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Policy

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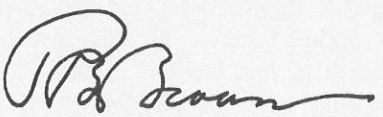
Christmas Message

Two thousand years ago, the promise of the Prophets was fulfilled on a holy night in Bethlehem when the Son of God became Man to bring hope to His people. Through the centuries, He has offered that hope to all who would follow Him. We celebrate His birth to give our thanks in the true Spirit of Christmas.

To the entire Medical Department family, I offer sincere wishes that your Christmas will be happy, and your New Year one of fulfilled hopes. To those who are separated from loved ones, I add a special wish that you may find comfort in the example of love and sacrifice shown by Christ, and that your families will soon be safely reunited.



R. B. BROWN
Vice Admiral, MC, USN
Surgeon General

PAINFUL FEET DUE TO HERNIATION OF FAT

Walter B. Shelley, MD, and Howard M. Rawnsley, MD,
JAMA 205(5):308–309, July 29, 1968.

An unusual cause for painful feet was found to be small papular herniations of subcutaneous tissue into the skin of the medial aspect of each heel. The herniation occurred only upon standing or upon application of pressure to the sole, and hence the papules were distinctively "piezogenic."

Cutaneous hernias are a rarity not described in dermatologic encyclopedias or references. Nonetheless dermatoceles do occur and have been recorded by both proctologists and ophthalmologists. The perianal examples appear as small 3- to 7-cm tumors, often following trauma, and are mistaken for lipomas. Marks has labelled these as "lipofascial hernias," and detailed their surgical care. The other example of cutaneous hernias masquerades as baggy lower eyelids. In this instance intraocular fat extends through defects in the septum orbitale into the subcutaneous tissue of the lower eyelids. Recognized since the last century, this entity can also be corrected surgically.

Still a third type of dermatolysis, previously unknown to us, is outlined here. In this instance, herniation of fat occurred into the skin of the medial side of the heel causing pain and discomfort. Diagnostically it could be recognized as a unique "piezogenic papule," ie, one appearing only when weight was placed on the foot.

Report of a Case

Tired, painful feet developed in a 20-year-old student after one week of summer employment as a railroad trackman. Although he had noted for several years some blanching of his fingers and toes on exposure to cold, he had previously been in excellent health. A tonsillectomy and appendectomy were the total of his surgical encounters. He gave no history of trauma to his feet and a careful vascular examination revealed no abnormalities.

At rest the foot appeared normal, but immediately on standing or applying pressure on the heel, firm papules developed along the medial aspect of the lower heel. Their induction by pressure was so characteristic that we have described these papules as "piezogenic." Numbering about a dozen on each foot, they could be made to appear and disappear as often as desired by simply regulating the pressure applications. Significantly, application of a blood-pressure cuff at suprasystolic pressure (200 mm Hg) failed to prevent their appearance, nor did intrasystolic pressure held at 150 mm Hg produce them when the patient was prone.

The extrusions were soft and became painful with the passage of time.

A 24-hour urinary amino acid chromatogram showed essentially a normal pattern. Administration of ascorbic acid, 100 mg three times daily for one month, failed to affect the condition. Relief was achieved only by avoiding long periods of standing.

Comment

The papules on the heels of this patient were viewed as true dermatoceles, ie, the herniations of fatty subcutaneous tissue into connective tissue defects in the fascial layer we consider the dermis. The extrusion of fat with its vasculature and associated nerves could be presumed to lead in time to anoxic pain and hence explain the initial complaint of "painful feet on standing." Such pressure-induced pseudopapules are unique in our experience, but can be viewed as yet another example of skin changes due to physical forces. The multiple nature of the small hernias made surgical correction appear less than appealing since the connective tissue defect would seem cribriform. Supportive external pressure devices were limited to well-fitting shoes and were not dramatically helpful. Avoidance of long periods of standing was at once the only obvious and conservative treatment.

Vascular examination was performed by Orville Horwitz, MD.

(The figures and references may be seen in the original article.)

From the Departments of Dermatology and Pathology, University of Pennsylvania School of Medicine, Philadelphia.
Reprint requests to 3400 Spruce St., Philadelphia 19104 (Dr. Shelley).

A TEN-YEAR REVIEW OF AMEBIC ABSCESS OF THE LIVER: 1956–1966

G. Douglas Cain, MD, Pruett Moore, Jr., MD,* and Marcel Patterson, MD,*
Amer J Dig Dis 13(8):709–717, August 1968.

Amebic hepatitis and abscess of the liver are the most common complications of amebic colitis, but the diagnosis is difficult if one insists on finding *Entamoeba histolytica.* The present 10-year series reviews our experience with 17 patients and represents a continuation of a previous 10-year (1946-1956) review from this institution. In the present series, we wish to re-emphasize the symptoms and signs that to us seem consistent and characteristic of this disease syndrome.

Clinical Picture

In our experience, amebic liver abscess is an illness of middle-aged men from lower socioeconomic backgrounds. The onset of the illness is vague and ill-defined; usually patients are sick from 2 to 4 months, but in one instance the illness had lasted 5 years. Although indefinite about the exact beginning of symptoms, patients find that the symptoms become quite profound and distressing. All but two of these patients felt feverish; night sweats were common, and over a third of the patients had shaking chills. Weight loss was striking and averaged 25 lb. All patients noted abdominal pain, usually well localized to the liver area; sometimes the pain was pleuritic, and at other times vague and ill-defined. Surprisingly, other gastrointestinal complaints are minimal. There was no nausea or vomiting. Bowel function remained relatively undisturbed. No patient had diarrhea at admission. Diarrhea had occurred previous to admission in 2 patients, but had subsided spontaneously. Cramping abdominal pain and bright rectal bleeding occurred in only 2 patients. In our experience, the patient with severe amebic colitis has not been the one to develop a liver abscess, nor were the past symptoms suggestive of colonic disease. One patient complained of jaundice, which should be of considerable differential diagnostic importance since the etiology indicates an inflammatory process of the liver or biliary tract, while the absence of jaundice contraindicates the diagnosis of diffuse liver disease or obstruction to bile outflow. The important features of the illness, derived from the patients' past histories, are summarized in Table 1.

The physical appearance and examination of these patients confirmed the severity of their complaints. All patients looked sick, weak, and debilitated, with evidences of recent weight loss. Right pleural effusions were detected in over half the patients, while one had bilateral fluid. In all but two, the liver was palpable and tender, sometimes massively enlarged, but usually 3-6 cm. below the right costal margin. Unlike metastatic liver disease that can produce liver enlargement without jaundice, these livers were smooth. Masses were described only in two instances—one in the left upper quadrant, and one on the right in association with hepatomegaly. All observers stress the striking evidence (by physical examination) of liver involvement in this condition without the usual stigmas that accompany chronic liver disease. For example, only 1 patient had splenomegaly, 1 had clubbed fingers, and 2 had ascites.

Sometimes the abscess points, and produces an identifiable bulge. In one instance, spontaneous perforation occurred, and a fistulous tract was seen in the right upper quadrant; however, these represent the exceptional, rather than the usual findings.

Rarely (in this series, on only one occasion), the abscess occurs in the left lobe of the liver. In this instance physical findings are atypical—the liver may not be felt or may not be identified as such. Here the clue may come from the displacement of the stomach as seen during the gastrointestinal X-ray series or from the liver radioisotopic scan. Table 2 summarizes the physical findings in all patients.

Anemia, leukocytosis, low serum albumin, elevated alkaline phosphatase, and abnormal sulfobromophthalein (BSP) were the important laboratory findings. Evidences of *E. histolytica* were found in only 7 patients—by stool examination in 3, by aspiration of ulcers at proctoscopy in 1, by liver biopsy in 1, and by positive hemagglutination test in 2. The pleural fluid of 1 patient was recorded as having 5 large, bizarre, unidentifiable cells per 100 white blood cells. Fluids aspirated from the chest

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Supported by Grant 5T01 AM 05304 06 from the National Institutes of Health, U.S. Public Health Service.
We wish to thank the Communicable Disease Center in Atlanta for performing the hemagglutination tests.
* Drs. Cain and Moore are National Institutes of Health Training Fellows.

