophyseal tumor, and (3) that of myocardial insufficiency, and of increasing arterial hypertension. It would be exceedingly interesting to follow the course in this case, and possibly we may be able to report to you much of interest later on.

A word should be said before closing regarding the joint changes in this patient. Much can be done to relieve the strain upon these joints: (1) by the reduction of weight, and (2) by suitable foot-plates, as the patient has outspoken flat-foot. Static arthropathies are very prone, as I said, to develop in obese patients. The possibility of a toxic-infectious component in the etiology of the joint trouble here should not be lost sight of. Certainly the pyorrhea alveolaris should be treated, and if there are any tooth abscesses the infected teeth should be extracted and their sockets cureted. You will recall, also, the old recurring tonsillitis. Of late she seems to have had but little tonsillar trouble, and I should not be inclined to do anything to the tonsils in this patient unless it becomes absolutely necessary. There is no enlargement of the glands at the angle of the jaw. The tonsils do not look actively inflamed now, though there is old scarring of the tonsils. A tonsil operation is a major operation. This patient would be very unwise to subject herself to a major operation at present, unless it were necessary to save her life. If we deemed treatment of the tonsils essential here, it would probably be wise to use radium or x -rays in order to bring about their atrophy. Of course, if she had a malignant growth in the uterus, her only chance would, in all probability, lie in surgery, with perhaps the use of radium subsequently; but even in that case the myocardium should be strengthened a little bit before hysterectomy was performed. I hope that the return of bleeding from the uterus in this patient does not mean malignancy; but it is important for the patient that we make sure.

Physicians can do much in the way of educating their patients to avoid the development of obesity. Here, especially, prevention is better than cure. If a practitioner sees a member of one of his families growing too stout, he should warn the patient and insist

upon a correction of the daily régime, insisting upon a suitable diet and plenty of exercise in the open air.

The treatment of the milder degrees of obesity and those of moderate grade is very rewarding. Patients in the early stage of obesity can be taught how to reduce their weight without any real hardship, and such education will do much to prolong life and to increase happiness and working hours.

[*Subsequent History of the Case.*—During the two weeks that the patient spent in the hospital she lost, on an average, a pound a day. Her nitrogen intake was continuously greater than the twenty-four-hour output on a constant diet of: Protein, 90 gm.; fat, 40 gm.; carbohydrate, 70 gm.

The patient felt well, was not weak, and had less dyspnea on exertion. The most marked change was in the condition of her hands and arms. The skin of the hands hung loosely and had become wrinkled. The fat of the arms and of the abdomen was much softer. There was no pitting (edema) anywhere.

The patient was discharged at the end of two weeks, and told to continue a 1200 calorie diet, to be increased if she continued to lose weight at the same rapid rate. She was advised to return in about two months.

The patient was readmitted on March 6, 1921. She had kept faithfully to the diet prescribed for her (1200 calories), and had lost in all 96 pounds. She said she felt very well. Her headaches had disappeared and she possessed more "endurance." She returned simply for observation and directions for further treatment. Her weight on readmission was 336½ pounds. Her ideal weight, as already stated, is 143 pounds. While in the hospital she continued to lose weight at the rate of a pound a day! Although there was nothing in the subjective findings nor in the laboratory tests to indicate that she was losing weight too fast, it was thought better to increase the diet to: Protein, 100 gm.; fat, 60 gm., and carbohydrates, 210 gm. From the time the patient was placed on this diet (1780 calories) her weight remained constant. She was discharged at the end of three weeks, with orders to keep in touch with the house officers by correspondence.]

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 XXIX. THE DIAGNOSIS AND TREATMENT OF GOUT

 AN OVERNOURISHED PATIENT OF THIRTY-TWO, SUFFERING FROM
 AN ACUTE ATTACK OF GOUTY ARTHRITIS

We have to present to you today an interesting example of the disturbance of metabolism, known as gout.

This disease has been known since the time of Hippocrates, and has been the subject of much interest and investigation, notwithstanding which our knowledge of it is still incomplete.

William Heberden in his "Commentaries," published in 1782, remarked:

“For though this distemper be older than any medical records and in all ages so common; and besides, according to Sydenham, chiefly attacks men of sense and reflexion, who would be able, as well as willing, to improve every hint that reason or accident might throw in their way, yet we are still greatly in the dark about its causation and effects and the right method in which it should be treated.”

Dr. J. H. Pratt, of Boston, who opens a recent article on gout with this quotation, remarks that although more than a century has passed since it was written, the statement that “we are still greatly in the dark about causation and effects” is as true today as it was then. And Dr. Pratt adds that the investigations of the past three years, made by the aid of a reliable method of analysis for uric acid in the blood, introduced by Folin and Denis, have shown that the writers and teachers of fifty to a hundred years ago knew more about the clinical characteristics of gout than many of those who have studied and written upon the disease in recent years.

The patient, Mrs. Flora E., thirty-two years old, has kindly consented to come from the Private Ward to the amphitheater, in order that the students may profit by the opportunity to observe a typical case of this interesting disease. She entered the hospital on March 15th, that is, ten days ago, complaining of “acute pain in the left foot, with swelling in the region of the left great toe.”

There is not so much in the *anamnesis* to help us as we might have hoped for. Her family history is practically negative. She has, earlier, always had good health, except that she has suffered from sick headaches, and once had an attack of otitis media, in consequence of which the drum of one ear was ruptured. She is subject to colds and is more or less troubled by nasal catarrh. At present she is more or less constipated, but she had no trouble of this kind before her present illness. Menstruation is normal and regular, but she has leukorrhea during the intermediate periods.

The patient has been moderately obese in spite of the fact that she is fond of exercise. At one time she weighed 169 pounds, but her weight on admission was 146 pounds. What is her height?

RESIDENT PHYSICIAN: Five feet, 3 inches.

DR. BARKER: Her normal weight then, is about 126 pounds, so she is still nearly 20 pounds over weight. Is there any history

of potatorium? We must always inquire about the use of alcohol in patients who suffer from this disease.

RESIDENT PHYSICIAN: An occasional cocktail or glass of wine at dinner. There is no history of the excessive use of alcohol.

PATIENT: I have always been fond of everything that is good.

DR. BARKER: In other words, she has been a "good liver"; but not all who live "well" live "wisely."

Four years ago she had her first attack of gout. She awoke one morning with an acute pain in the left foot, with swelling of one great toe joint. Since then she has had a similar attack every summer, each of them lasting for eight to ten days, except the last, which continued for a month. In these attacks the skin over the affected joint is red, shiny, and extremely sensitive.

During the four years since her first attack she has been troubled with heartburn, constipation, and indisposition to exertion. When she reached 169 pounds in weight, she put herself for some time on a reducing diet, consisting chiefly of buttermilk—3 quarts daily—and under this regimen she has lost 23 pounds. But, notwithstanding a restricted diet, she had a very severe attack of pain last summer, which, as I have just said, lasted a month.

Her arthritic attacks are all alike in their features and onset, presenting the typical characteristics of paroxysms of gout. The patient goes to bed feeling quite well and is awakened in the early morning by pain in the left foot, especially in the metatarsophalangeal joint of the great toe, which is swollen and exquisitely tender. The skin over the affected joint is reddened and shiny. The attacks are accompanied by considerable fever; and in one of them the patient was delirious. They vary in duration from a week to a month. Between the attacks the patient has no symptoms whatever connected with the foot, and is able to walk or dance with ease.

Three years ago she noticed hard deposits around two of the finger-joints on her right hand. These have gradually increased in size, but have never been inflamed or painful. One of the deposits, removed about a year ago, proved, on examination, to contain a milky, chalk-like substance. Evidently they are gouty tophi.

On *physical examination*, the interesting features are the increased weight, the heightened blood-pressure, and the condition of the joints. Her musculature is in fair condition. The pupils and eye-grounds are normal. The thyroid isthmus is thickened

and a little nodular. There is a slight tremor of the fingers. The thorax is symmetrical. The heart and lungs are normal. The abdominal walls are relaxed. Liver, spleen, and kidneys are not palpable. The deep reflexes are hyperactive; the abdominal reflexes are sluggish. Babinski's sign is negative. Pelvic examination shows nothing except a few nodules in the vaginal wall that are probably small vaginal cysts.

On the inner side of the left metatarsophalangeal joint there is a reddened area, overlying a definitely thickened deposit in the capsule of the joint. There is slight tenderness on pressure over it, but no limitation of motion of the joint. Some of the phalangeal joints on the right hand are thickened, especially the distal joint of the middle finger. On the palmar surface of the distal joint of the first finger on the right hand is a small, firm, white tophus. There are no tophi in the ears.

The *x-ray findings* indicate a marked hallux valgus of the left great toe, and closer examination of the plates shows two characteristic deposits. Thus, there is a peculiar area upon the lateral surface of the left metatarsophalangeal joint (probably a mass of crystals), and a hemispherical area in the adjacent bone. In the proximal phalanx there is an area that may also be due to crystals deposited in the bone substance. You can get a good idea of the shape that such deposits assume in *x-ray* pictures by examining the *x-ray* plate of these joints.

Dr. H. A. Christian, in a recent article on gout and infectious arthritis, describes three types of gout distinguished by the *x-ray* findings in the joints. In the first variety there are obvious depositions of urates in the bone or in the cartilage, or in both. In the second, instead of these bony deposits, there are chronic arthritic changes with exostoses and associated atrophy of the cartilage, etc., sometimes with deposition of urates in the soft parts adjacent to the bones, but not in them. In the third form there is very little change in the joints, and no obvious deposition of urates in the soft parts about the joints or in the bones or the cartilages. In all three types there may be deposits of urates (tophi) in the ears.

The presence of urate deposits in the bone gives rise, as we have for some time known, to a punched-out appearance of the bone. Lime salts are present in very small quantities, if they are present at all in these areas, so that the *x-ray* penetrates readily; hence,

instead of getting the ordinary shadow of bone or cartilage, we get a punched-out appearance. Dr. Christian is of the opinion, and I am in agreement with him, that in the present state of our knowledge, a positive diagnosis of gout is not justified from the x-ray picture unless it shows a punched-out area, with thickening of the bony material around that area.

Examination of the *blood* in our patient shows a leukocytosis of 10,600; the hemoglobin is 83 per cent. The Wassermann reaction is negative.

The *blood-pressure* on admission was 160/110; this has decreased since the patient has been in the hospital to 150/100. Evidently, there is a beginning arterial hypertension; the systolic pressure is somewhat increased, the diastolic pressure relatively more so. In cases of gout, arterial hypertension generally develops, sooner or later, along with atherosclerotic changes.

The *urine* contains a faint trace of albumin, but no casts at present, and no sugar. Doubtless, a few hyaline casts will appear in it from time to time. The specific gravity is 1011. These are the findings that we should expect in a slight gouty nephropathy with arterial hypertension and beginning atherosclerosis.

From the time that Wollaston, in 1797, first demonstrated that gouty deposits in the joints contain urates, the fact that gout was in some way connected with the formation and elimination of uric acid has been generally accepted. It is now established that it is a disturbance of the metabolism of purins, through which an excess of uric acid accumulates in the blood and in the tissues.

The blood of a normal individual, living on an ordinary diet, generally contains only a little uric acid, but in gouty subjects the amount may be in excess to the extent of 4, or 5, or even as much as 10 mgm. per 100 c.c. of blood. Pratt has recently tested the amount of uric acid in 21 gouty patients, irrespective of diet, and found that the average was 3.7 mgm. per 100 c.c. of blood. Adler and Ragle, in another series of investigations, made upon 15 non-gouty individuals, found the amount of uric acid to be 1.7 mgm. per 100 c.c. of blood. Our patient, on admission, was placed upon the ordinary light hospital diet for a few days, and at the end of that time the amount of uric acid in the blood was found to be 4.12 mgm. per 100 c.c.

This determination of the uric acid content of the blood and

urine on an ordinary ward diet gives us the amount of combined endogenous and exogenous uric acid; but much more important for judging of purin metabolism is to know how to determine the endogenous uric acid content of the blood and urine, that is, the content after the patient has been kept for a few days on a purin-free diet. If a normal person is placed upon a purin-free diet for three days the uric acid content of his blood and that of his urine will soon assume constant values, and after these endogenous uric acid values have been determined, the study of the way his body deals with exogenous purins becomes feasible. The purin-free diet we use while making the test is made up as follows:

Breakfast.—Fruit, 250 gm.; milk, 250 c.c.; one roll.

Dinner.—Pudding (consisting of 100 gm. wheat flour, 150 c.c. milk, 3 eggs, and 50 gm. butter); 200 gm. stewed fruit.