TABLE 1. *Features of Illness Derived From Histories of 17 Male Patients*

Patient No.	*Age (yr.)*	*Race*	*Duration of illness (mo.)*	*Wt. loss (lb.)*	*Fever* (°F.)*	*Chills*	*Pain†*	*Anorexia*	*Malaise‡*	*Cough*	*Night sweats*	*Bowel movements*
1	52	White	6	15	—	—	RLQ 1 wk. sharp intermittent RUQ to rt. shoulder	+	+	+	—	Bloody diarrhea 1 wk.
2	23	Negro	2	25	I	—	Began RLQ, dull RUQ & pleuritic	—	NO	Mild mucoid	Profuse	Normal
3	34	Negro	2	18	I	+	RLQ 2 days then dull RUQ & pleuritic	—	NO	—	Profuse	Normal
4	52	White	1	18	101–103	+	Vague gen. abdom. pain	+	NO	—	+	Diarrhea (early)
5	47	White	4	29	I	—	Dull RLQ, RUQ 1 mo.	+	+	—	—	Normal
6	54	White	2	13	I	+	Rt. lower lung, pleuritic	—	NO	Hemoptysis	+	Normal
7	71	Negro	60	10	—	—	LUQ dull ache for 5 yr. intermittent	—	NO	—	—	Normal
8	37	Negro	3	22	I	—	Deep dull RUQ pleuritic 2 wk., worse with motion	—	+	—	+	Normal
9	38	White	5	35	I	+	Epigastric pressure	—	NO	Mucoid 3 wk.	+	Diarrhea (early)
10	32	Negro	2	18	+	—	Severe RUQ pain	—	NO	—	+	Colic & bright blood
11	77	Negro	3	40	100–104	—	RUQ pressure sensation	+	NO	—	—	Constipated
12	29	White	2	30	+	—	Constant periumbilical, pleuritic pain	+	+	Nonproductive	—	Normal
13	40	Latin Amer.	5	35	+	—	Epigastric discomfort	+	+	—	—	Normal
14	62	Latin Amer.	4	41	I	+	Intermittent, sharp epigastric & RUQ pain	—	NO	—	—	Normal
15	28	Negro	6	35	—	—	Throbbing rt. lower chest & left pleuritic pain	+	+	Brown sputum	+	Normal
16	53	White	3	25	+	+	Rt. pleuritic pain	—	+	2 wk.	+	Normal
17	52	Latin Amer.	4	Yes	+	+	Full epigastric after meals	—	+	—	+	Normal

* I, intermittent.
† RLQ, right lower quadrant; RUQ, right upper quadrant; LUQ, left upper quadrant.
‡ NO, not observed.

or the liver were described as serosanguineous, chocolate-colored, brick-red, or gray, and odorless. Cultures were sterile and no parasites were found. Chest X-rays confirmed pleural effusions. An elevated right diaphragm was demonstrated in 9 patients, and in only 3 was the chest film recorded as being normal. Only 5 patients had liver scans, but all 5 had "cold areas"—1 in the left lobe, 2 in the right upper lobe, 1 in the right lower lobe, and 1 involving the entire right lobe. Table 3 summarizes the laboratory findings. Table 4 lists the frequency of the symptoms, signs, and pertinent laboratory data.

All patients responded dramatically to amebicidal drugs, with rapid defervescence and abatement of symptoms in a few days. The case of Patient 14 is presented in detail as typical.

Case Report (Patient 14)

A. J., a 62-year-old Latin American laborer, gave a 4-month history of sharp, recurrent epigastric and right upper quadrant pain. He had had chills and fever and had lost 40 lb. On admission, his temperature was 103°F., and he weighed 124 lb. He was obviously thin, malnourished, and sick. There were findings of a small pleural effusion in the right lower chest. A very tender liver was enlarged 7 cm. below the costal margin in the right mid-clavicular line. The proctoscopic examination was negative. Hematologic test results were: hemoglobin, 6.8 gm./100 ml.; normochromic normocytic indexes; reticulocyte count, 4.8 percent; white blood cells, 11,300/cu. mm., with 74 percent neutrophils, 17 percent lymphocytes, 8 percent monocytes, and 1 percent basophils. The glucose tolerance curve was that of a diabetic. The prothrombin time, cephalin flocculation, serum glutamic oxalacetic transaminase (SGOT), and serum glutamic pyruvic transaminase (SGPT) were normal. The alkaline phosphatase was 6.5 sigma units (normal 2.8). Repeated examinations of stools for ova, cysts, and parasites were negative.

TABLE 2. *Physical Findings in 17 Male Patients*

Patient No.	*Lung*	*Liver*	*Wt. (lb.)*	*Fever (°F.)*	*Other*
1	Effusion, rt. base	6 cm., very tender	115	—	Ascites, spleen 3 cm.
2	—	4 cm., tender	153	102	—
3	Effusion, rt. base	Iliac crest very tender	122	103	Rt. c.v.a. pain
4	—	Mass ?, RUQ tender, RMQ to umbilicus	169	100	—
5	—	10 cm., tender	135	102	Bronchitis, tender RLQ
6	Dull rt. base with rales, friction rub	—	164	—	—
7	—	10 × 20 cm. LUQ tender	141	—	Fluctuant warm mass
8	Effusion, rt. base	6 cm.	154	101	Tender rt. lower ribs
9	—	2 cm., tender	?	101	—
10	Normal (2/20/61) Rt. effusion (6/1/66)	Normal Huge & tender	168	98–102	Icteric
11	Dull, rt. base	6 cm.	129	—	Draining RUQ fistulas
12	Effusion, rt. base	5 cm., very tender	122	103	Rt. c.v.a. pain
13	—	Large, pain	—	108	Distended abdomen
14	Effusion, rt. base	8 cm., tender	124	103	—
15	Friction rub, left base bilat. effusion	8 cm., tender	129	103	—
16	—	—	104	102–105	Clubbed fingers, lymphadenopathy, generalized
17	Effusion, rt. base	14 cm., tender	132	None	Anasarca

Abbreviations used in table: RUQ, right upper quadrant; LUQ, left upper quadrant; RLQ, right lower quadrant; cva, costovertebral angle.

TABLE 3. *Relevant Laboratory Data Before Therapy*

Patient No.	*Bilirubin (mg./100 ml.)*		*BSP (%)*	*Alk. phos.**	*SGOT*	*SGPT*	*Serum protein (gm./100 ml.)*			*Hgb (gm./100 ml.)*	*WBC (per cu. mm.)*	*WBC Differential*	*Amebas †*
	Total	*Direct*					*Total*	*Alb.*	*γ-glob.*				
1	0.7	0.4	20	4.7 BU	—	—	6.2	2.4	—	10.0	6,500	Normal	Trophozoites in stool
2	0.67	0.16	—	2.0 BU	—	—	6.9	4.2	—	10.4	16,900	Normal	NF
3	0.8	0.3	10	10.3 BU	—	—	7.4	3.1	—	8.0	15,350	Left shift	NF
4	0.94	0.57	10	7.7 BU	—	—	6.2	4.2	—	8.7	15,200	Left shift	Trophozoites from rectal ulcer
5	1.14	0.54	—	16.2 BU	—	—	5.0	3.1	—	11.7	18,900	Left shift	NF
6	—	—	—	—	—	—	7.2	4.8	—	14.8	11,500	Left shift	NF
7	0.7	0.3	—	1.3 BU	—	—	7.1	3.3	—	9.9	5,800	Normal	NF
8	0.6	—	12	1.9 BU	—	—	7.1	3.5	—	15.0	6,500	Normal	NF
9	0.6	0.44	10	5.7 SU	3	14	5.8	2.49	—	10.0	12,000	Left shift	NF
10	3.65	2.76	6	9.3 SU	100	420	8.9	3.3	—	8.0	16,800	Left shift	Trophozoites in stool
11	0.53	0.12	5	5.6 SU	48	21	—	—	—	12.0	10,900	Left shift	NF
12	0.3	0.1	—	16.4 SU	40	29	—	1.44	—	8.8	18,000	Left shift	NF
13	0.4	0.3	—	3.6 SU	25	26	—	1.44	—	8.6	15,000	Left shift	Precysts by liver biopsy
14	0.6	0.3	35	6.5 SU	28	34	7.9	2.13	—	10.8	11,300	Normal	Pos. hemagglut.
15	0.4	0.2	11	3.7 SU	17	13	—	1.14	3.72	8.8	11,900	Eosinophilia	Pos. hemagglut.
16	0.5	0.3	13	8.4 SU	26	18	6.3	1.6	2.05	8.4	15,400	Normal	Negative
17	0.8	0.65	24	9.3 SU	34	20	5.0	0.99	—	9.4	14,200	Left shift	Trophozoites in stool

* BU, Bodanski units; SU, sigma units.
† NF, not found.