Supper.—Cereal (consisting of 50 gm. meal, 750 c.c. milk, 20 gm. sugar); fruit (raw or stewed), 250 gm.; one roll; butter, 50 gm.

During the day a liter of water should be taken in addition to the fluids of the above diet.

It is only necessary to add a known quantity of purin-containing food to the otherwise purin-free diet, and then to make further determinations of the uric acid content of the blood and urine, to determine the amounts of uric acid in excess of the constant endogenous uric acid values. In the gouty patient the administration of a known amount of a purin-containing food is followed by quite different results from those obtained in normal persons, for the excretion of the exogenous uric acid is, in gout, greatly delayed. Normally, exogenous uric acid is fully excreted within twenty-four to forty-eight hours, but in gouty patients four or five days or even more are required for full excretion. The curve of excretion in a healthy person, after a purin-free diet, followed by a meal of sweetbreads, is represented by Fig. 58, A. The curve of excretion in a patient suffering from the disturbance of metabolism known as gout is shown in Fig. 58, B; you observe that the uric acid has not been excreted as quickly as under normal conditions. In making a diagnosis of gout in patients who have no visible tophi, this sweetbread meal test is one of the most valuable of the means at present at our disposal.

In the patient before us, however, no elaborate quantitative chemical tests of the purin metabolism are necessary to establish the diagnosis of gout, for the patient exhibits definite tophi, on needling

which a little material can be obtained in which, under the microscope, urate crystals are easily recognizable. If you examine this patient's right hand you can see a characteristic gouty tophus—there is only one at present—at the bend of the first finger, between the terminal and middle phalangeal joints. On palpation it is felt as a small, firm nodule. A larger one, situated on the lateral surface of the terminal phalangeal joint of the second finger, has been removed, and on examination it was found to consist of crystals of monosodium urate, which yielded the characteristic murexide reaction.

Tophi may occur over the elbows or the ankles as well as on the fingers, but they are most often present in the ears. It is interesting that in this particular case there are none at all in this latter

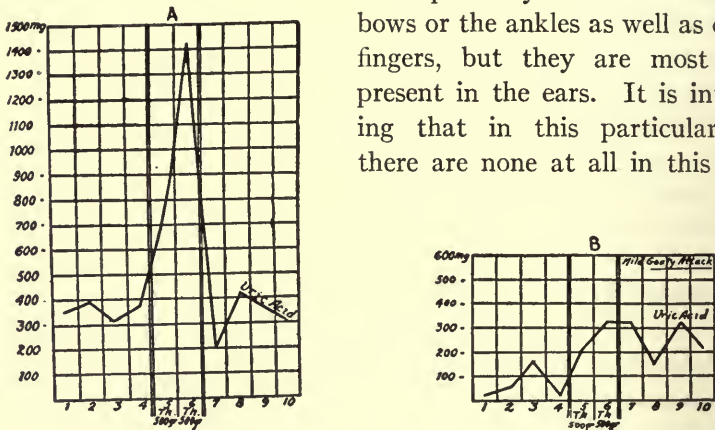


Fig. 58.—A, Uric acid output following ingestion of thymus gland in normal person. B, Uric acid output following ingestion of thymus gland in gouty person. (After F. Ueber, *Lehrb. d. Ernährung u. d. Stoffwechselkrankh.*, published by Urban and Schwarzenberg, Berlin.)

situation. Tophi usually occur about the joints first affected by the gout, but they often appear in some distant part of the body where there has been no inflammation whatever.

This patient, then, has an *arthritis urica*, *gouty tophi*, *obesity*, *beginning arterial hypertension*, and *slight nephropathy*.

There is, strange to say, no history of gout in her family. Her general health is good, though she is still somewhat overweight. She has come here for a careful metabolic study in the hope that we may so instruct her how to live that she may escape further acute attacks like those from which she has suffered during the last four years.

Gout is an exquisitely hereditary disease. In gouty families

even persons who live with great restraint and do not indulge in excesses of any kind may have attacks of gout.

Much of the gout that you hear about, however, is not real gout at all, and the gout so much talked about at certain watering places and mineral springs is most often not gout, but chronic infectious arthritis. I once observed a physician at one of these resorts while he was examining such a case. He lifted the patient's leg carefully, with one hand on the knee and the other on the heel, and then remarked "You are full of uric acid!" Unfortunately, this explanation is usually entirely satisfactory to the patient. In Pratt's article, already cited, he mentions that of all the arthritic patients whom he had known to be sent to a certain health resort (name not given) only one brought back an assurance from the physician in charge that he did not have gout, and this man was the only patient out of the whole number who actually did have the disease, the diagnosis being subsequently assured by the appearance of tophi. Physicians of the kind formerly employed at some of these resorts made it a practice to prescribe a liberal diet, in conformity with the appetite of the patient rather than his metabolic needs. The custom was to give the patient a list of foods, those that were permitted to him being underlined. The patient was grateful when he found underlined foods generally believed to be harmful to the gouty. Those not underlined were foods he would not care to eat under any circumstances! There was formerly a good deal of humbug in the treatment of gout at the Spas, but there has, fortunately, been marked improvement of late years. When you hear, or read, of gout you should keep in mind, then, that many who speak and write of it have not learned to discriminate between true gout and other forms of arthropathy.

You will sometimes hear "poor man's gout," the *arthritis pauperum* of the older writers, spoken of. This name was given in 1800 not to true gout, but to an entirely different disease, namely, *primary progressive polyarthritis*, which is an infectious arthritis and not an arthropathy associated with a disturbance of purin metabolism at all. There is, however, a true "poor man's gout," for gout may occur, when they are predisposed to it, in poor people, and in those in easy circumstances who lead abstemious lives, as well as in wealthy high livers.

Abernethy was accustomed to advise gouty patients who led

idle, luxurious lives to "live on sixpence a day and earn it." It is a good prescription. If people would take sufficient bodily exercise, drink plenty of pure water, and eat sparingly, choosing mainly foods of low purin content, there would be very little gout, even among those who have hereditary claims upon it. Dr. Thomas B. Futcher, one of our best authorities on gout, goes to the heart of the matter when he says that "neither the quantity of the food nor its quality does so much harm as the fact that, as Ewart puts it, 'it is unearned by muscular exertion.'"

There has been much discussion of the question, To what is the condition known as gout really due? As a matter of fact, we are in ignorance as yet as to its cause, despite all the work that has been done upon it.

A great many of the chemical investigations made upon it were worthless, and I regret that much time, energy, and money are still expended upon estimating uric acid in urines when no account is kept of the purin intake. A few years ago it was customary to estimate the uric acid and the urea in almost every specimen of urine sent to a clinical laboratory. We know now that such examinations are worthless unless we are at the same time in possession of reliable data concerning the quantity and quality of the food intake.

Though we are still woefully ignorant of the ultimate cause and nature of gout, we have learned many facts that have a *bearing* upon the causation of the disease and upon its pathological physiology. First, the amount of uric acid in the blood is considerably greater in gouty patients than in normal persons. This is true not only with ordinary diets but also with diets low in purins. Second, an acute attack of gout is preceded by a period in which a little less uric acid than usual is given out, whereas, during the acute attack, the output of uric acid in the urine is increased. After the acute attack is over there is again a period of diminished excretion. Third, exogenous purins are eliminated by the kidneys more slowly and less completely in gouty patients than in normal persons. Fourth, deposits of monosodium sodium urate—the so-called tophi—are frequently present in or about cartilages and connective tissue in gout. Fifth, during an acute attack of gout some of the uratic deposit in the region of the affected joints undergoes solution, and with this solution the pain in the joints becomes manifest, the dissolved urates apparently acting as a violent irritant of the local tissues, including

the nerve endings. Sixth, a gouty attack may, in the predisposed, be precipitated by dietary indiscretions, by excessive alcoholic indulgence, or by physical or mental overstrain. Seventh, the children of a gouty parent are much more likely to suffer from gout than are children of parents who have never suffered from gout.

As regards the treatment of gout we rely mainly upon a dietetic-hygienic régime. We advise regarding the habits of life, imposing regularity, urging the avoidance of fatigue, prohibiting the use of alcohol, arranging for daily exercise in the open air of all the muscles of the body, and prescribing an abundant water intake, and a diet with limited purin content. In addition, we can do much for the acute attacks by using certain drugs, which I shall speak of in a moment, and between attacks we favor the elimination of uric acid by keeping the bowels open, and by giving at intervals substances that have a powerful effect in hastening the elimination of uric acid in the urine. Thus, cincophen or atophan (2-phenyl-chinolin-4-carbonic acid) causes an increased output of uric acid in the urine, especially during the first two days of its administration, soon reducing the uric acid content of the blood.

There is very little evidence that the human body of itself has power to destroy uric acid. We know that in animals uric acid is converted into urea and other substances by means of a uricolytic ferment, the so-called *uricase*, but according to our biochemist, Dr. Walter Jones, who has made especial studies of the metabolism of purins, this ferment is lacking in human beings. Miller and Jones have shown, further, that the several ferments that are responsible for the metabolizing of nucleins and their purin derivatives have the same distribution in the organs of a gouty man at autopsy as in the organs of persons who have been free from gout.

In contracted kidney, uric acid is retained in the blood and a so-called "renal gout" may occur in some patients who suffer from this form of chronic renal disease. Ordinary gout, or so-called "metabolic gout," may also be renal in origin for all that we yet know. Thus, the retention of uric acid in the blood may possibly be due to a renal defect that manifests itself only in this way. The kidney, we know, behaves differently as regards different substances; its eliminative power for sodium chlorid, for example, is independent of its eliminative power for urea and for kreatinin. Our tests of renal function, clinically, are as yet very crude. We must learn to

test the eliminative power separately for each of a whole series of substances.

In gouty patients from the beginning or, at any rate, from a very early period there is an enfeeblement of the capacity of the kidney to eliminate uric acid. It may be that in the gouty, uric acid reaches the kidney in some combination that makes its excretion difficult. According to the current view uric acid is present in the blood-serum as the biurate of soda, *i. e.*, monosodium urate. Gudzent asserts that this salt occurs in the blood-serum in two isomeric forms. At first it exists in the *laktam* form, which is unstable, but soluble in blood-serum to the extent of 18.4 mgm. per 100 c.c. of blood. In course of time it passes into the *laktim* form, which is soluble only to the extent of 8 mgm. per 100 c.c. of blood. This difference in solubility of the two forms of monosodium urate is associated with, perhaps, also different thresholds for its excretion, and if so, may be of importance in helping to explain the deposition of urates in the tissues.

Some investigators believe that uric acid may sometimes exist in the blood in colloidal solution, and they suggest that such a colloidal phase may be that which characterizes gout. But more work must be done upon the blood, both in gout and in normal states, before we can make definite statements.

I have often wondered whether or not the power of the kidney to eliminate uric acid and urates may depend upon some other substance brought to the kidney, or to the renal nerves by the blood from a distance, say a substance of hormonal nature. It is not long since I showed you a patient suffering from diabetes insipidus; a disease in which the kidneys separate a urine of very low specific gravity, and demonstrated to you how pituitrin, given hypodermically, quickly made it possible for the patient's kidneys to excrete a concentrated urine. Perhaps we shall later be able to discover some natural product within the body that increases the power of the kidney to excrete uric acid rapidly. Not unthinkably such a substance might, in its chemical composition, be related to cincophen!

Gout is certainly not a very common disease in this country, though it probably occurs more frequently than is generally supposed. Dr. Osler was convinced that it often went unrecognized in the United States. During the first twenty-four years of the Johns Hopkins Hospital, which terminated on May 15, 1913, only 92 cases

of gout had been recorded out of a total of 36,871 medical admissions. Pratt considers that chronic tophaceous gout is more common in Baltimore than in Boston. This will, perhaps, not surprise you. You know that Baltimore is proud of the table she sets, though Boston, as anyone who has been a guest there will affirm, also "knows how to live!" In confirmation of his view Pratt presents statistics from the Massachusetts General Hospital, where, during the period between 1821 and 1916, or nearly a century, only 41 cases were diagnosed as gout out of 199,518 patients admitted to the medical wards. In the Out-patient Department, between August, 1903 and May, 1916, a diagnosis of gout was made only 42 times out of 298,000 patients admitted to all clinics. He suggests that the increased number of recognized cases during the last decade may, to some extent, be due to the use during the last three years of Folin's method of determining uric acid in the blood. At any rate, the incidence, as you will gather from the figures I have cited, is small.