The BSP retention was 35 percent in 45 min. Protein determination revealed: albumin, 2.13 gm./100 ml., a_2-globulin 1.19 gm./100 ml., and γ-globulin 1.88 gm./100 ml.; the other globulins were normal. The gallbladder and upper gastrointestinal series and the barium enema were normal. The chest X-ray revealed blunting of the right costophrenic angle and an elevated right diaphragm. Liver scan revealed a 10-cm. filling defect in the right lower lobe. An amebic hemagglutination was positive.

A total of 650 ml. of thick, red-brown sterile material was aspirated from his liver on two different occasions. One month later he was asymptomatic, his liver was not felt, and he weighed 134 lb. Three

TABLE 4. *Summary of Symptoms, Signs, and Laboratory Findings*

Parameters	*Patients (%)*
Symptoms	
Weight Loss	100
Pain	100
Pleuritic	47
Right upper quadrant	41
Right shoulder	12
Epigastric	2
Periumbilical	2
Left upper quadrant	2
Signs	
Large tender liver	88
Fever	70
Signs of right pleural effusion	58
Laboratory	
Cold area on liver scan (5 patients tested)	100
Positive hemagglutination test (2 patients tested)	100
Leukocytosis	82
Increased BSP	82
Hypoalbuminemia (16 patients tested)	80
Anemia	75
Elevated alk. phosphatase (16 patients tested)	56
Amebas found (16 patients tested)	31

months later, he weighed 165 lb.; his hemoglobin was 14.2 gm./100 ml.; and he had a white blood cell count of 6200/cu. mm. with a normal differential. His chest X-ray had not changed. His BSP retention was 6 percent in 45 min., and his alkaline phosphatase was 3.7 sigma units.

Discussion

Amebas form single or multiple colonies in the liver sinusoids and then invade the outer areas of the tissue with resulting necrosis. Why amebas produce necrosis and abscess formation is not clear. Jarumilinta and Kradolfer report that *E. histolytica* organisms have proteolytic enzymes. In in-vitro studies, these authors found *E. histolytica* capable of destroying leukocytes, but similar enzymes were found in *Entamoeba coli* and the small "nonpathogenic" race of *E. histolytica.*

Amebic abscess can be fatal, but if recognized it can be safely and effectively treated; therefore, a correct diagnosis is imperative. In our experience, the clinical picture is very characteristic. Isotopic scanning of the liver should be of considerable aid in localizing the lesion, particularly for accurate needle aspiration of the abscess. The diagnosis can be assumed when typical brown or brick-red, relatively odorless sterile fluid is obtained. Ultrasonic hepatograms (echohepatograms) may distinguish abscesses from solid masses, but this test requires more evaluation and use. The hemagglutination test for amebiasis seems promising. An elevated diaphragm or pleural fluid detected with chest X-rays are valuable clues. Stools properly collected after a saline purge and examined fresh, as well as the examination of aspirate from ulcers seen at proctoscopy and tissues removed by rectal biopsy, are helpful in making a definitive diagnosis.

Most reliable, in our and others' experience, is a diagnosis based on the patient's therapeutic response. When an abscess is suspected, the patient should be treated by closed needle aspiration and chloroquine diphosphate (1 gm. b.i.d., for 2 days followed by 0.5 gm. b.i.d. for 3 weeks). Diiodohydroxyquin, 630 mg t.i.d. for 3 weeks, is given to eradicate any amebic colitis. A careful follow-up is desirable, since some patients do not respond to treatment and others become reinfected.

Summary

A 10-year review of 17 patients with amebic abscess of the liver is presented. In our patients, a clinical picture occurred consistently enough to make one strongly suspect amebic liver abscess. Usually, the patient was a male with a 2- to 4-month history of weight loss, and right pleuritic or right upper quadrant pain. During examination, fever, signs of a right pleural effusion, and a large tender liver were found. Once a diagnosis is suspected, definitive steps should be taken to demonstrate an abscess, since this potentially fatal disease is curable.

(The figures and references may be seen in the original article.)

SURGICAL INFECTIONS—PATHOGEN VERSUS HOST

J. Wesley Alexander, MD, J Surg Res 8(5):225–233, May 1968.

Microbial infections continue to be a major problem in surgical practice partly because increasing numbers of patients undergoing operations have "an increased susceptibility to infection" or "a diminished host resistance." Both of these terms, however, serve only to reflect our ignorance concerning the basic physiological derangements involved. The purpose of this presentation is to review briefly the mechanisms of host resistance against bacterial and fungal infection, to classify the deficiencies thereof, and to relate these abnormalities to surgical practice. It is not intended to be exhaustive, and represents only an attempt to stimulate an interest in and an awareness of specific deficiences of host resistance so that they may be dealt with more effectively.

Every surgeon has had the opportunity to observe that massive bacterial contamination can occur without resulting in infection. Open traumatic wounds are frequently encountered in which bacterial contamination is virtually always associated with the injury. In these, and in experimental wounds in which fecal material or bacterial cultures are sometimes used to inoculate the wounds, infection is not always a sequel. Altemeier and Todd have emphasized the relatively low incidence of infection in emergency thoracotomy done without aseptic or antiseptic preparation of either the patient's skin or the surgeon's hands. Even in clean operative procedures, bacterial contamination of surgical wounds is frequent, as can be shown by careful culturing of the wound at the time of surgical closure. Since most individuals with open traumatic or surgical wounds have some degree of bacterial contamination, and relatively few develop overt infections, it is obvious that small numbers of bacteria will not ordinarily overwhelm host resistance mechanisms. To every practicing surgeon, however, it is painfully obvious that an individual patient cannot be depended upon to cope with even minimal uncontrolled bacterial contamination. To understand the reasons for individual variations in susceptibility to infection, we must clearly define host resistance.

Basic Mechanisms of Host Resistance

Common to all higher organisms, we live in what is virtually a sea of bacteria, fungi, and viruses. No portion of our epithelial surfaces is sterile, with the possible exception of the lower respiratory tract, part of the genitourinary tract, and ductal portions of those organs having excretory functions. These epithelial surfaces constitute an amazingly effective barrier against the penetration of bacteria. For the skin this is accomplished by desiccation and by providing a noxious environment high in fatty acids and other antibacterial substances. In the respiratory and gastrointestinal tracts, constant bathing of the epithelium by mucus probably represents the most important barrier to bacterial invasion. Epithelial surfaces, however, are frequently broken with violation of the internal environment of the host by living microbes. When this occurs, a well-defined sequence of events follows which normally provides protection against invasive infection.

Vasoactive mediators, released either from injured tissue, from microbes, or both, produce an initial change in the microvasculature which is usually characterized by constriction of venular sphincters at the junction of the venules and the collecting veins, partially obstructing the flow of blood at this point. This results in increased venular and capillary pressures with dilatation of these vessels and partial separation of the endothelial cells at their junctions. Concomitantly, an alteration of the endothelial surfaces of the venules and capillaries occurs whereby these surfaces become "sticky." Phagocytic cells, the neutrophils and monocytes, flowing through these vessels become adherent to the endothelial membrane upon contact, causing their plasma membranes to acquire an increased adhesiveness. The actively motile phagocytes exit into the extravascular tissues through the intercellular spaces along with an exudation of plasma. If antibodies are present in the exuded plasma which have specificity for the bacterial surface antigens, they will react with these antigens and activate complement. Antibody and complement together serve as opsonins to alter the bacterial surface, making it a more attractive object for ingestion by phagocytes, and in addition, they aid intracellular killing of the bacterium. Chemotactic substances are also released by activated complement which further promote the removal of these bacteria. Once inside a phagocytic cell, bacteria are normally destroyed by a process of intra-

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cellular digestion. Degranulation is an essential step in this process and merely represents emptying of the lysosomal granules, which contain high concentrations of hydrolytic enzymes, into the phagocytic vacuole. Susceptible organisms are thus destroyed and digested by these enzymes. The short-lived neutrophils which usually expend their life-span in the inflammatory lesion play the major role in this process. Mononuclear phagocytes remove dead neutrophils and debris, contribute to antibacterial killing, and, perhaps most important, assimilate antigenic material for transfer to immune component cells which then become committed to the production of specific antibody. Several publications may be of help to those interested in expanding this sketchy review.

Classification of Deficiences

Abnormalities of host resistance occur in a wide variety of conditions encountered in surgical practice. A simple classification of these abnormalities is possible, as shown below, despite the diversity and complexity of the diseases which produce them.