When we consider the therapy of gout we may conveniently deal with it under two headings, namely, the treatment of acute attacks, and the treatment of the metabolic conditions leading up to them with the object of preventing their recurrence.

The symptom in the acute attack from which the patient cries out for relief is *pain*. An acute attack of gout is characterized by the most atrocious pain. In its typical form the patient is awakened in the early morning by excruciating pain in the affected joints, usually the metatarsophalangeal joint of one great toe or the joints of the tarsus. As described by Sydenham, "the pain insinuates itself with exquisite cruelty among the numerous small bones of the tarsus and metatarsus, in the ligaments of which it is lurking." Only one who has suffered from such an attack, or has seen someone suffer from it, can conceive what the pain is. He who suffers may try to comfort himself with the old saying, attributed to Sydenham, who himself suffered from the gout, "that more wise men than fools have this disease." There is an interesting old Dutch painting in which the patient is depicted as suffering agonies of pain from gout. The face shows every indication of extreme suffering, there is swelling of the metatarsophalangeal joint, and objects, resembling crabs, can be seen clawing at it!

The pain in an acute attack is so severe that it must be controlled in one way or another. In its extreme severity the pain lasts from

twenty-four to forty-eight hours, or sometimes longer. It has been known to continue for more than a week. For the immediate relief of pain codein and aspirin may be used. But in the more severe cases they are not sufficient. In the most severe cases you will have to use morphin, but it is best to avoid this drug if you can get along without it. Applications of lead and opium lotion will sometimes give relief, as will, sometimes, local hydrotherapy. Some patients are more benefited by the application of cold, and others by the application of heat. There is one drug in particular that will sometimes control the pain very quickly, and that is colchicum, but we do not know just how it acts. It may be that it temporarily arrests the solution of uric acid. I know one man, a doctor, who has frequent visits from his old enemy; he gets great relief from a French preparation of colchicum (*Liqueur de Laville*), and always carries it with him. He said to me on one occasion: "If I could not get another bottle I would not part with this one for a thousand dollars." The dose of the wine of colchicum is a teaspoonful every three or four hours until intestinal symptoms make their appearance. There are other good preparations of colchicum. Each gouty patient of experience has his favorite form of this remedy. And I have noticed that those who suffer much and often from gout always come, finally, to colchicum therapy. The relief of pain by drug treatment in acute gout is something for which your patients will be very grateful.

There are certain other measures that should be adopted in treating an acute attack of gout. The limb should be kept at absolute rest, wrapped in cotton batting. The best diet during the first two days of an acute attack is milk and barley-water (Cæsar's diet), after that a more nourishing diet, but one still purin poor, may be allowed.

The extreme irritability of the patient suffering from an acute gouty attack must receive due allowance, for "A fit of gout is also a fit of irritability." The relatives of the patient and the physician must try to suffer this irritability gladly, for the unfortunate gouty patient has a hard enough time without being subjected, in addition, to reproaches because of his peevishness.

After the acute attack of gout is over there is sometimes a good deal of depression, both mental and physical, accompanied by disturbances of digestion. Iritis, neuralgias, or eczemas may make their appearance. Similar symptoms are often suggestive of the approach

of an attack. The resources of the therapist will sometimes be severely taxed in coping with the symptoms of patients suffering from acute attacks of gout or from their complications and sequels.

In the intervals between attacks it is essential that the gouty patient live upon a simple diet, that is to say, one easily digested, palatable, and calculated to keep the body within 5 pounds of its calculated ideal weight. The diet should consist mainly, therefore, of milk, cream, cheese, eggs, bread and butter, cereals, nuts, certain vegetables, and fruits. The only difficulty with such a régime is to keep it from being too monotonous. Meat, chicken, fish, sweet-breads, liver, and kidneys—all of which are rich in purins—add greatly to the pleasure of life, as does an occasional glass of beer or wine, and if you have been accustomed to them and have to do without them for any considerable period of time you miss them. Nevertheless, one can get on without them if he must do so. I remember a story once told by President Eliot: "A good old lady once lay dying, surrounded by her children and grandchildren to the second and third generation, and the clergyman attending her, thinking it an opportune time to bring home a lesson to those present, asked her: 'What, of all things, my dear friend, has given you most pleasure in life?' To this she replied: 'Parson, if I must tell the truth, I think it has been my vittles.'" Undoubtedly, none of us wants to cut off any of his victuals unless he is obliged to do so. So, in advising our gouty patient, we should do our best to give him a diet that will yield satisfaction and enjoyment without doing harm. We must find out just how much purin he can take without bad results. All gouty patients require at least one, or two, or three purin-free days each week, and on those days the purin-free food should be made as tempting as possible. It is a good thing that our present patient can remain in the hospital long enough to permit us to work out a dietary for her, controlled by careful laboratory investigations. The *Apsley Cookery Book* of Mrs. Webster and Mrs. Llewellyn, published in 1915 by P. Blakiston's Son & Co., of Philadelphia, contains a good collection of receipts for purin-free dishes. You will find it helpful in planning gouty dietaries. In addition to a carefully regulated diet and an abundance of pure water, the gouty patient should take daily an adequate amount of exercise in the open air—horseback-riding, walking, playing golf, tennis, Badminton, or other games. He should pay strict attention to his personal hygiene,

bearing in mind that excess of any kind, whether physical or mental, will often precipitate an attack, especially in the spring or autumn. For further details of the treatment of gout I advise you to consult Dr. Fletcher's excellent article on *Gout* in Osler and McCrae's *Modern Medicine*.

[*Subsequent History of the Case.*—The patient was put on a general diet for three days; then on a purin-free diet for three days. Following this she was put on a purin-poor diet, on the first day of which 200 gm. of sweetbread was added. The uric acid of the blood was determined at the end of the period of light diet, and at the end of the period of purin-free diet. The result of the first test was 4.12 mg. per 100 c.c. The result of the second test was 3.06 mg. per 100 c.c. The uric-acid secretion of urine was determined during the purin-free test diet and for eight days following it (see chart).

REPORT OF EXAMINATION OF URINE

Date.	Amount of urine, c.c.	Uric acid per 100 c.c., mg.	Total amount of uric acid, mg.	
Purin-free diet {	March. 18-19	1940	4.875	945.75
	19-20	1740	4.125	721.75
	20-21	1760	4.125	726
Ordinary ward diet {	21-22	1800	4.5	810
	22-23	1220	31.5	3343
	23-24	1700	31.125	5287
	24-25	1550	33.75	5223
	25-26	2010	20.625	4140
	26-27	1900	15.375	2907
	27-28	1420	19.875	2811.6
28-29	1310	21.75	2842.7	

The patient was discharged on March 30th as "improved," with instructions as to diet and control of weight.]

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DISEASES OF THE GLANDS OF INTERNAL SECRETION

XXX. FATAL AIR-EMBOLISM DURING OPERATION FOR GRAVES' DISEASE

A COLORED WOMAN OF THIRTY-SIX, WITH SIGNS OF GRAVES' DISEASE (STRUMA VASCULOSA, TACHYCARDIA, EXOPHTHALMOS, TREMOR, ACCELERATED METABOLISM), ENLARGED THYMUS, ARTERIAL HYPERTENSION AND FOCAL INFECTIONS; OPERATION; AIR-EMBOLISM; DEATH; AUTOPSY.

IDEAS concerning the thyreopathies and especially concerning their treatment are in such a state of flux that it would seem desirable, at least once each session, to present one or more cases of thyroid disease to the class in order that current opinions may be discussed and contrasted with those of preceding years.

The patient to be brought before you today illustrates exceedingly well the majority of the phenomena that we are accustomed to attribute to overactivity of the thyroid gland. From the standpoint of etiology, too, the case is an interesting one, since several factors that predispose to hyperthyroidism may have been operative in this patient. Moreover, the problem of therapy in this particular case is well worth discussing, for there might easily be differences of opinion regarding the best measures to adopt or, at any rate, regarding the serial sequence in which several different therapeutic measures may best be employed. I shall ask the clinical clerk, Mr. F., to give you an epitome of the anamnesis in this case.

STUDENT: The patient, Louisa P., is a colored woman, thirty-six years of age, a housewife. She was admitted to Ward O of this hospital (service of Professor Thayer) on November 18, 1920, complaining of "swelling of the neck, nervousness, nausea, and bulging of the eyes."

DR. BARKER: May I interrupt you to ask you to speak just a little louder? One of the advantages of these clinics is to give the senior students an opportunity to become accustomed to speak before medical audiences. If you will permit me, I will give you one hint that I have found useful, and that is to look at the most

distant person in the room and to address what you have to say to him. If you make sure that he hears, you can be confident that those who are nearer can hear also.

STUDENT: The *family history* of the patient seems to have but little bearing upon the case. Two of her brothers died in infancy, and her father suffered from palpitation of the heart.

DR. BARKER: The latter point may be of some interest. The father's palpitation may have been a sign of a thyreopathy in him. Certainly, thyroid disease tends to run in families. We are forced ever more to the conclusion that the several classical endocrine syndromes develop in persons who exhibit anomalies of constitution. In other words, the endocrinopathies are, as a rule, primarily genotypic in origin.

STUDENT: On inquiring into the patient's *past history*, we have found that she has suffered from various infections, including whooping-cough, measles, chickenpox, and one attack of pneumonia some years ago. She states that she has also had rheumatism, off and on, for some nine years, and that she still suffers from aching pains in various joints. She has repeatedly suffered from sore throats (tonsillitis) and has had frequent attacks of toothache. Several of her teeth have been extracted. She thinks her eyes have always been rather prominent. She has had a little cough from time to time and has frequently suffered from indigestion, but the latter seems to have followed, as a rule, indiscretions in eating, especially taking large meals late at night. Though only thirty-six years old, she has been pregnant nine times. Four of her children were stillborn and one child died in infancy of rickets.

No history of venereal infection in the patient or her husband could be elicited.

As to her *present illness*, the patient states that it began last May, some six months ago, when she noticed that her neck was growing larger. At first there were no other symptoms, and her only concern was the unsightliness of the swelling in the neck. This enlargement of the neck progressed steadily for several months, reaching a maximum about three months ago, since when she has noticed no further enlargement. She states that there has been no tenderness in the swelling at any time.

On inquiry, the patient admitted that she had been nervous since her marriage, and that she had noticed, at times, some palpita-

tion of the heart. A few weeks after the swelling in the neck appeared her nervousness increased. She became irritable, suffered from marked palpitation of the heart, and from shortness of breath on exertion. She states, also, that she became easily frightened without adequate cause. Recently she has been losing weight rapidly, despite the fact that she has a good appetite and eats abundantly. Her sleep has not been disturbed. Her eyes have gradually grown more prominent, and of late she has found that reading has been interfered with, as her eyes soon become painful on attempting to read.

DR. BARKER: She entered the hospital five days ago. What was her physical condition on admission?

STUDENT: The first *physical examination* was made by the house officer, Dr. Reinoff. The patient was markedly undernourished. She was nervous and fidgety, but suffered no actual pain nor any marked local discomfort. Her temperature was normal. The pulse-rate was 140 and the respiration rate 27 to the minute. There was some hyperhidrosis, the sweating of the palms of the hands and of the forehead being particularly marked. The patient seemed weak and looked rather toxic. The bony framework was gracile and the musculature only moderately well developed. There was very little subcutaneous fat.

DR. BARKER: What was her height and weight?

STUDENT: She was 5 feet tall, and, on admission, weighed $86\frac{1}{2}$ pounds stripped.

DR. BARKER: What is the calculated ideal weight for an adult whose height is 5 feet?

STUDENT: One hundred and ten pounds.

DR. BARKER: Yes; according to Dr. Clyde Guthrie's convenient formula, we allow 110 pounds as the calculated ideal weight for 5 feet and add $5\frac{1}{2}$ pounds for each additional inch. Adopting this standard, the patient was $23\frac{1}{2}$ pounds below her calculated ideal weight on admission. I understand that she has lost weight since she came into the hospital.

STUDENT: Yes; she lost $4\frac{1}{4}$ pounds during the first three days, in spite of the fact that she ate well.

DR. BARKER: She is now between 27 and 28 pounds below her calculated ideal weight, and is evidently emaciating rapidly. That is a very important symptom in this disease. To what does it point?

STUDENT: To an acceleration of her metabolism.

DR. BARKER: Yes, undoubtedly. We shall return to that point later. Will you please continue with the description of her physical status on admission?