I. Abnormalities of the deposition of phagocytic cells in contaminated foci
  A. Abnormality of mediators
    1. Complement deficiency
    2. Possible factor in old age or prematurity
  B. Abnormality of vascular response
    1. Drug-induced—usual cause, e.g., ethanol, salicylates, opium, cortisone
    2. Radiation-induced
    3. Nutritional deficiencies
  C. Abnormality of blood flow to affected area
    1. Anatomical variations—e.g., pretibial vs. face; fat vs. muscle
    2. Foreign bodies, seromas and hematomas, necrotic tissue
    3. Low flow states
      a. Shock, injury
      b. Drug-induced, such as with vasopressors
      c. Mechanical obstruction

II. Abnormalities involving opsonic substances
  A. Antibody deficiencies
    1. Lack of prior experience—usual cause
    2. Hereditary abnormalities
      a. Agammaglobulinemia—several varieties
      b. Dysgammaglobulinemia—several varieties
    3. Acquired abnormalities
      a. Decreased synthesis—many causes
      b. Consumptive states—occurs with active infection
  B. Complement deficiencies
    1. Hereditary abnormality
    2. Acquired abnormality—usually consumptive but may be drug-induced, especially locally

III. Abnormalities of phagocytic cells
  A. Insufficient production or release, e.g., myelofibrosis; cyclic neutropenia
  B. Abnormalities of phagocytosis
  C. Abnormalities of intracellular killing
    1. Hereditary, e.g., fatal granulomatosis of childhood
    2. Acquired
      a. Abnormal degranulation
      b. Abnormality of lysosomal enzymes—e.g., burn injury
    3. Cyclical variation in normal persons—affects males predominantly

At the turn of the century, Metchnikoff emphasized the importance of phagocytic cells in host resistance. While his views were not accepted by his contemporaries, his monumental work serves as a basis for our present understanding of host resistance, and it is now fully recognized that integrity of the function of phagocytes is essential to providing antimicrobial defense. The development of inflammatory lesions and the production of opsonic substances in all vertebrate animals constitute ancillary mechanisms which aid the system of phagocytic cells.

Abnormalities of the Deposition of Phagocytic Cells in Contaminated Foci

No single biological mediator of the vascular response has been found to be important to the exclusion of others. Numerous mediators have been described ranging from rather simple polypeptides to poorly characterized macromolecular substances derived from tissue extracts. Both histamine and bradykinin are important mediators which produce early permeability changes.

Hageman factor and other plasma proteins such as complement components have been shown to be important in the sustained vascular response associated with leukocyte emigration. Products of the leukocytes themselves have been shown to be a factor in the full development of inflammatory lesions. With the exception of conditions associated with a deficiency of complement, abnormalities of the vascular response associated with deficiences of mediators have not been well defined in clinical circumstances. Inflammatory responses have been found to be abnormal in old age and prematurity, but whether this reflects an abnormality of the vessels themselves or of the mediators inducing vascular change remains unclear.

The reactivity of the vessels to a given stimulus is as important as the nature of the stimulus. Uremia; malignancy; several drugs, including ethanol, salicylates, opium, and cortisone; radiation injury; and severe nutritional deficiences may diminish the responses to an inflammatory stimulus. The mechanisms of action are largely unknown but may affect either endothelial activity or the reactivity of the venular sphincters.

If there is insufficient flow of blood to an affected area, deposition of phagocytic cells may be inadequate even when vasoactive mediators are sufficiently present and the available vessels are capable of

response. Availability of reactive blood vessels is an important consideration since this may vary markedly with anatomical location. Every surgeon knows that lacerations of the face become infected less frequently than lacerations of the pretibial area and that healthy muscle withstands bacterial contamination more readily than adipose tissue. The number of reactive capillary vessels increases progressively at the margin of a wound during the first few days after injury, and increasing numbers of bacteria introduced into a healing incision during the postoperative period are necessary to induce an infection as the healing period progresses. It is by virtue of an increased availability of reactive vessels that a delayed primary closure is effective in preventing infection in bacterially contaminated wounds. Elek showed that approximately 1,000,000 viable *Staphylococci* were necessary to produce an infection in normal humans when introduced either intradermally, subcutaneously, or into a small incision. However, infections ensued when as few as 100 organisms were introduced with a foreign body, in this instance a silk suture. Monofilament suture materials withstand contamination better than multifilament sutures because bacteria can gain entrance into the interstices of the multifilament suture whereas the entrance of phagocytic cells is impaired. Studies in our laboratory have supported the experimental and clinical observations of numerous investigators that virtually any type of foreign body will potentiate the development of infection. Hematomas and necrotic tissues effectively act as foreign bodies in surgical incisions since they do not possess an effective blood supply. Any condition associated with a diminished flow of blood to a contaminated focus effectively reduces the availability of phagocytic cells. Low flow states associated with hemorrhagic shock, massive injuries such as a large thermal injury, the administration of vasoconstrictor drugs such as norepinephrine, and mechanical obstruction of major vessels all have been shown to be associated with an increased susceptibility to bacterial infection.

Abnormalities Involving Opsonic Substances

Both neutrophils and mononuclear phagocytes will ingest microbes in vitro in the absence of detectable serum opsonins, but the presence of these opsonins in optimal quantities markedly promotes their effectiveness. Serum opsonins for practical purposes belong to two groups of serum proteins—antibody and complement. Specific antibody will combine with specific antigens on the surface of a microbial membrane, and the union of antigen and antibody, with certain exceptions depending upon the type of antibody, will activate the nine components of complement. Full activation of the complement system has several important functions in defense against microbial disease, including alteration of the microbe to render it susceptible to phagocytosis and intracellular killing, chemotaxis, immune adherence, release of vasoactive mediators, and lysis of susceptible membranes. In the antibody-complement system, antibody serves largely to provide specificity for the site of activation of complement. Complement can be activated by conditions other than antigen-antibody interaction, but the reaction between antigen and antibody is the only one of practical importance for our discussion. Other serum components with antibacterial properties are probably of little importance in vivo.

The susceptibility to infection of man and experimental animals having deficiences of antibody is well known. Lack of prior experience with a given antigenic stimulus is the most common cause of antibody deficiency but cannot be considered to be an abnormality since it represents the natural state of a nonimmunized animal. Hereditary abnormalities of antibody synthesis are relatively uncommon, but there are several varieties of agammaglobulinemia and dysgammaglobulinemia which should be suspected in patients with recurrent infections for which no other cause can be found. Acquired abnormalities of antibody synthesis may also arise from a variety of causes ranging from diminished synthesis in acquired idiopathic hypogammaglobulinemia or malignant conditions of the lymphoid tissues to consumptive states associated with active infections. Acquired abnormalities are encountered much more frequently in surgical practice and deserve particular consideration.

Abnormalities of the complement system may also be a causative factor in the development of infection. The hereditary deficiencies that occur in man are not associated with a susceptibility to infection. This seeming variance with our established concept of complement function occurs because full expression of membranolytic activity by complement need not be present for the full expression of activity related to phagocytosis and intracellular killing. Our own preliminary observations would indicate that C'1 is more important for potentiating phagocytosis and intracellular killing than other components. Acquired abnormalities of complement function are usually of a consumptive nature such as may be present with massive burn injury, infection, and

certain immunological disorders. Probably of greater importance to the surgeon is the observation that complement activity may be inhibited at local sites by a variety of agents which have an anticomplement activity. Among these are free hemoglobin and a variety of polysaccharides including mucin and heparin.

Abnormalities of Phagocytic Cells

Phagocytic cells are present in every animal from man to the lowly ameba, in which such a cell constitutes the entirety of the organism. Metchnikoff, in a very clear and careful study of their phylogenetic development, pointed out that these cells retain their digestive properties throughout the animal kingdom. With the development of a hematopoietic system, a new type of phagocyte arose, the polymorphonuclear granulocyte. Not surprisingly, specific opsonins which evolved with the primitive vertebrates, influence phagocytosis and intracellular digestion of bacteria by granulocytes more than by mononuclear phagocytes. As in all higher vertebrates, there are two classes of phagocytes, the mononuclear phagocytes and the granulocytes. The neutrophilic granulocyte has the greatest responsibility in the initial defense of the host against microbial infections. Its importance in this role cannot be overemphasized, for in the absence of neutrophils the host will soon die of overwhelming sepsis. Mononuclear phagocytes of both wandering and fixed types also ingest and kill bacteria but do so much less efficiently. Two major functions of mononuclear phagocytes are processing of antigen and removal of effete or dead cells. It has often been stated that the mononuclear phagocytes of the fixed reticuloendothelial system are the primary line of defense against organisms introduced systemically, such as by the intravenous route. Ordinarily, bacteria are presented to the host in this manner only after a primary infection becomes established. Because of the striking correlation of abnormalities of neutrophils to the development of primary infections, these deficiencies will be discussed in this presentation. It has not been determined whether or not abnormalities of neutrophils and mononuclear phagocytes regularly coexist.