STUDENT: There was marked exophthalmos, and she could close the eyelids only with difficulty. There was a marked "stare" on fixation of the eyes. On following the examiner's finger downward with her eyes the upper lids lagged. Convergence, too, was defec-



Fig. 59.—Patient with outspoken Graves' syndrome (anterior view).

tive and it was poorly maintained. Winking was infrequent. There was tremor of the closed lids. On extending the hands there was considerable fine tremor of the fingers.

She had a marked pyorrhea alveolaris, considerable dental caries, and some dead teeth, which are to be investigated. The right tonsil was enlarged and looked infected.

In the neck there was a large goiter (Figs. 59 and 60), the swelling involving the whole thyroid gland, though the enlargement

was maximal in the isthmus. Each lateral lobe, however, was enlarged to the size of a hen's egg. The surface of the goiter was smooth or only slightly granular. On palpation, a definite thrill could be felt at each systole, and on auscultation a systolic bruit was audible over the whole gland. The goiter extended well into the jugulum, but did not appear to descend behind the sternum. There was no palpable enlargement of the glands in the neck, nor was there any general glandular enlargement.



Fig. 60.—Patient with outspoken Graves' syndrome (lateral view).

The thorax was flat and narrow and the epigastric angle measured less than 90 degrees. Aside from slight impairment of the percussion note at both apices, a little more marked on the left than on the right, the examination of the lungs was negative.

The apex of the heart was palpable. There was vigorous pulsation in the fifth interspace, just about in the mammillary line, the heart being enlarged a little to the left. A systolic murmur was audible at the apex and also at the base; it was maximal in the pul-

monic area. The pulse was a little collapsing on palpation, and a capillary pulse could be seen, but there was no diastolic murmur audible over the heart. The peripheral arteries were not demonstrably thickened. Definite retromanubrial dulness could be made out, and this dulness extended a little to the left of the sternum as well; this dulness was thought to indicate the presence of an enlarged thymus gland.

The abdomen was scaphoid, but the abdominal walls were not tense. The lower pole of the right kidney was easily palpable. The abdominal examination was otherwise negative.

The skin was everywhere thin, moist, and delicate in texture. No objective changes were made out in the aching joints. There was a little scoliosis of the thoracic spine. The superficial and deep reflexes were all normal, and there was no disturbance of motility or sensation. Pelvic examination was negative except for retro-position of the uterus.

DR. BARKER: What laboratory examinations have been made in this patient?

STUDENT: The blood, the urine, and the basal metabolism have been examined.

The *blood examination* was as follows: R. B. C., 5,480,000; W. B. C., 6400; hemoglobin, 75 per cent. The differential count of the white corpuscles showed polymorphonuclear neutrophils, 50 per cent.; small mononuclears, 45 per cent., and large mononuclears and transitionals, 5 per cent.

DR. BARKER: Evidently, there is a slight hemoglobin-anemia present, though there is no diminution in the number of red cells. There is no leukocytosis, but there is a relative lymphocytosis. Do you think that this is of any significance?

STUDENT: I do not know.

DR. BARKER: It is a rather important sign. Certainly, the majority of patients presenting Graves' syndrome have a relative lymphocytosis. In this case the small mononuclear elements are not only relatively increased but also somewhat increased absolutely. The polymorphonuclear eosinophils are absolutely diminished. This means that the lymphadenoleukopoiesis is somewhat increased in this patient and that the myeloid leukopoiesis is decreased, or, if a normal number of neutrophils have been produced, more than a normal number have been destroyed. Many of these patients that

suffer from Graves' disease have also a tendency to status thymico-lymphaticus. As you know, many of the Basedow patients are "thymus carriers." This patient has marked retromanubrial and some paramanubrial dulness; it is probable that this dulness is due to an enlarged thymus.

Has a roentgenogram of the chest been made yet?

STUDENT: No; not yet.

DR. BARKER: One will doubtless be made soon; it may show a shadow due to an enlargement of the thymus.

Has a Wassermann test been made?

STUDENT: Yes; the Wassermann reaction in the blood-serum is negative.

DR. BARKER: Will you report on the urine?

STUDENT: The color of the *urine* was normal; reaction, acid; specific gravity, 1010. A little albumin was present and there were some hyaline and granular casts. Tests for sugar were negative.

DR. BARKER: Evidently a slight nephropathy exists. It would be interesting to know to what it is due. One thinks at once of the oral sepsis, of the chronic tonsillitis, and of the thyreo-intoxication as possible causes of this nephropathy.

Is the blood-pressure increased?

STUDENT: The *blood-pressure* on admission was 160 systolic, 90 diastolic. Since admission, however, the blood-pressure has gradually fallen, until now it is 120 systolic and 70 diastolic.

DR. BARKER: Evidently, there is a slight tendency to arterial hypertension in this patient; it is a very common finding in Graves' disease. The fact that the pressure has fallen, however, to normal would indicate that, as yet, we are dealing only with a functional hypertonia rather than with an organic change in the walls of the arterioles (arteriolar sclerosis). It is always fortunate to get a patient before the arterial hypertension becomes fixed; that is to say, before organic sclerosis of the arterioles in the precapillary areas sets in. I wish we knew the mechanism of this presclerotic, functional, arteriolar hypertonus. If we can get the clue to it we shall have gone far toward understanding the pathogenesis of chronic arterial hypertension.

You say that the basal metabolism has been tested in this patient. Will you give us the results?

STUDENT: The basal metabolism was tested by Dr. John T.

King, Jr. He reports as follows: "Height of patient, 151 cm.; weight, 38.6 kg.; area of body surface, as calculated, 1.29 square meters. The CO₂ eliminated per square meter per hour was 22.02 grams. This is 85.7 per cent. above the average for the patient's age and sex. It indicates a high metabolic rate and a severe hyperthyroidism."

DR. BARKER: This report on the basal metabolism is very interesting, and is quite in accord with the clinical phenomena presented by the patient, namely, the marked tachycardia and the rapid loss of weight, despite an abundant food intake. Many patients suffering from Graves' disease eat ravenously, ingesting large quantities of food, and still lose weight. The degree of tachycardia when the patient is at rest is a very good measure also of the metabolic rate. One must remember, however, that the pulse in these patients is very labile, and nervous excitement might, temporarily, cause an acceleration of the pulse, which would, perhaps, mislead one if he were to try to deduce the metabolic rate from it. If, however, the patient lie quietly in bed, and be protected from influences that excite the nervous system, one can judge fairly well of the rapidity of the metabolic processes by an examination of the charted pulse-rate.

Workers in medical clinics everywhere are now much interested in studies of accelerated metabolism in Graves' disease and in its relation to the tachycardia. I shall pass around an article by Irene Sandiford, published in *Endocrinology*; it deals with the basal metabolic rate in exophthalmic goiter and gives a brief description of the technic used in the Mayo Clinic. Dr. Boothby and Dr. Sandiford, working with Dr. Plummer in the Mayo Clinic, have made a large number of metabolic-rate determinations upon thyroid patients. It seems clear that studies of the basal metabolic rate are of real value in connection with thyroid disorders, since the metabolic rate appears to be an accurate index of the degree of functional activity of the thyroid gland. Dr. Sandiford states that in 182 cases of exophthalmic goiter before any treatment was instituted the average basal metabolic rate was 51 per cent. above normal, and the average pulse-rate 115. You will find in this article, also, data concerning the effects of rest and of strumectomy upon the basal metabolic rate and upon the tachycardia. This paper refers to the cases studied in 1917 only. I visited the Mayo Clinic last October again myself, and was much

impressed with the careful basal metabolic studies now being carried on there under the direction of Dr. Boothby. A large number of determinations are being made at that clinic in a very accurate way, and we shall all look forward with interest to the results that will from time to time be published. Three or more of our clinical laboratories here in Baltimore are now making studies also of basal metabolic rates, and it will be interesting to compare the results obtained here with those emanating from the Mayo Clinic, the clinics in Boston, and the other clinics in this country. Metabolic rate determinations are undoubtedly useful not only for establishing diagnoses but also for measuring more accurately than has been possible hitherto the results of therapy of different kinds. I think it quite possible that, after metabolic rates in thyroid diseases have been followed in this accurate way for some time, we shall be able to judge sufficiently well for ordinary diagnosis, and ordinary therapy, without determinations of the metabolic rate; but for the present it is very comforting to be able to control our clinical studies by accurate metabolic rate determinations.

The studies thus far made in the patient before you permit us to make certain definite statements regarding the diagnosis. The patient is suffering from a typical Graves' syndrome, as manifested by the struma vasculosa, the tachycardia, the protrusio bulborum, and other eye signs, the fine tremor of the fingers, the emaciation and accelerated metabolism, the functional nervous symptoms, the lymphocytosis, and the tendency to arterial hypertension. In addition, she has an enlarged thymus, a chronic tonsillitis, an oral sepsis, a slight secondary anemia, a slight nephropathy, a chronic infectious arthritis, and a retroposition of the uterus.

Has the patient improved since she entered the hospital?

STUDENT: She is, perhaps, a little less nervous since she has been at rest in bed. The blood-pressure is lower, but she is rapidly losing weight in spite of rest in bed and an abundant diet.

DR. BARKER: If you were responsible for the treatment of this patient, what measures would you adopt?

STUDENT: I think I should have the patient operated upon.

DR. BARKER: I think that a great many physicians and surgeons would agree with you; but would you operate at once? And, if so, what would you operate upon first, the thyroid, the tonsils, the teeth, the thymus, the uterus, or what?

STUDENT: I had operation upon the thyroid in mind. I think I would have a lobectomy done.

DR. BARKER: Doubtless many would agree with you in this recommendation. The treatment of this syndrome is, however, much under discussion. Recently a certain reaction against surgical therapy for Graves' disease has been noticeable in the literature as well as in several of our leading clinics. There are still many who maintain that every case of Graves' disease should be operated upon, but there is also a group of physicians who maintain that Graves' disease is a non-surgical process, and that the patient should never be operated upon for it. When you find two large groups of opposite opinion, the truth usually lies somewhere in between the two extreme positions. Undoubtedly, a considerable number of patients suffering from Graves' disease recover under medical treatment. Undoubtedly, a large number seem to be markedly benefited by strumectomy. The disease is exceedingly common, and large bodies of statistics are gradually becoming available for study and comparison. Unfortunately, these statistics too often fail to give us information regarding the ultimate outcome of the cases. It will be very interesting to know, later on, what the permanent results are in the two groups of cases—those that have been treated medically only, and those that have been treated surgically only. As a matter of fact, there probably are no cases that are treated surgically only, for the surgical cases have prolonged medical treatment after the operation, and some of them have had considerable medical treatment for a long period of time before operation. I am of the opinion that patients who suffer from Graves' disease, and who apparently recover, either after medical or surgical treatment, are rarely entirely well. Most of them continue to suffer, more or less, from thyreopathic disturbances. They rarely attain to vigorous and robust health. To a certain extent they remain permanently invalided in the sense that they are less equal to the rough and tumble, the hurly-burly of life than are normal persons. All "thyreopaths," even so-called "cured" cases, require some protection and a very carefully ordered life if they are to remain fairly well.

You may be interested in looking over this article by Dr. Bram, of the Jefferson Medical College, of Philadelphia, entitled, *The Rational Therapeutics of Exophthalmic Goiter*. He has brought together as many arguments as he could find against the surgical

therapy of exophthalmic goiter, as well as those in favor of careful non-surgical management, which he believes is capable of completely and permanently curing the majority of cases of hyperthyroidism within from six months to two years. On the other hand, if you will consult most surgical treatises, you will find that the surgeons complain bitterly that medical men treat their cases of Graves' disease too long before turning them over to surgeons for operation. These surgeons maintain that early operation cures the patient and prevents the permanent invalidism that too often develops in patients in whom thyreo-intoxication is permitted to continue for a long time before strumectomy is done.

In view of this clash of opinion, you will readily understand that the general practitioner may often be in doubt as to the best course to pursue in a given case of Graves' disease. As a matter of fact, the whole medical profession is, at present, feeling its way rather cautiously in the hope of ultimately arriving at more definite criteria that may serve as guides in the choice of therapy in Graves' disease.