Susceptibility to microbial infection is found in a wide variety of conditions associated with neutropenia. Whether severe and prolonged neutropenia is caused by displacement of the marrow by myelofibrosis, by drug administration, by cyclic neutropenia, or by injury such as massive irradiation, the usual end result of overwhelming infection is the same. When neutropenic conditions persist, the host finds itself in the same position as an army with an inadequate supply of ammunition.

Even if the number of phagocytic cells is adequate, they must be deposited in sufficient numbers at a site of contamination, and they must be capable of phagocytosis and intracellular digestion. Abnormalities of phagocytosis and intracellular killing by human neutrophils can be measured separately by an in vivo test recently described by Alexander, Windhorst, and Good. In patients thus far studied, deficiences of ingestion (phagocytosis) have been encountered infrequently, and the diseases associated with this type of defect have not been well defined. However, abnormalities of intracellular killing of ingested bacteria are frequent. These deficiences may be inherited or acquired. Fatal granulomatosis of childhood is an inherited sex-linked disease, carried on the X-chromosome, which is accompanied by a severe susceptibility of the affected male child to infection. Physiologically, the disease is characterized by a defect in degranulation and an inability to kill ingested bacteria. This abnormality is a serious one, and no child so affected has lived to adulthood. Acquired disorders of intracellular killing may result from abnormalities of degranulation or deficiencies in the quality or quantity of the lysosomal enzymes. Defective degranulation was once felt to be a contributing factor to an increase in susceptibility to infection in individuals treated with high doses of steroids, since these agents have a stabilizing effect on isolated lysosomal membranes in vitro. In our laboratory we have been able to demonstrate only slight abnormalities of neutrophil function in leukocytes exposed directly to steroids in vitro or in leukocytes taken from both patients and experimental animals treated with relatively high doses of steroids. Similar findings have been reported by Hirsch and Church. Undoubtedly, inhibition of degranulation could occur in a variety of acquired conditions, but these have not yet been defined, and our test of function does not allow this distinction. Likewise, the diseases associated with deficiencies of specific lysosomal enzymes have not been well defined, but it has been shown in patients with severe burn injury that selected lysosomal enzymes of neutrophils become abnormally low. The greatest degree of deficiency occurred between the sixth and tenth postburn day, at a time when this group of patients is particularly susceptible to infectious complications. Subsequent studies have shown that the degree of abnormality of intracellular killing by the leukocytes of patients with severe thermal injury paralleled that

which could be anticipated from the enzyme deficiencies demonstrated previously.

Our studies on neutrophil function during the past year have uncovered an unexpected finding which may be of considerable importance in defining abnormalities of host resistance in surgical patients. In serial observations of the function of cells from a normal individual who was used repeatedly as a control, it was noted that the cells occasionally failed to function as well as might be expected. At first this appeared to be an eccentricity of the test, but when the tests were plotted as a function of percent of the initial inoculum killed during a specified period of incubation, there appeared to be a cyclical variation in the function. Subsequently, a study was planned whereby neutrophil function tests were to be performed three times weekly for a period of six weeks on 3 adult men and 3 adult women. The study was incomplete because of unscheduled absences, but, nevertheless, a great deal of information was obtained. Each of the women was studied during mid-cycle and at the beginning of their menstrual periods. The neutrophil function of each of these individuals was compared with the neutrophil function of the remaining persons for each day, expressing this as a ratio of the remaining viable bacteria in the tests without antibiotics for the individual compared with the average for the group. Each of the men in the study showed clear evidence of a cyclical variation in neutrophil function. This variation was associated with abnormalities of both phagocytosis and intracellular killing. In one individual the poor function was related more clearly to diminished phagocytosis, while in another it was related more clearly to an abnormality of intracellular killing. One of the subjects was able to relate the variation in neutrophil function to a fluctuation in libido, the latter increasing as the efficiency of killing of bacteria by his neutrophils diminished. This observation suggests that neutrophil function may be hormonally regulated. It is well established that serious infections occur more frequently in males of all age groups than in females. A cyclical variation of neutrophil function which predominantly affects males could explain this increased susceptibility. In addition such a variation could contribute to the development of infection in individuals undergoing clean surgical procedures. It is apparent, however, that additional information must be obtained before these hypotheses can be established as facts.

Diagnosis and Evaluation

Three questions deserve consideration in an evaluation of a patient who appears to have an increased susceptibility to infection or an evaluation of etiological factors responsible for the development of an unexpected surgical infection: (1) Is there a sufficient number of normally functioning phagocytic cells; (2) Can they be mobilized to the area of bacterial contamination; and (3) Are there sufficient opsonins to aid the phagocytes in the removal and destruction of bacteria? A few simple tests are help-

TABLE 1. *Selected Conditions Associated with Abnormal Host Resistance*

Disease or Agent	Abnormality of Inflammatory Lesion	Abnormality of Opsonin	Abnormality of Phagocyte
Shock	+	−	−
Traumatic injury, massive	+	±	+
Prematurity	+	+	+
Old age	+	±	?
Steroid treatment	+	±	+
Azathioprene	?	±	+
Narcotics	+	−	−
Ethanol	+	−	−
Salicylates	+	−	?
Foreign bodies, necrotic tissue, seromas and hematomas	+	−	−
Vasopressors	+	−	−
Hypogammaglobulinemia	−	+	−
Malignant condition	±	±	±
X-irradiation	+	+	±
Mucin (local) and other anticomplement agents	?	+	−
Multiple vitamin deficiency	+	+	?
Diabetes	+	−	+
Uremia	+	−	−
Obesity	+	−	−
Fatal granulomatosis of childhood	−	−	+
Neutropenia (any cause)	−	−	+

ful in detecting and defining any existing abnormalities. The number of available phagocytes can be determined simply by a leukocyte count and differential. Bactericidal function of the neutrophils can be measured by the recently described neutrophil function test, which further differentiates between abnormalities of phagocytosis and defects in intracellular killing. The neutrophil function test can also be used to detect deficiencies of serum opsonins by using patient serum as the source of opsonins in comparative tests with normal cells. Serum electrophoresis and measurements of hemolytic complement can also be used as tools for screening abnormalities involving serum opsonins. Measurement of the ability of an individual to mobilize phagocytic cells to sites of injury is much more difficult. The skin window technique can be used to detect qualitative differences in cellular exudates, but no acceptable quantitative tests are available which can be used in humans. Other techniques, such as the rabbit ear chamber and inflammatory pouches, have provided valuable information in experimental animals. By combining these few tests with a judicious clinical evaluation the presence and nature of an abnormality may be detected in the majority of instances.

Table 1 lists several selected conditions associated with abnormal host resistance, and a categorization of the types of abnormalities caused by each. The major types of abnormalities, in most instances, can be further characterized as listed earlier.

Summary

An attempt has been made to present a useful classification of the etiological factors in the development of surgical infections. The role of the host has been emphasized, but the author in no way wishes to draw attention away from the importance of strict adherence to aseptic and antiseptic principles.

A few simple tests combined with a thorough clinical evaluation will usually detect the nature of abnormalities of host resistance. A newly developed test for measuring neutrophil function appears to be particularly useful. A cyclical variation in the neutrophil function of healthy persons has been discovered which may be of importance in the pathogenesis of unexpected infections.

(The figures and references may be seen in the original article.)

LIVE, ATTENUATED RUBELLA-VIRUS VACCINE *

Maurice R. Hilleman, PhD, DSc, Eugene B. Buynak, PhD, Robert E. Weibel, MD, and Joseph Stokes, Jr., MD, DSc, New Eng J Med 279(6):300–303, August 8, 1968.

High priority is being given in the United States and Europe to the development of an effective live, attenuated rubella (German-measles) virus vaccine. To be acceptable, a rubella vaccine should cause little if any clinical reaction, should induce lasting immunity in essentially all recipients, should be noncontagious to susceptible contacts, especially pregnant women, and should be prepared with the use of a safe and acceptable cell culture.

First studies by our group of a highly purified and concentrated killed rubella-virus vaccine showed development in children of heat-labile (56°C) neutralizing antibodies that were not protective on challenge with live virus. Reports by others of preparation of immunogenic killed rubella-virus vaccines remain to be confirmed. Problems of low potency, short duration of immunity after killed myxovirus vaccines and untoward clinical reactions in natural rubeola among children who had previously received killed virus vaccine diverted interest almost entirely to the live-virus approach for rubella vaccine.

Cell Cultures and Virus Strains

Rubella virus propagates well in a variety of cell cultures, and at least four different virus strains are known to have been attenuated for man. Hence, the field has not wanted either for viruses or for means for propagation. Most notable progress has been made to date by four groups of workers using the cell-virus systems shown in Table 1. Our group employed the Merck (Benoit) strain and the Meyer-Parkman (HPV-77) strain grown in duck-embryo cells; Meyer and his co-workers used their HPV-77 and HPV-120 rubella viruses grown in grivet-monkey-kidney (77 and 120 passages) and in dog-kidney (HPV-77 and 12 additional dog-kidney passages). Peetermans et al. used the Cendehill strain grown in rabbit kidney cells and Plotkin and his associates tested RS 27/3 virus propagated in the human diploid WI-38 cell strain. Various incubation temperatures were employed for propagating the viruses in cell culture.

TABLE 1. *Principal Cell Cultures and Virus Strains Used to Prepare Rubella Vaccines*

Cell Culture *	Virus Strain
Duck embryo	Merck
	HPV-77
Grivet-monkey kidney	HPV-77 & 120
Dog kidney	HPV-77
Rabbit kidney	Cendehill
WI-38 (diploid human cell strain)	RA 27/3

*All primary cell cultures except WI-38.

All four strains appear to be potentially acceptable for vaccine purpose. More important, perhaps, is the matter of cell used to prepare the vaccine. This is subject to differences in judgment based, in part, on precedent for use in existing vaccines and on individual preference or prejudice. Unfortunately, the commonly employed chick-embryo cell culture permits only limited proliferation of rubella virus and the adaptation to these cells effects rapid overattenuation, with resulting reduction in immunogenicity for man. Monkey-kidney cells are used to prepare poliovirus and adenovirus vaccines, and dog-kidney cells to prepare rubeola vaccine. Rabbit and duck tissues are used to prepare rabies vaccines, though not in cell culture. Serially propagated cells, such as WI-38, are not presently licensed for vaccine use. Historically, animal cells and cultures have been found to harbor a variety of viruses, some of which are oncogenic, but no evidence of harmful effect from use in man has been found to date. All such extraneous agents discovered in vaccines to date have been eliminated. Our interest in duck-embryo cells arose because of the relatively long gestation period of the duck, as compared with chick, which appeared to permit and to promote virus growth in more primitive cells, because duck cells are of nonmammalian origin and because spontaneous neoplasms of Pekin ducks (the breed that supplied eggs used to prepare our vaccine) are rare.

Vaccines prepared for clinical testing are generally assayed for infectivity, identity, and safety along the guidelines established by the United States Public Health Service for live rubeola-virus vaccine. Additionally, in vivo and in vitro marker tests for attenuation have been applied.

* From the Division of Virus and Cell Biology Research, Merck Institute for Therapeutic Research, West Point, and the Department of Pediatrics, University of Pennsylvania School of Medicine, Philadelphia (address reprint requests to Dr. Hilleman at the Division of Virus and Cell Biology Research, Merck Institute for Therapeutic Research, West Point, Pa. 19486).

Clinical Trials

Duck-Embryo Vaccines

Our first studies were undertaken for the purpose of developing an attenuated rubella virus for use in man that would cause no clinical illness, would not be excreted from the pharynx, would not be contagious to susceptible contacts and would induce high antibody titers in essentially all vaccinated persons. The vaccines shown in Table 2, which represented various levels of attenuation for man, were dried and given subcutaneously, and the infectivity titers were $10^{-1.5}$ to $10^{-2.9}$ per 0.1 ml. Controlled clinical tests were carried out among children in institutions. Blood samples for hemagglutination-inhibition (HI) titrations were taken just before vaccination and 60 days later. This period was ample to measure primary antibody response in the vaccinated children, and in contact controls as well, if transmission had taken place.

The clinical testing began on January 25, 1965, and was carried out among children in institutions. Vaccine at attenuation level A caused very mild clinical rubella with rash, lymphadenopathy and low fever—the temperature did not exceed 102°F by mouth. Antibody developed in all the recipients. Furthermore, they excreted the virus, and this was contagious to contacts, two of whom had clinical signs of rubella.

Further passage of the virus to provide levels B through E eliminated all illness in vaccinated susceptible children and contagion to susceptible contacts. However, such passages were increasingly at the expense of antibody response. Level E appeared desirable in that it failed to cause pharyngeal excretion of virus, but the antibody responses were inadequate. The findings in these tests have been confirmed by Drs. Harry M. Meyer, Jr., and Paul D. Parkman and their co-workers and by Dr. Saul Krugman and his associates.

The important conclusion from these data was that virus excretion seemed to be a necessary attribute for rubella vaccine if adequate immunity was to be achieved. However, there was no inherent danger in such excretion since B-level and further passage vaccines were not contagious to susceptible contacts. B-level Merck vaccine was judged optimal in eliciting highest antibody titers without causing illness or contagion. Tests of Meyer-Parkman HPV-77 virus serially passaged five times in duck-embryo culture showed results comparable to B-level or C-level Merck-strain vaccine.

The duck-embryo vaccines were then considered worthy of clinical trial in the open community. During September and October, 1966, 265 rubella-susceptible children in families were vaccinated in the Havertown-Springfield suburb of Philadelphia using HPV virus grown five passages in duck embryo. None of the children had clinical signs or symptoms referable to the vaccine. As shown in Table 3, 97 percent of the children developed rubella antibody with a geometric mean HI antibody of 53. Most important, none of 262 susceptible sibling contacts and none of 34 susceptible mothers (three of whom were pregnant) who were in contact with their vaccinated children developed rubella antibody. This study was of greatest importance in establishing the lack of spread from vaccinated person to susceptible contact and opened the way to the mass vaccination programs among children in families and schools now being undertaken in the United States and abroad.

The findings in a study of the Merck B-level vaccine prepared in duck cells that was carried out in

TABLE 2. *Influence of Cell Culture Passage of Rubella Virus on Virulence and Immunogenicity*

Virus Strain	Attenuation			Clinical Result		HI-Antibody Response			Dates of Tests
	Level	Passages		Rubella Illness	Pharyngeal Virus	Vaccinated		Contact Controls	
		grivet kidney	*duck embryo*	(%)	Recovery (%)	*conversion rate* (%)	*geometric mean*	*conversion rate* (%)	
Merck *	A	11	10	86	100	100	156	86	1/25/65
	B	19	20	0	67†	100	323	0	1/14/66
	C	11	20	0	25†	92	39	0	6/30/66-6/13/67
	D	11	25	0	41	83	14	0	6/13/67
	E	11	30	0	0	65	9	0	3/17/67-5/11/67
HPV-77	—	77	5	0	100	100	64	0	6/13/67

* Also passed 1 time in embryonated eggs.
† Possibly low owing to insensitivity of cultures used to detect virus.

TABLE 3. *Large-Scale Controlled Study of HPV-Strain Rubella Virus in Duck-Embryo Cell Culture among Children in Families*

Initially Seronegative Groups	Rubella HI-Antibody Response			
	Cases in which Antibody Developed *	Total	Sero-conversion Rate (%)	Geo-metric Mean Titer †
Vaccinated children	256	265	97	53
Sibling contact (controls)	0	262	0	0
Mothers (controls)	0	34	0	0

* Interval between bleedings 8 wk.
† Reciprocal of serum dilution.

an institution are shown in Table 4. The findings were similar to those obtained with HPV virus in duck cell culture except for the greater mean antibody titer obtained with the Merck-strain vaccine—namely, 148 versus 53.

Monkey-Kidney and Dog-Kidney Vaccines

Meyer and Parkman and their colleagues initiated clinical trials of their HPV-77 virus grown in cell cultures of grivet-monkey kidney in October, 1965. Their initial studies, which have since been considerably expanded, were carried out primarily among retarded children in an institution. These workers recorded inoculation of 200 susceptible persons with HPV-77 monkey-kidney virus, 27 with HPV-120 monkey-kidney virus and 40 with HPV-77 virus that had been passed an additional 12 times in dog-kidney cells. The antibody responses were excellent, causing seroconversion in 95 to 100 percent of recipients. Illness did not occur in the vaccinated children, and none of 213 susceptible contacts developed antibody, indicating lack of contagion even though all the vaccines were shown to cause excretion in 72 to 92 percent of recipients.

Most important, Meyer and Parkman challenged 10 children by the nasal route with virulent rubella virus of human origin. None of five persons who had been vaccinated with HPV-77 virus became ill or excreted the virus whereas, by contrast, all of five unvaccinated controls did. These findings established the protective efficacy of the vaccine and the association between circulating rubella antibody and immunity.