During the past thirty years I have, with interest, watched the pendulum swing to and fro between surgical and non-surgical therapy for exophthalmic goiter, and I have, personally, observed many cases treated by each of these methods. As the result of my own observations I have arrived at certain conclusions:

1. Some patients do fully as well under medical measures as under surgical treatment.
2. Some patients do not do sufficiently well under medical measures, and are much benefited by surgical treatment.
3. Medical measures should always be given a fair trial before surgery is resorted to. This is particularly true, in my opinion, of patients under thirty years of age. It is only occasionally that a young person, under thirty, requires surgical treatment for Graves' disease.
4. The medical measures that seem to have been most beneficial are the following: (a) Mental and physical rest with an abundant mixed diet; (b) the removal of foci of infection, since the overactivity of the thyroid gland seems sometimes to be a response to infection or intoxication [oral sepsis, tonsillitis, paranasal sinusitis, cholecystitis, appendicitis, pelvic inflammatory disease, chronic constipation, etc.]; (c) ice-bags over the thyroid gland and over the heart; (d) slowing of the rate of metabolism by pharmacotherapeutic measures [quinin

hydrobromid, ergotin, arsenic]; (e) psychotherapeutic influences; (f) lessening of thyroid activity by the applications of the x-ray, or of radium, to the thyroid gland, to the thymus, or to both.

When, however, the response to these medical measures, or to the surgical removal of the foci of infection and intoxication, is not sufficient, surgical operation upon the thyroid gland should not be too long postponed. It is, in my opinion, not fair to the patient, nor to the surgeon, to reject surgical interference for so long a period as to permit irreparable damage to be done to the heart muscle, to the nervous system, or to the gonads.

Many patients who respond very favorably to the medical measures outlined above do not, however, make a full recovery, and in these cases resection of the thyroid gland often helps to further the cure.

Surgical treatment will often give quicker relief than medical treatment, even when the ultimate results obtainable by medical treatment may be just as good as those obtainable by surgical treatment. This quicker favorable response from surgery must be kept in mind when the social and financial status of the patient would make a prolonged medical therapy impracticable on account of necessary absence from occupation and of financial cost.

When surgical therapy has been decided upon, careful consideration by the surgeon as to the mode of operation to be employed is essential. In the first place, most surgeons refuse to operate upon a patient who is in a very acute stage of hyperthyroidism, or who is in such a nervous state that he feels sure the outcome of the operation will be fatal. In the severer cases the surgeon may begin by ligation of an artery, and follow this by a ligation of a second artery. A little later on he may do a lobectomy or a resection of the thyroid gland. What special precautions must be taken at such operations?

STUDENT: The surgeon must avoid direct injury to or cutting off the blood-supply to the parathyroid glands.

DR. BARKER: Yes; it is exceedingly important to observe such precautions if we are to avoid the production of a postoperative tetany. Tetania strumipriva is practically always due to injury to the parathyroids at the operation, either by rough handling or by cutting off some of the blood-supply. Of course, tetany can be produced in other ways in these patients; for example, it has followed

the injection, as a therapeutic measure, of sodium bicarbonate into the blood.

After surgical operations on the thyroid have been performed the patients should be returned to the internist or to the general practitioner for careful supervision and for a continuation of medical treatment, unless the surgeons themselves are prepared to conduct such treatment. You are doubtless familiar with the rules formulated by Ochsner, of Chicago, to be followed by his patients after strumectomy. They include a number of points. Let me read them to you. They are as follows:

"1. You should avoid all excitement or irritation, like attending receptions, shopping, church work, or politics.

"2. You should get an abundance of rest by going to bed early and taking a nap after luncheon.

"3. You should have an abundance of fresh air at night; consequently you should sleep with wide-open windows or on a sleeping-porch.

"4. You should eat and drink nothing that irritates the nervous system, like tea, coffee, or alcohol. Of course, you should not use tobacco in any way.

"5. You should eat very little meat. If you are very fond of meat, take a little beef, mutton, or breast of chicken, or fresh fish, once or twice a week, or, at most, three times a week.

"6. You should drink a great deal of milk or eat things that are prepared with milk, such as milk soup, milk toast, etc.; cream and buttermilk are especially good for you.

"7. You should avoid beef soup, or beef tea, or any kind of meat broths.

"8. You should eat an abundance of cooked fruits and cooked vegetables, or very ripe raw fruits, or drink fruit-juices prepared out of ripe fruits.

"9. You may eat eggs, bread, butter, toast, rice, and cereals.

"10. You should drink an abundance of good drinking-water, or if this is not available, you should boil your drinking-water for twenty minutes or drink distilled water."

Clearly, in the treatment of these cases of Graves' disease, there should be the closest co-operation between surgeons and internists. Surgeons should perhaps be somewhat more patient than they are in the trial of medical measures before resorting to operation; medical

men should, perhaps, be less dilatory than they are in turning patients who do not respond to medical measures over to the surgeons for operation; and patients who have apparently recovered from Graves' disease should report at regular intervals to their medical supervisors for a "check-up."

As I said at the beginning of the clinic, ideas are in a state of flux, especially regarding the therapy of Graves' disease. I have given you my impression of the present status of the subject; but a year from now our knowledge may have advanced to a point where essential modifications of these measures may seem advisable. There is no field in medicine that is being more actively tilled at present than that of the endocrinopathies, and especially that of the thyreopathies. From all the work that is going on in the great clinics of this and other countries we have reason to anticipate that rapid advancement in our knowledge of diseases of the thyroid will result.

You will want to know what happens in the near future to this patient that you have seen this morning. I shall hope to report to you later the results of our further studies and of the therapy instituted.

[*Subsequent History of the Case.*—The patient was transferred to the surgical service about a week later. Operation was performed on December 3d by Dr. J. M. T. Finney. The major part of both thyroid lobes was removed. As the wound was being closed, bleeding just above the suprasternal notch was observed. The bleeding area was caught in a clamp, but on elevation of the clamp, a second spurt of dark blood took place, instantly followed by a sound of in-rushing air. This was succeeded by two or three respiratory excursions during which it seemed as though air were being sucked in and out of the suprasternal notch. Artificial respiration was employed, but death took place immediately.

The rush of air back and forth, accompanied by the bubbling of black blood, might indicate the presence of pneumothorax. But the rapid exitus seemed to exclude this hypothesis. In the opinion of one of the surgeons it was most probable that an air-embolism had occurred, the air having entered through a vein in the neck.

Report on Tissue Removed at Operation (Dr. E. Hanrahan).—*Gross Examination* (Pathological Report No. 27,196): "Right and left lobes of thyroid gland. Specimen rather larger than normal size of thyroid gland. On section, it was homogeneous in appearance;

there were no adenomata. It was of quite noticeable increase in consistency, and of a deep, rather purple-red color. No colloid seen; quite friable."

Microscopic Examination.—"Typical hypertrophy of exophthalmic goiter. Diminished colloid; collapsed hyperplastic lining epithelium. There is lymphoid and small round-celled infiltration. *Diagnosis:* Thyroid gland hypertrophy (exophthalmic goiter)."

Abstract of Autopsy Report (No. 6418; Dr. Athens).—"Exophthalmic goiter. Recent surgical operation for removal of thyroid; exophthalmos; hyperplasia of the thymus; air in the ventricle and in the coronary veins. Bilateral fibrous pleural adhesions. Hyperplasia (slight) of mesenteric and retroperitoneal lymph-glands. Old adhesions around the left fallopian tube and ovary.]"

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XXXI. ACROMEGALY WITH EUNUCHOIDISM AND STATUS LYMPHATICUS

A RUSSIAN OF THIRTY, WITH A HISTORY OF ACROMEGALIC ENLARGEMENT OF THE BONES, EXTENDING OVER NINE YEARS, ACCOMPANIED BY HEADACHES, PAINS IN THE LIMBS, AND VISUAL DISTURBANCES, AND ASSOCIATED WITH HYPOPLASIA OF THE TESTICLES, HYPOTRICHOSIS, TYPUS FEMININUS, HYPERPLASIA OF THE PHARYNGEAL AND PALATINE TONSILS, AND RELATIVE LYMPHOCYTOSIS.

For the opportunity of showing you today an interesting example of the results of marked disturbance of function in one of the endocrine glands I am indebted to the surgical service. The clinical clerk, Mr. J. A. Ward, will give you an epitome of the history of the case.

STUDENT: The patient, Isaac H., a groceryman, thirty years old, entered the hospital three days ago complaining of "stomach trouble and cough." He also said that his "bones were too large." Neither his family history nor his past history, up to maturity, contain anything bearing upon his present condition. There is no record of similar abnormality of the skeleton in his family.

He is a Russian by birth, and came to the United States eleven years ago, when he was nineteen years old. He says that at that time he was a tall, strong, healthy boy. His habits have been good, except for the excessive use of tobacco.

After he had been in this country about two years he noticed that the bones in the back of his chest on the right side were growing larger and bowing out. About the same time his face, as well as his hands and his feet, began to increase in size. The change came on very slowly—to use his own words, "Just a little bit at a time."

He has suffered more or less for several years from headache, which has become worse during the last few weeks, though it has never been very severe. It is not localized in any particular area.

A few years ago he became aware that he was losing the sight of his right eye, so that, gradually, he became almost completely blind on that side. For about the same length of time, he thinks, he has been growing deaf in his right ear; his hearing is now slightly affected in the left ear also.

His teeth have been giving him trouble for some time. He has lost a good many of them, and at present has several carious roots and considerable pyorrhea. He says he has never had tonsillitis or sore throat of any kind, though there is some evidence of chronic pharyngitis. For the last two years he has been short of breath on exertion. He has had an inguinal hernia for about six years. There is no history of Neisser infection and the patient denies lues. The Wassermann test is negative. Six years ago he married; and he has one child, living and well. His wife has never had any miscarriages.

DR. BARKER: Has there been any disturbance of libido sexualis or of potentia?

STUDENT: No.

DR. BARKER: That is an interesting point. In cases of this kind some diminution of either, or of both, is usually reported.

The locomotor system of the patient is, I understand, negative, except for the enlargement of the bones, and for some soreness and pain in the limbs. Has the pain been in the bones or in the joints, or in both?

STUDENT: Mostly, he says, in the bones.

DR. BARKER: There are no skin lesions. The patient's habits are regular. He drinks coffee and alcohol in moderation and smokes rather to excess. His maximum weight is 185 pounds, and he says he has not lost weight recently. How tall is he?

STUDENT: Five feet, 5 inches.

DR. BARKER: The ideal weight for that height is about 138 pounds; he is, therefore, apparently about 45 pounds above ideal weight.

STUDENT: He says that when he was twenty-one, before the present trouble began, he was 6 feet tall.

If he were 6 feet tall when he was twenty-one, how does he come to be 5 feet 5 inches now that he is thirty?

STUDENT: He has developed a kyphoscoliosis.

DR. BARKER: In that case we should calculate his ideal weight on the basis of 6 feet rather than of 5 feet 5 inches. For a height

of 6 feet he is only about 10 pounds over weight. Please continue your summary of the history.

STUDENT: The patient is positive that there was nothing unusual about his figure when he was twenty-one, and at that time he considered himself a normal man. The kyphoscoliosis began at about the same time that he noticed the enlargement of the bones. During the last nine years his health, as a whole, has gradually deteriorated, but there were no acute symptoms until about two weeks ago, when he began to have attacks of nausea and vomiting, with cough, accompanied by expectoration of thick, tenacious mucus. He says also that he has had a chill, and he thinks, some fever every day during the past two weeks with excessive sweating at night. There has evidently been an infection of some kind, probably of the respiratory system. His temperature and pulse-rate are now normal.

DR. BARKER: Now let us examine him for ourselves. You notice that his face is long and rather heavy in type (Fig. 61). The record made in the ward shows that the face measures 25 cm. in length from the hair line to the tip of the chin. It is somewhat hexagonal in form, and the lower jaw is markedly enlarged. Indeed, this enlargement of the mandible of the patient is a very striking feature (Fig. 62). In this class of cases the head, as a whole, is enlarged, though, on close examination, the facial skull is seen to be much more involved than the cranial skull, the result being the peculiar distortion of the countenance, known as the acromegalic face. When you look at this patient you see at once the unusually great distance from the forehead to the chin. But if we cover up the lower part of the face, as I am doing now, so that only the forehead and eyes are visible, the head does not look especially abnormal. The forehead of the acromegalic is small in comparison with the large size of the face. In other words, the cranial skull is but relatively little affected. There are, it is true, some abnormalities in the cranial skull, as we shall see presently, but they are comparatively inconspicuous. It is in the facial skull that we notice the very extensive changes. In some cases of this disease the changes in the facial skull are even more marked than they are in the patient before you, though the changes here are pronounced enough (Figs. 61 and 62).

When we come to examine the eyes we must bear in mind that the patient has been blind in the right eye for nearly two years. Did that eye react to light when it was tested in the ward?

STUDENT: Yes; but the reaction was very sluggish.

DR. BARKER: I get no reaction at all to light in the right eye at this moment. (To patient): Can you see anything at all when I hold this electric torch before your right eye?

PATIENT: I see a "shine."