Rabbit-Kidney Vaccine

Peetermans et al. developed a high passage (51st passage) Cendehill-strain vaccine in rabbit-kidney cell culture. In 13 initially seronegative infants given the vaccine rubella antibody developed in high titer without accompanying illness. Rubella antibody was not found in the serums of susceptible contacts taken six weeks after vaccine was given. Serum samples of contacts taken two months after vaccine was given would have been more assuring in proving lack of contagion. Tests for virus excretion were not reported.

Human Diploid Cell (WI-38) Vaccine

Plotkin et al. tested in children various passage levels of RA 27/3 rubella virus grown in WI-38 cells. In all of 17 susceptible children in institutions given 21st-passage or 25th-passage virus antibody developed, and one showed clinical rubella with rash and lymphadenitis. Virus excretion was reported in only a small portion of the children. None of seven susceptible contacts displayed rubella antibody in serums taken six weeks after 21st-passage virus was given. More data will be required to establish, conclusively, the excretion rates and lack of contagion.

TABLE 4. *Controlled Study of B-Level Merck-Strain Rubella Virus in Duck-Embryo Cell Culture among Children in an Institution*

Initially Seronegative Groups	Rubella HI-Antibody Response			
	Cases in which Antibody Developed *	Total	Sero-conversion Rate (%)	Geo-metric Mean Titer †
Vaccinated children	33	33	100	148
Contacts (controls)	0	11	0	0

* Interval between bleedings 8 wk.
† Reciprocal of serum dilution.

Discussion

The last major epidemic of rubella that occurred in the United States (in 1964) was estimated to have caused congenital defects in about 20,000 infants and to have caused a similar but unknown number of fetal deaths. The next large-scale epidemic might be expected to occur within two or three years. Testing of rubella-virus vaccines has now reached a high level. With such an advance, and barring unforeseen problems, rubella vaccine seems on the horizon. Judicious application of the vaccine might help to forestall the next expected epidemic of rubella, with its anticipated high toll in infant deformity.

(The references may be seen in the original article.)

MEDICAL ABSTRACTS

MENTAL SYMPTOMS AS AN AID IN THE EARLY DIAGNOSIS OF CARCINOMA OF THE PANCREAS

I. Fras, MD, E. M. Litin, MD, and L. G. Bartholomew, MD, Gastroenterology 55(2):191–198, Aug 1968.

The incidence, character, and differential diagnosis of the mental symptoms associated with carcinoma of the pancreas are presented on the basis of a study of 46 patients with this diagnosis and 79 control patients. These mental symptoms, consisting of depression, anxiety, and feelings of premonition of serious illness with several specific features, are frequent and can be used as an aid in the early diagnosis of carcinoma of the pancreas. Careful history taking and awareness of the specific aspects of the mental symptoms in carcinoma of the pancreas are necessary to distinguish carcinoma of the pancreas from certain psychiatric problems.

URTICARIA AND ANGIOEDEMA

J. S. Thompson, MD FACP, Ann Intern Med 69(2):361–380, Aug 1968.

Urticaria may be the sole symptom of a minor reaction or it may be a manifestation of a progressive, fatal connective tissue or neoplastic disease. At least five basic pathogenetic pathways may initiate histamine release from mast cells. These are complement factors; chemical liberators; immunologic mechanisms; biologic, physical, and neurogenic factors; and general modifying phenomena. The interrelationship of these pathways has been shown, particularly stressing the potential significance of chemical liberators and complement-mediated events in several mechanisms. Implication that hormonal and neurohumoral substances may modify the entire mast-cell degranulating system has been entertained as important speculation awaiting confirmation.

Diagnosis and therapy is discussed using these principles. In addition to a careful history and physical exam, determination of blood eosinophiles, total complement activity, quantitation of isolated complement components, selected skin tests, elimination regimes, and controlled provocative tests may be useful in individual cases.

Although antihistamines constitute the principal means of therapy, their method of action impairs an early effect, and beta adrenergic amines must be given when stock or potentially fatal angioedema occur. Corticoids and immunosuppressive agents may be necessary for control in some of the serious underlying disorders. Three modes of experimental therapy are also discussed.

FLUID AND ELECTROLYTE BALANCE IN PENETRATING HEAD WOUNDS

LCDR P. J. Pitlyk, MC USNR and LCDR G. S. Moss, MC USNR, Surgery 63(3):396–409, Mar 1968.

The dependence of the body upon a constant extracellular volume and osmolal concentration for the continuance of its varied metabolic and physiologic activities is readily appreciated. The mechanism by which this is maintained within narrow limits has been the subject of investigation, with the result that these processes are now partly understood. Additionally, observed deviations in fluid and electrolyte relationships subsequent to surgery and trauma have been studied, and some conclusions elucidating the mechanisms have been drawn. Moore and coworkers have contributed much to the understanding of this subject in both the healthy and diseased state.

Fluid and electrolyte disturbances uniquely associated with head injuries are known, and explanations for the various patterns manifested have been offered. Some of these as pointed out by Wise are related to fluid management, while others reflect the responses known to occur following bodily insult. Still others, though, escape explanation.

Since serum electrolyte values reflect the concentration rather than absolute content, quantitative information is lacking. Balance studies add this dimension and supply data regarding net gain, loss, and total body amount of the electrolytes and fluid.

During the current hostilities in Southeast Asia, the authors were assigned to the U.S. Naval Hospital near Da Nang, where battle casualties were brought by evacuation helicopter within a short time (50 percent in less than three hours after injury) for both resuscitation and definitive management of neurosurgical conditions. Balance studies on fifty missile-inflicted head wounds for the purpose of studying fluid and electrolyte behavior in response to them

were carried out. Admittedly, study conditions were not ideal in this forward facility, but data in forty cases were complete enough for inclusion in this report.

THE USE OF FLUORESCENT ANTIBODY METHODS FOR THE DETECTION AND IDENTIFICATION OF ACTINOMYCES SPECIES IN CLINICAL MATERIAL

C. H. Blank and L. K. Georg, J Lab Clin Med 71(2):283–293, Feb 1968.

This study was undertaken to evaluate the use of the FA technique for the direct detection and identification of Actinomyces species in tissue or exudate smears. Human tonsils, removed at routine tonsillectomies, were used as the clinical material. FA reagents, previously shown to be specific for the various Actinomyces species, were used as test agents. Results indicated that the FA technique provided rapid and specific evidence for the presence of several Actinomyces species in clinical material, thus fulfilling the objectives of the experiment. The test was helpful also in monitoring for the presence of Actinomyces species in culture media containing mixed bacterial flora obtained from the tonsillar material. Finally, it provided a definitive identification of the Actinomyces species which were isolated in pure culture.

EXTRA-ADRENAL PHEOCHROMOCYTOMA: LITERATURE REVIEW AND REPORT OF A CERVICAL PHEOCHROMOCYTOMA

J. G. Fries, MD, and J. A. Chamberlin, MD, Surgery 63(2):268–279, Feb 1968.

Pheochromocytomas are functionally active tumors of sympathetic nerve cells that most commonly occur in the adrenal medulla but can also develop in extra-adrenal sites. These tumors produce epinephrine and norepinephrine, and thus cause sustained or paroxysmal hypertension. Their incidence in all hypertensive patients is estimated at 0.5 to 0.7 percent. They actually represent one of the few forms of hypertension which can be corrected. Annually, 800 deaths from pheochromocytomas are reported in the United States. In patients with unrecognized pheochromocytomas, surgery of any type or for any reason can be associated with a mortality rate of approximately 50 percent. Such tumors are certainly not rare, and newer diagnostic tests and safer techniques for removal have taken them out of the category of necropsy curiosities.

DENTAL SECTION

EVALUATION OF THE STIMULATION OF OSTEOGENESIS BY HOMOGENOUS FREEZE-DRIED BONE

LCDR P. W. Connole, DC USN, and LCDR D. J. Smith, DC USN.

Freeze-dried bone homografts have proved clinically successful in the contaminated environment of the oral cavity, but it is not known whether freeze-dried bone stimulates osteogenesis or acts only as a compatible, resorptive space filler. The purpose of this study was to evaluate the effect of freeze-dried bone homografts on osteogenesis in dogs. For comparative study of the rate and quality of osseous healing, two 8-mm defects were trephined in each side of the mandibles of five dogs. One defect on each side was filled with cancellous freeze-dried bone while the adjacent defects, which served as controls, were allowed to heal spontaneously. Homogenous freeze-dried bone was found to be a compatible grafting material in dogs, and no histological evidence of rejection was noted. Clinical evidence of healing was correlated with histological evidence of actual bone deposition. Although gross examination and radiographic appearance gave a clinical impression that more repair had occurred in the grafted defects, in all cases histological examination revealed evidence of more bone deposition in the spontaneously healed defects. It was concluded that freeze-dried homogenous bone should be used to obliterate large defects but not to stimulate osteogenesis.