Fig. 61.—Anterior view of head of patient with acromegaly. Note the hexagonal face, the enlargement of the mandible and nose, the thick succulent lips, and the up-turned chin.

DR. BARKER: Then there is still slight perception of light in the right eye. When we come to examine the left eye, we find that the left pupil contracts very well on stimulation of the eye by light. There is nothing abnormal about the ocular muscles on the left.

Now let us test the motility of the right eye. (To patient): Look at my finger as I move it, please. You notice that the right eye is pulled lateralward by the lateral rectus; there is a failure of the eye properly to converge.



Fig. 62.—Oblique lateral view of upper part of body of patient with acromegaly. The nut-cracker profile is obvious. Note the enlarged clavicles and the marked kyphosis.

When we look at the ears we see at once that they are much increased in size, the left ear measuring 8.3 cm. in its longest diameter; the right ear, 7.5 cm. The nose is distinctly larger than normal; it measures 7 cm. in length. There is a slight nasal discharge.

The teeth, you will observe, are far apart. There is considerable caries and some pyorrhea. I would have you notice these teeth and jaws particularly. The patient has lost most of those in the upper jaw, but the lower teeth remain, and they are of considerable interest. (To patient): Close your mouth, please, biting hard, and then open your lips. You see that if the upper teeth were still present the lower teeth would project several millimeters beyond them. That is what is known as mandibular prognathism. Another point to be observed here is the marked spacing of the teeth. You can see it quite plainly in those remaining in the lower jaw, for they are widely separated. This separation has been caused by an enlargement of the mandible that has developed after the teeth have been formed. Such spacing of the teeth is often seen in the jaws of acromegals, resulting in the appearance (in the upper jaw) of what are known as "hag's teeth." Shakespeare mentions the occurrence of such teeth in connection with an increase of libido. It is possible that there is some physiological reason for this association of ideas, for in some cases there is certainly an increased sexual libido during the early stages of acromegaly, probably due to hyperpituitarism. Later on in the disease, as the hyperpituitarism gives place to hypopituitarism, libido is usually diminished.

Increase in the distance between the malar bones and enlargement of them, causing them to appear as striking prominences, are also features characteristic of the acromegalic face. In this particular patient, however, the enlargement of the malar bones is not so marked as it usually is in acromegaly. I would also have you observe, especially, the thickness and succulence of the upper and lower lips in this patient (Fig. 62). The upper lip is markedly thickened and it is turned somewhat upward. It would project even more than it does if the upper teeth were still in place; but it is plain that it is distinctly enlarged. Notice, please, how thick and "juicy" it is. It looks as if it were edematous, though it is not really so. The lower lip, too, is thick, "juicy," and everted. Another point that I desire to emphasize is that when you look at the upturned chin you see that the groove between it and the lower lip is distinctly deepened; the chin is turned upward, resulting in the form called by the French *en galoche*. This projection of the chin is quite characteristic of acromegaly. In many cases the whole face is of the type known as the "nut-cracker" profile, the face of Punchinello

in the Italian puppet-show. You are all familiar with the face of Mr. Punch as it is represented on the cover of the English comic paper; if you will recall the features of Punch you will recognize that they are those of an acromegalic.

The next thing to be noted in this patient is the way his hair has grown in the front of the head. It comes down low upon the middle of the forehead, forming an apex, commonly known as "a widow's peak." This distribution of the hair, also, is characteristic of acromegaly. Still another rather characteristic finding is the marked increase in depth of the transverse rugæ in the forehead; remember that this patient is only thirty years of age, and yet his forehead is deeply grooved. The external occipital protuberance is well marked, and above it the skull is somewhat flattened. Patients suffering from acromegaly often have a deep sulcus just above the external occipital protuberance.

When we come to examine the position of the eyes we find that they are farther apart than is usual, and that there is a slight enophthalmos, though the latter is not marked. There is certainly no protrusio bulborum, though there is slight widening of the lid-slits, and Dalrymple's sign is present, as well as a slight von Graefe's sign. The supra-orbital margins are somewhat overprominent, but the eyebrows are not noticeably heavy, as they frequently are in acromegaly. In most acromegalic patients the hairs of the head, of the eyebrows, and of the barba are heavy and coarse, but this man has scanty supracilia and rather a sparse beard, not very heavy in texture. He says that he has never had more beard than he has now. You see that he is unshaven at this moment, but in spite of that there is not much beard to be seen. (To patient): How often do you shave?

PATIENT: Every three weeks.

DR. BARKER: The hairs of the beard and the supraciliary hairs are certainly diminished in number, though the hair of the head is abundant. There are almost no hirci. The crines pubis are sparse and show a horizontal upper limit, corresponding to the feminine type (*typus femininus*) rather than to the masculine type. There is, then, a hypotrichosis rather than a hypertrichosis, and a feminine type of distribution of the hair, neither of which belongs to typical acromegaly. We shall have to try to explain these discrepant signs when we come to discuss the several endocrine factors in this patient.

In cases of acromegaly the tongue is often enlarged (glossomegaly), making mastication, and sometimes speech, difficult. (To patient): Let me see your tongue, please.

You can all see that his tongue is abnormally large. It is protruded steadily, however, in the middle line. The roof of his mouth shows a very high arch. The right tonsil is red and enlarged, and there are some signs of chronic pharyngitis.

I would also call your attention to the patient's voice. Enlargement of the larynx is one of the results of the disease, and in consequence of it the voice becomes lower in pitch and hoarse. The characteristic change in this particular respect is very well marked in this man. You have doubtless noticed the peculiar *timbre* of his voice.

The neck is rather short and the thyroid isthmus is slightly thickened. The fulness of the neck suggests a slight struma, but neither lateral lobe of the thyroid seems to be enlarged. There is no pulsation palpable in the thyroid. Notice the large size of the Adam's apple. This enlargement of the larynx, of which I have just spoken, is quite common in acromegaly.

We come now to the patient's chest. There is a marked increase in the anteroposterior diameter of the thorax, with prominence and eversion of the margins of the inferior thoracic aperture. The manubrium sterni is large and the angulus sterni is prominent. The corpus sterni projects, giving rise to the so-called "keeled breast" (*pectus carinatus*), sometimes referred to as "pigeon-breast" or "chicken-breast." The clavicles are not so much enlarged as they sometimes are in acromegaly; still, they can be seen to stand out prominently, and they slope upward and lateralward.

When we examine the back we find that there is really an extraordinary degree of kyphosis resulting in great deformity (Fig. 63). There is also marked scoliosis, the convexity in the midthoracic region being toward the right, whereas, in the lumbar region, the curve is reversed. When the stature of a full-grown man decreases from 6 feet to 5 feet 5 inches the change is usually due to kyphosis.

How about the heart? Is there any enlargement?

STUDENT: It has been difficult to form a satisfactory opinion about the exact size and position of the heart owing to the marked deformity of the thorax.

DR. BARKER: I can understand that. The wall of the thorax is rather thick, too. Not only is percussion difficult here, but the

abnormal posture makes it impossible to secure a satisfactory tele-roentgenogram of the heart. No heart murmurs are audible. Examination of the lungs reveals many rhonchi in both lower lobes. There has been dyspnea on exertion for several years and the patient has



Fig. 63.—Lateral view of whole body of patient with acromegaly, showing the marked kyphosis.



Fig. 64.—Anterior view of whole body of patient with acromegaly.

hippocratic fingers. The recent respiratory infection doubtless added markedly to the patient's difficulty in breathing. The kyphoscoliotic runs great risk if he gets an acute pulmonary infection. Often, too, the heart becomes hypertrophied in kyphoscoliosis.

It has been found that in acromegaly not only the bony frame-

work, but the internal organs also undergo enlargement; in other words, a general splanchnomegaly accompanies the disease. In this case, however, the abdominal viscera are not palpably enlarged. The abdomen is scaphoid in form, the epigastrium being shaped like the bow of a boat. There is no muscular rigidity, nor is there any tenderness to be made out anywhere. No abnormal mass is to be felt. Looked at from in front the patient appears "short-coupled" and "knock-kneed" (Fig. 64).

On examining the urogenital system we find that the testes are small, soft, and atrophic. Rectal examination is negative. The



Fig. 65.—Hands of patient with acromegaly. Note the quadrangular finger-tips and the prominent rugæ over the joints.

external genitalia are practically normal except for the transverse crines pubis, already mentioned. In acromegaly the external genital organs are often hypertrophied rather than atrophied. In this particular case there is no marked hypertrophy, owing, perhaps, to the same cause as the hypotrichosis and the soft, velvety texture of the skin, to which we are to return.

Examination of the extremities reveals a definite enlargement of the bones, especially at the acra. You can all see plainly what large hands this patient has, though one often sees still larger hands in acromegaly. They are good examples of the so-called "spade-

like hands"; they are broad, thick, and rather elongated (Fig. 65). These hands are characteristic of acromegaly. The soft parts, as well as the bones, are enlarged, though not so much so as we often see. The fingers show the usual acromegalic form of enlargement, though the caliber is not so uniform from the root to the tip, as we often see in the so-called "sausage fingers" of the acromegalic. The fingertips are somewhat bulbous. The nails are broad and short, and the lunulæ at their bases are absent or only slightly visible. There is evidence of some longitudinal as well as some transverse curving of the nails. There is a marked contrast between the size of the hands and that of the rest of the upper extremities.

When we come to the lower extremities we see that this man has very large feet. (To patient): What size shoe do you wear?

PATIENT: Twelve and a half.

STUDENT: He says that when he was twenty-one, before his health began to fail, he wore a No. 8 shoe.

DR. BARKER: I should think that shoes of the size he now wears would not be readily purchasable in the market. (To patient): Can you buy your shoes ready-made in a store?

PATIENT: My uncle has a shoe store, and when I want a pair of shoes I tell him a week or two beforehand and he gets them made for me.

DR. BARKER: You see what enormous feet the patient has, and what huge great toes! They are shaped like pears (Fig. 66).

We have here in the clinic the complete skeleton of an acromegalic. The case was studied clinically most carefully by Dr. Thayer, and he was fortunate, later, in securing the skeleton. You will be interested, I am sure, in studying it in your leisure hours.

On examining the functions of the nervous system certain abnormalities can be made out. The volume of the muscles is rather small, but the reduction in volume is hardly sufficient to account for the fact that the patient has for some time tired easily on walking, and that his arms and hands are weak. As a rule, one would hesitate to test a man's grip when his hand was the size of this patient's. Still, under the circumstances, we must take the risk! (To patient): Grip my hand, please. Not too hard! Is that the best you can do? Try again. His grip is, certainly, rather weak. Movements of all the joints of the upper and lower extremities are well performed, though there is some evident general weakness. There is no tremor,

and no fibrillary twitching. The tonus of the musculature of the extremities seems to me to be a little diminished. No objective disturbances of cutaneous or of deep sensibility have been made out on careful examination in the ward. There is, however, a diminution of response on testing all the deep reflexes. On testing the superficial reflexes the responses are normal.

The patient has had some pains off and on in his extremities, but pain has certainly not been dominant in the clinical picture



Fig. 66.—Feet of patient with acromegaly. Note the huge, elongated, pear-shaped great toes.

as it is in the so-called “painful form” of acromegaly. (See the Paris thesis of Jean State.) One is reminded, however, by the muscular weakness and sluggish deep reflexes, of the “amyotrophic form of acromegaly” described by Duchesneau, in which amyotrophia occurred in all four extremities without reaction of degeneration, though there was no change in the reflexes or, at most, slight diminution. (To patient): Have you any numbness anywhere?

PATIENT: No; I haven't noticed any.

DR. BARKER: The sluggishness of the reflexes is in this case possibly due to a slight toxic neuritis, associated perhaps with the oral sepsis or the recent respiratory infection.

Psychically there is some impairment. There seems to be some slowing of the mental processes, though the memory is good. No pathological ideas or sense deceptions have been reported by the assistants in the surgical ward.

How about the laboratory tests?

STUDENT: The *urine* showed a trace of albumin and a few casts; its specific gravity was 1026.

DR. BARKER: The fact that the specific gravity is 1026 is interesting, for it shows that the patient is able to pass a concentrated urine; in other words, that the pars intermedia of the hypophysis is able to perform its normal function; that is to say, it produces enough pituitrin to prevent the development of diabetes insipidus. There is a slight nephropathy, due, in all probability, to the concurrent infections (oral sepsis; nasopharyngitis; otitis media with otorrhea; subacute bronchitis); such infectious processes could easily account for the existence of a slight toxic nephropathy. Recently he has had fever, chills, and night-sweats. How about sugar in the urine?

STUDENT: The tests for sugar were negative.

DR. BARKER: No glycosuria. In marked hyperpituitarism there is sometimes glycosuria; whereas in marked hypopituitarism there is increased carbohydrate tolerance and obesity. This man is slightly overweight. His actual tolerance for carbohydrates has not yet been tested.

Next, as to this patient's *sputum*. For the last seven years he has been troubled with dyspnea on exertion, and for the last two weeks he has had a cough, with a moderate amount of thick tenacious sputum. What did the examination of the sputum reveal?

STUDENT: No tubercle bacilli were found on examination of the sputum, but there were pus-cells and streptococci.

DR. BARKER: How about the blood-tests?

STUDENT: Examination of the *blood* showed normal numbers of red and white cells.

Red blood-cells	4,960,000
White blood-cells	6,750
Hb.	90 per cent.

The differential count, made at the same time, showed:

Polymorphonuclear neutrophils	42.5	per cent.
Polymorphonuclear eosinophils	1.5	"
Polymorphonuclear basophils	1	"
Small mononuclears	29	"
Large mononuclears	17	"
Transitionals	4	"

DR. BARKER: These are interesting findings. There is a relative diminution of the polymorphonuclear neutrophils and a relative increase in the small mononuclears. This marked relative lymphocytosis may be of importance from the endocrine side, as we shall see later on.

Has a special examination of the *eyes* been made? What was observed in the eye-grounds? Have charts of the visual fields yet been made?

STUDENT: Yes. Examination of the visual fields with the perimeter shows complete blindness of the right eye. In the left eye the vision is defective in the temporal field only (Fig. 67). There is optic atrophy on the right side.

DR. BARKER: Under such conditions as these there must be lesions—where?

STUDENT: In the optic chiasm.

DR. BARKER: Yes; these signs are pathognomonic of a lesion of the optic chiasm. There is plainly total atrophy of the optic nerve on the right side, with partial atrophy of the optic nerve on the left side. It is probable that the visual symptoms began here—in such cases they usually do—as a bitemporal hemianopsia, caused by pressure upon the middle of the chiasm, with loss of function of the nasal half of each retina. The pressure has been a little more marked to the right of the middle line than to the left, with the result that total atrophy of the right optic nerve has occurred; this accounts for the blindness of the right eye.

We come now to the report on the *ears*. From the history we learn that the patient has had a moderate amount of purulent discharge from the right ear since the onset of the recent illness, about two weeks ago. This would indicate the presence of suppurative otitis media on the right side. He has been deaf in the right ear for the last two years. A watch held on that side is heard only when it is quite close to the ear. The tuning-fork, also, can be heard only

when it is loud and near the ear. The hearing on the left side is less defective than it is upon the right. Weber's test, when applied, showed, as we should expect, that bone conduction is better than air conduction. The aurist's report states that the right drum is perforated, and that the canal contains a purulent discharge. The canal on the left side is so contracted that the drum cannot be seen.

As regards the *nose*, the specialist's report states that both inferior turbinates are enlarged and slightly polypoid. There is a septal

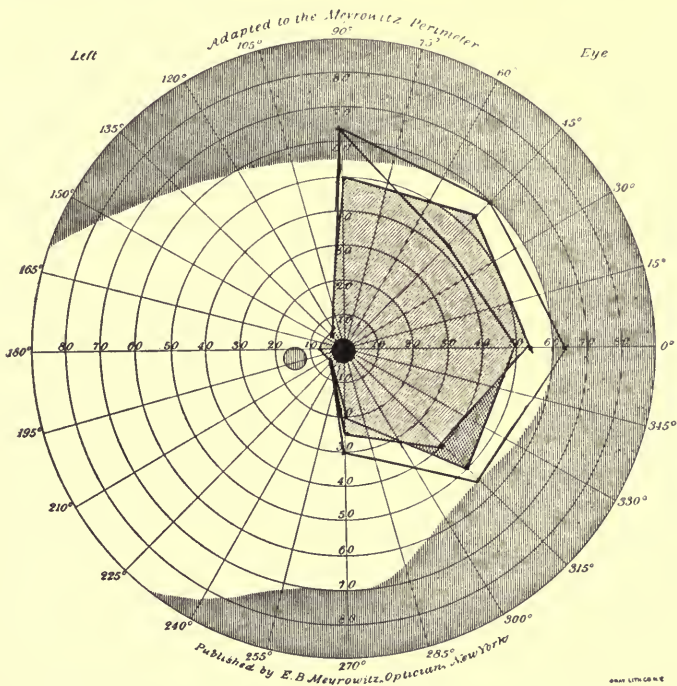


Fig. 67.—Chart showing disturbances of visual field of left eye on perimetric examination.

spur, posteriorly, on the right side. A large mass of adenoids can be seen, with some mucoid discharge. The palatine tonsils are large and adherent.

A *roentgenogram of the skull* shows enlargement of the sella turcica, exaggerated occipital protuberance, and enlargement of the frontal and sphenoidal sinuses.

We have now come to the point where we may conveniently summarize the data we have accumulated for the purpose of diagnosis.

This groceryman of thirty began at the age of twenty-one to notice enlargement of the bones of the feet, hands, face, and chest; he states that in a few years he lost several inches in stature, owing, we feel sure, to the development of an outspoken kyphoscoliosis. Six or seven years ago he noticed shortness of breath on exertion, a symptom that has been present ever since. Two years ago he began to lose the sight of the right eye, and recently he has been totally blind in that eye. Vision in the left eye has also been defective, especially in the temporal field. For the past two years he has been growing deaf, hearing in the right ear being involved more, however, than that in the left. Slight headaches have occurred for two years; recently they have been more severe. About two weeks ago he suffered from an acute respiratory infection, with cough, purulent sputum, fever, chills, and night-sweats; with it there was some disturbance of digestion, with temporary nausea and vomiting. He has of late noticed some loss of muscular power.

On physical examination we have made out: (1) characteristic acromegalic changes in the skeleton and soft parts, with typical acromegalic roentgenographic formula of the skull; (2) scanty supercilia, barba, hirci, and crines pubis (general hypotrichosis), with transverse upper limit to the crines pubis, soft, velvety skin, and broad hips (*typus femininus*); (3) nasopharyngeal catarrh, hypertrophic pharyngeal and palatine tonsils, bronchitis, bilateral otitis media with otorrhea dextra; (4) blindness in the right eye and in the temporal field of the left eye, with bilateral descending optic atrophy; (5) relative lymphocytosis (46 per cent. of white cell count); (6) dental caries and pyorrhea alveolaris; (7) slight albuminuria and cylindruria (slight toxic-degenerative nephropathy); (8) hypoplasia of the testicles; (9) slight struma; (10) neuralgic pains in the extremities, weakness of the voluntary muscles with some hypotonicity and sluggishness of the deep reflexes, and (11) slowed mentality, with possibly a subnormal intelligence.

Evidently we have to deal in this patient with a complex situation. The pathological-physiological findings point to wide-spread disturbances and enable us to predicate pathological-anatomical changes in a large series of structures (osseous, cutaneous, respiratory, hemopoietic, urogenital, nervous, and endocrine), the nature of which we must try to decide upon.

Certainly, the most striking of the changes are those of the skeleton

—the enlargement of the acra (acromegaly) and the kyphoscoliosis, which has reduced a tall man to a short one; even the tyro in diagnosis would scarcely have any difficulty in recognizing this form of skeletal change as typically acromegalic in nature. For there is but little resemblance to the changes seen in Paget's disease, to those that occur in rickets, or to those of leontiasis ossea. A beginner might, perhaps, if he looked at the hands and feet alone, confuse the conditions present here with those of so-called hypertrophic pulmonary osteo-arthropathy (the Marie-Bamberger disease), especially as there has been dyspnea for years, signs of a bronchitis are present now, and there is an outspoken kyphosis. But the mandibular enlargement, the enlargement of the sella turcica, and the compression of the optic chiasm could not be due to a hypertrophic pulmonary osteo-arthropathy. Of course, one might have (and we may, even in this case, have) a hypertrophic pulmonary osteo-arthropathy superimposed upon acromegalic skeletal changes. If so, its existence can be determined by *x*-ray examinations, since in the Marie-Bamberger disease there is an ossifying osteoperiostitis, which, on *x*-ray examination, is seen as a characteristic diaphyseal deposit on the long bones.

To what do we now attribute the bony changes in acromegaly?

STUDENT: To abnormal stimulation of bony growth, due to disease and overactivity of the hypophysis cerebri.

DR. BARKER: Yes; the hypophysis cerebri, otherwise known as the pituitary gland. It consists, you recall, of three parts, namely, the anterior lobe, the posterior lobe, and the pars intermedia. Which part of the gland do you think is affected in this case?

STUDENT: The anterior lobe.

DR. BARKER: Yes. Overactivity of the anterior lobe is believed to be responsible for acromegaly. When overactivity of this lobe occurs in a child, what is the result?

STUDENT: Gigantism.

DR. BARKER: Yes. The anterior lobe, it is believed, produces an internal secretion that has to do with the growth of bone, and also with the stimulation of that endocrine function of the gonads that is concerned in the development of the secondary sexual characters. T. Brailsford Robertson has recently isolated a substance from the hypophysis that he calls "tethelin"; it is his opinion that this tethelin is the chief growth-controlling principle of the anterior

lobe. It will be interesting to see whether or not the researches of other investigators support this view.

No matter what the final decision about tethelin turns out to be, it seems to have a remarkable growth-promoting influence on surface epithelium, and has been used successfully, locally, to hasten the healing of leg ulcers. Some think that it will aid the healing also of gastric ulcers!

The patient we have here today is, or rather was, 6 feet in height. A man of that stature is not, of course, a giant, but if he has been as much as 6 feet, he must, even at the time in his life before his epiphyses united with his diaphyses, have had an active hypophysis. When a stimulus to overgrowth of bones occurs after the union between the epiphyses and the diaphyses of the long bones, what is the result?

STUDENT: Enlargement of the bones.

DR. BARKER: Yes; but only at the ends of the bones—the acra of the head and of the extremities. When the overgrowth occurs before the epiphyses and the diaphyses are united, the shafts of the long bones become elongated, and we have an overtall person, or gigantism. In the skull the bony enlargement of acromegaly affects chiefly the lower jaw.

What is it that determines the closure of the epiphyseal lines, normally limiting the length of the diaphyses, and, accordingly, the stature of a person?

STUDENT: The internal secretion of the gonads.

DR. BARKER: Yes; that is the current opinion. There seems to be, normally, a certain balance between the activity of the anterior lobe of the hypophysis and that of the internal secretory function of the gonads (testes in the male; ovaries in the female). Thus, during adolescence, gigantism may be due to a disturbance of the balance that involves a preponderance of hypophyseal activity, whereas dwarfism may be due to a disturbance of the balance that involves a preponderance of gonadal activity.

What are some of the causes of the hyperpituitarism, or hyperhypophysism, that leads to acromegaly? Roussy, I may say, thinks that it is dyspituitarism rather than hyperpituitarism that is responsible for acromegaly; that is, a perversion of function rather than an increase of function of the hypophysis.

STUDENT: The overactivity of the hypophysis may be due to

the development in it of some form of tumor, most frequently an adenoma, or a so-called struma, of the hypophysis.

DR. BARKER: Yes. It seems to be due nearly always to some form of epithelial growth situated in the gland itself or in its neighborhood. Formerly these tumors with which acromegaly is associated were supposed to be sarcomatous in nature, but it is now believed that they are epithelial tumors which have their origin in the glandular cells of the anterior lobe of the hypophysis, or in the cells of an accessory hypophysis. The flat-celled epithelial tumors of the hypophysis do not cause acromegaly. It may be that occasionally some change other than tumor, say a cyst, a hemorrhage, or an inflammation of the hypophysis, may stimulate it to overactivity, though this is not yet certain.

What signs are there in this patient, besides those of acromegaly, that point to tumor of the hypophysis cerebri?

STUDENT: The enlargement of the sella turcica revealed by the x-ray examination.

DR. BARKER: Yes. Can you mention any other signs that point to tumor of the hypophysis in this man?

STUDENT: The bilateral optic atrophy and the changes in the visual fields, especially the evidence that there has been, earlier, a bilateral hemianopsia.

DR. BARKER: Yes; these changes point to a lesion of the optic chiasm. And this particular form of chiasmal lesion is most often due to hypophyseal tumor. We can be very sure, I think, that this man has a tumor of his hypophysis. Why hasn't he had a choked disk?

STUDENT: Tumors of the hypophysis are, as a rule, not large enough to cause a marked general increase of intracranial pressure.

DR. BARKER: That is right. And, of course, an ordinary decompression operation would not relieve the symptoms in such a case. It is intrasellar pressure (or perisellar pressure) that is doing the damage here, not an increase of the general intracranial pressure.

Hypophyseal disease is an endocrinopathy. Are any of the other glands of internal secretion functioning abnormally in this man?

STUDENT: The pars intermedia of the hypophysis must be functioning, for he has no diabetes insipidus.

DR. BARKER: Yes, that is evident, if the view that diabetes insipidus is due to a loss or diminution of activity of the pars inter-

media is correct. Recent studies seem to point, however, to the gray matter in the floor of the third ventricle as the site of lesions causing diabetes insipidus. How about his thyroid?

STUDENT: The isthmus of the thyroid is slightly thickened, but there are no marked signs of overactivity or of underactivity of the thyroid gland.

DR. BARKER: The signs, if any, pointing to the thyroid are, as you say, slight. There are some eye signs (v. Graefe and Dalrymple's signs are slightly positive and there is faulty convergence), but there is no tachycardia, the test for hypersensitiveness to epinephrin is negative, and there are no signs of myxedema. Sometimes acromegaly and myxedema are found in association.

How about the internal secretion of the gonads in this patient?

STUDENT: He has small, soft testicles. There is general hypotrichosis, as shown by the sparseness of the eyebrows, of the hairs of the beard, and of the axillary and pubic hair. The crines pubis have a transverse upper limit. The skin is soft and velvety. The hips are broad, and the femora are long. The patient is a little heavy.

DR. BARKER: Yes. Do those signs point to overfunction or to underfunction of the testicular internal secretion?

STUDENT: To underfunction.

DR. BARKER: Yes. This man is an example of moderate hypogonadism. In other words, he is slightly "eunuchoid."

In addition, he shows some signs of status thymicolymphaticus, namely, hypertrophy of the pharyngeal and palatine tonsils, and a relative lymphocytosis in the blood in association with the feminine type of external habitus.

From the endocrinopathic side, then, we may conclude that he exhibits predominantly a hyperhypophysism (or dyshypophysism), along with moderate hypogonadism (or eunuchoidism) and hyperthymism (or status thymicolymphaticus). We know, too, that the thymic cases generally show a congenitally defective chromaffin system, though that such exists in this patient we are not certain. As you go on with endocrine studies, you will be interested, I feel sure, to find how often in a patient in whom there is an outstanding affection of one endocrine gland, there will also be discoverable, on careful testing, phenomena referable to minor affections of other glands of the hormonopoietic system. It is, in reality, rare that endocrinopathies are single; most of them are multiglandular affec-

tions.¹ This man's major endocrinopathy is of hypophyseal origin; but he has, apparently, also minor endocrinopathies of gonadal and thymicolymphatic origin, for besides his acromegaly, he is somewhat eunuchoid and shows some signs of status thymicolymphaticus.

Now we come to the question, What can we do to help this patient? What do you think could be done?

STUDENT: Surgery offers the best prospect of relief. But, even if an operation were successful, it could only arrest the bony change. It would not remove the changes that have already occurred.

DR. BARKER: Yes. Certainly, the bones will not grow smaller again. But in other respects the patient's condition might be improved by it. Unless the pressure on the optic chiasm be removed this man will soon be entirely blind I fear. What surgical procedure do you think should be employed?

STUDENT: Removal of part of the hypophysis.

DR. BARKER: How about removing the whole of it?

STUDENT: Experiments on animals have shown that life is impossible without the presence of some portion of it.

DR. BARKER: Could you not feed enough to take its place?

STUDENT: I think not.

DR. BARKER: You would be afraid to trust to it? In the event of operation, would you take out all of the tumor?

STUDENT: I should think it would be necessary to take out at least enough to relieve the pressure in its neighborhood.

DR. BARKER: Yes. Up to the present time it has not been found possible, as a rule, to remove tumors of the gland in their entirety, but I think this has been partly because the methods employed were not sufficiently developed. In such operations the nasal approach has been strongly advocated and largely employed. For all details of hypophyseal diseases and of operative measures to relieve them, as developed up to the time it was written, you should consult the admirable monograph of Dr. Harvey Cushing, formerly of this hospital, now at the Peter Bent Brigham Hospital in Boston.

Quite recently Dr. Heuer, here, has suggested that operation by the nasal approach must be regarded purely as a palliative measure except in the few rare cases of hypophyseal cyst, because it labors under the disadvantages of (1) a septic approach; (2) very limited

¹See the interesting case of acromegaly with multiglandular syndrome reported by Bendell in 1915.

exposure of the region affected, and (3) a restricted field of activity. The intracranial operation, however, as it was performed up to the time at which he wrote (1915) was not satisfactory, because it necessitated a more formidable approach, without providing much better exposure of the hypophysis. In Dr. Heuer's opinion the further development of hypophyseal surgery must depend upon a satisfactory intracranial approach to the hypophysis, and in 1915 he introduced a method of operation possessing the advantages of (1) a much more extensive view of the chiasmal region and even to a certain extent, of the region behind the chiasm; (2) the easy exposure of both carotids, and (3) the complete control of the entire field of operation. In 1916 he was able to report 6 cases operated upon by this method. Recently Dr. Dandy, here, has employed this method of operation for removal of a hypophyseal tumor in a physician. I had the privilege of examining this physician both before and after the operation, and the result, thus far, has been gratifying.

I think that, in the case of our patient, the removal of the entire hypophyseal neoplasm might possibly be accomplished, provided the tumor has not invaded the bone. When that has taken place, what happens?

STUDENT: The tumor is apt to return after operation.

DR. BARKER: Yes. One interesting point in Dr. Heuer's operation is that he cuts straight through one or other of the optic nerves in order adequately to expose the sellar region. In fact, this procedure forms, I believe, a definite feature of the operation. What objection would there be to doing this?

STUDENT: It would cause permanent total blindness upon the side on which the nerve was severed.

DR. BARKER: But this man has already lost the sight of the right eye altogether. That being the case, if the Heuer operation were performed, which nerve should be selected for section in this case?

STUDENT: The right.

DR. BARKER: Yes, of course. In such a case as this the surgeon, if he were to perform the Heuer operation, would go in on the right side of the head, and would sever the optic nerve on that side. The operation is begun by making a large, low, frontal osteoplastic flap. Following this the dura is opened almost as widely as the bone defect. Lumbar puncture is then performed and the head tilted back, when the frontal lobe falls backward by gravity. Further exposure can

be obtained, if necessary, by retraction with a spatula, introduced laterally, *i. e.*, just in front of the temporal lobe. This is the method that has been employed recently in this hospital. The operation is, however, a formidable one, not lightly to be entered upon. It is too soon, as yet, to pass judgment upon its merits as compared with earlier methods.

Now, let me tell you something. When you get into practice you will from time to time doubtless see cases of hypophyseal disease in its early stages, and it is important that you should be able to recognize such disease at its beginning. Dr. Walter Timme, who has contributed some valuable papers to the literature upon this subject, has expressed an opinion in regard to this particular point that deserves to be emphasized. "We are all," he says, "familiar with the text-book descriptions of disturbance in the pituitary gland, with its accompanying symptoms, such as acromegaly, gigantism, infantilism, adiposis dystrophia, sexual inversion, eunuchism, and eunuchoidism, together with restriction of the visual fields, hemianopsia, atrophy of the optic nerve, etc. But, if we look for all these clinical signs before we recognize disturbance of the pituitary gland, we shall fall into the error of non-recognition of transitional, compensatory, or abortive forms of pituitary disease, the clinical significance of which is placed to the credit of neurasthenia, hysteria, idiopathic epilepsy, and even of the psychoses." These incomplete forms (*formes frustes*) of acromegaly, on the one hand, and of dystrophia adiposogenitalis, on the other, are far more numerous than the well-developed forms. But let me warn you that there is also danger on the other side. A good many rash and unwarranted endocrinopathic diagnoses are being made at present. Clinicians are trying to go farther both in the diagnosis and therapy of the endocrinopathic disturbances than is in reality justifiable in the present undeveloped state of our knowledge in this new field.

It is, however, precisely in the early period of hypophyseal diseases that therapeutic efforts should be applied, and especially in hypophyseal neoplasms, we must act early if we are to save the eyesight. A few months ago I saw a patient who was rapidly losing her eyesight from, as I believed, the pressure occasioned by a hypophyseal tumor. No other signs of the growth were present when I saw her except amenorrhœa and obesity, and as the menopause was approaching, it was possible to regard both these latter symptoms as occurring

in the natural course of events. The sella was only slightly enlarged as seen in the *x*-ray plate. Now this patient has "everything to live for" provided she is not handicapped by blindness. Therefore, notwithstanding the gravity of the surgical procedure, I advised her to have an operation upon the hypophysis. I admit that this was rather a radical decision, but the visual symptoms strongly suggested an early stage of a lesion of the optic chiasm, and the patient's condition, in general, seemed to me to indicate a tumor developing in the hypophysis. The whole situation was, of course, explained to the patient and to her husband. It was emphasized that, if the operation were performed, it should be of an exploratory character, with the understanding that, if a growth of the hypophysis were found, an attempt should be made to remove it. Not all medical men, however, take this point of view, and in the case of this particular patient the majority of consultants were not in favor of the operation. I could not blame the patient, in the circumstances, for deciding against operation, but at last report her vision had become progressively more impaired, and she will soon, I am afraid, be totally blind, in which case life will lose a large part of its value for her, as it would for most of us. Whether we decide for or against operation in a case of this sort, we assume, as physicians, a very grave responsibility, but as for myself, I cannot help but agree with Cope, who, in the course of an interesting article on methods of approach to the pituitary fossa, remarks: "It is greatly to be regretted that so many patients are now permitted to become almost blind before operative treatment is advised."

Within the last few years some attempt has been made to treat disturbances of the hypophyseal functions, including those accompanied by defects of vision, by means of organotherapy. Two years ago de Schweinitz and How reported a case in which a woman fifty-one years of age developed a blurring of vision, first in the right eye, and then in the left, with marked increase of headaches, from which she had suffered for years. Visual examination revealed bi-temporal hemianopic scotomata in both eyes, and *x*-ray examination showed a typical enlargement of the sella turcica, suggesting neoplasm, or struma, of the hypophysis. The patient declined operation, and after some fluctuations in her condition, she was put upon tablets of thyroid and pituitary extract, $2\frac{1}{2}$ grains each. Between July 1, 1914 and February 24, 1916 she took about 1400 tablets.

A series of visual charts taken during this period of time showed a gradual return of the visual fields, chiefly from below upward, until they were practically restored to their normal extent. Vision was considerably improved in both eyes, the patient's general condition was better, and the headaches had practically disappeared. This case is an interesting one, but there is, so far, but little other evidence in favor of organotherapy in hypophyseal tumor. I believe that, at present, our chief reliance when tumor exists must be upon surgery, though the case of de Schweinitz and How would make it seem wise to give organotherapy a preliminary trial.

As regards the particular patient before us I can only say that if I were the patient I should certainly wish to get into shape to have the operation performed, because, otherwise, the blindness must steadily increase. Moreover, the later stages of acromegaly are in themselves very distressing. The headache and the pains in the limbs grow constantly worse, and I am sure most of us would take a big risk to escape such an issue. But I am convinced that the risk with improved operative technic is much less than that attending earlier operative methods. At present the patient is suffering from bronchitis, and one would not, of course, advise his taking an anesthetic until he has recovered from it. After this and the other local infections he has have received due attention I believe it would be a good plan to ask Dr. Heuer and Dr. Dandy what they think in regard to the advisability of operation.

I am very glad to have had the opportunity of showing you a patient who we believe has a tumor developing in the hypophysis, for the case illustrates well the symptoms associated with the condition. It will bring you, also, to a realization of the possibilities of operative treatment in such cases, and the importance of resorting to surgery in the earlier stages of the disease. Not many years ago a famous surgeon is said to have remarked that it was "tempting Providence to operate in the region of the hypophysis cerebri." Ten years ago, no doubt, ample support could be found for such an opinion, but, as Cope says in the article I have referred to, "The last decade has witnessed the birth and development of hypophyseal surgery, and the next decade should witness the employment of such surgery at increasingly earlier stages."

[*Subsequent History of the Case.*—The patient remained in practically the same condition for about eight months. His eyesight

did not become worse and his headaches showed no increase. During the influenza epidemic of 1918 he contracted pneumonia and died of it in December, 1918. No autopsy was obtained.]

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