(Abstract by Research Work Unit: MR005.19-6052 by LCDR P. W. Connole, DC USN, and LCDR D. J. Smith, DC USN.)

The opinions and assertions contained herein are those of the authors and are not to be construed as reflecting the views of the Navy Department or the naval service at large.

RECURRENT APHTHOUS STOMATITIS

Arch Derm 97:30, Jan 1968.

Recurrent aphthous stomatitis is often associated with trauma, stress, chemical irritants, and, in women, hormonal changes. Infection with herpes simplex virus does not cause recurrent aphthous stomatitis. Recently Graykowski et al have suggested that a pleomorphic transitional L-form of an alpha-streptococcus plays a role in the pathogenesis of this disease. They recovered pure cultures of these organisms from both intact and biopsied lesions and observed compatible organisms in 93 percent of biopsy specimens (compared with 40 percent in nonaphthous lesions and 47 percent in normal oral mucosa). They found that tetracycline administered both locally and systematically was the most effective treatment. In women with premenstral exacerbation of aphthae Bishop et al reported improvement or remission with estrogens administered orally in a dosage sufficient to prevent ovulation. Topical corticosteroids are also effective for existing lesions. However, topical administration of neither corticosteroid or tetracycline prevents recurrences.

(Abstracted by: CAPT George H. Green, DC USN.)

PERSONNEL AND PROFESSIONAL NOTES

Christmas Greetings

Again the excitement of the happy season of Christmas is with us. May the true Christmas spirit bless all who are striving for a just and honorable peace. Christ gave freely and unselfishly of himself. Let us ennoble ourselves with thoughtful prayers and actions characterized by a genuine concern for those in need.

May the spirit of this Yuletide Season abide upon the officers, enlisted personnel and civilians of the Naval Dental Corps, their families and loved ones.

Merry Christmas and a Happy Year.

E. C. RAFFETTO
Rear Admiral, DC, USN
Assistant Chief of the Bureau of Medicine and Surgery (Dentistry) and Chief, Dental Division

LONG COURSES AT CIVILIAN UNIVERSITIES

The Dental Training Committee convened in the Bureau of Medicine and Surgery in September to select dental officers for long courses of instruction at civilian universities in Fiscal Year 1970. Thirty-two dental officers were selected and recommended for approval.

Long Courses at Civilian Universities—Approved (32)

Oral Surgery Training
Approved (5)

1. LCDR T. E. Bollinger
2. LCDR L. P. Chandler, Jr. (continuation)
3. LCDR P. C. Charbonneau
4. LCDR H. C. Howarth
5. LCDR T. N. Salmon

Prosthodontics Training
Approved (4)

1. LCDR R. A. Hesby
2. LCDR J. C. Kelly, Jr. (continuation)
3. LCDR G. E. Monasky (continuation)
4. LT D. R. Morris

Periodontics Training
Approved (7)

1. LCDR P. B. Carroll (continuation)
2. LCDR R. C. Jann
3. LCDR T. F. Kravets
4. LCDR T. E. Muir
5. LCDR J. R. Sconyers
6. LCDR R. J. Stepnick (continuation)
7. CDR J. E. Williams, Jr.

Endodontics Training
Approved (6)

1. CDR J. H. Burke (continuation)
2. LCDR R. E. Cassidy
3. LCDR F. H. Kellner (continuation)
4. LCDR P. C. Lehman
5. LCDR G. M. McWalter
6. LCDR O. T. Watkins

Operative Dentistry Training
Approved (2)

1. LCDR J. V. Gourley (continuation)
2. LCDR P. P. Hatrel

Oral Medicine
Approved (1)
1. LCDR C. J. Smith

Oral Pathology
Approved (3)
1. CDR R. L. Corio (continuation)
2. LCDR B. E. Crawford, Jr. (continuation)
3. LCDR J. M. Foley

Orthodontic Training
Approved (2)
1. LT J. H. Harnett
2. LCDR J. L. Heibel, Jr. (continuation)

Dental Education Training
Approved (1)
1. CDR H. C. Pebley

Public Health/Preventive Dentistry
Approved (1)
1. LCDR J. E. Vaught

U.S. NAVY AND OLD DOMINION COLLEGE TO TRAIN DENTAL HYGIENISTS AND ASSISTANTS

At a signing ceremony recently in the office of the Commanding Officer, Naval Dental Clinic, Norfolk, Virginia, Old Dominion College and the U.S. Navy effected an agreement whereby students in the College's dental hygiene and dental assistant programs will obtain part of their training at the Naval Dental Clinic.

Signing the agreement for Old Dominion College was Edgar A. Kovner, Dean of the Division of Technology. Rear Admiral Maurice E. Simpson, DC USN, Director of Dental Activities, Fifth Naval District, signed for the Navy. Also in attendance was Doctor Gene W. Hirschfeld, Chairman of the Dental Hygiene Department at Old Dominion and Captain Joseph F. Link, DC USN, Executive Officer of the Naval Dental Clinic.

Doctor Hirschfeld, commenting on the agreement, stated that the affiliation is similar to the part of student nurses training that is obtained in hospitals throughout the country. "All members of a health services team must learn to apply academic knowledge in the actual treatment situation. Our hygienist and dental assistant students will gain clinical experience at the Naval Dental Clinic in their role as a member of the dental health team. They will assist dental officers and work with oral hygienists, dental assistants, dental laboratory technicians and X-ray technicians in all the specialties of dentistry."

Rear Admiral Simpson said, "The responsibilities of dental auxiliary personnel, such as hygienists and dental operating room assistants, are increasing rapidly as the dental profession endeavors to find ways to make more treatment available for our increasing population. We are pleased to know that our affiliation with Old Dominion College will contribute to the training of a future supply of auxiliary dental personnel for the Hampton Roads Area including the several naval installations."

JAPANESE DENTIST VISITS NAVAL DENTAL SCHOOL

Doctor Katsuyasu Yamaguchi, an instructor in Pedodontics at the Kanagwa Dental School, Yokosuka, Japan, recently visited the Naval Dental School, Bethesda, Maryland. Doctor Yamaguchi is presently visiting dental schools throughout the United States.

Prior to his arrival in the United States, the doctor spent three months in Peru, South America, on an archeological expedition with the Tokyo Dental College Mountaineering Club.

Doctor Yamaguchi lives in Yokohama. His father, also a dentist, practices in Shemabara City, Nagasaki Prefecture, on the island of Kyushu. His brother is in his sixth year of study at the Tokyo Dental College.

The Naval Dental School is commanded by CAPT William C. Wohlfarth, Jr., DC USN. CAPT Wohlfarth previously was Commanding Officer of the U.S. Naval Dental Clinic, Fleet Activities, Yokosuka.

NURSE CORPS SECTION

THE IMPORTANCE OF EMOTIONAL SUPPORT IN THE INTENSIVE CARE UNIT

The following comments are by LTJG Margaret A. Murray, NC USNR, stationed at the Naval Hospital, Newport, Rhode Island. LTJG Murray attended the short course on Intensive Care Units and Recovery Room Nursing held at the National Naval Medical Center, Bethesda, Maryland earlier this year.

Nursing has become increasingly specialized, more scientific, more efficient, and more administrative. It has also tended to become less personal and nurses have tended to withdraw from the bedside into the nursing station.

"The primary purpose of an intensive care unit is to provide high-level nursing care for patients who require continuous, comprehensive observation and detailed intensive care in an atmosphere of compassion and understanding." Both the medical and nursing staff on a busy intensive care unit often seem to emphasize and to value physical care the most. We find ourselves involved in giving expert physical care but tend to overlook a very important part of what is meant by intensive care—that of meeting the emotional needs of a patient, as well.

Not only are we involved in meeting the physical needs of the patients but we are often tied down by a great deal of paper work which is no doubt necessary but very often a hinderance.

"Separation from the normal life situation associated with the stress of illness or disability is likely to produce tension, anxiety, and fear in anyone who is admitted to the hospital but is intensified for the patient in the intensive care unit." The patient is housed in a strange and threatening environment. The nature of the equipment, the number of personnel and the constant activity of numbers of people hovering over him or other patients may create an illusion of constant crisis.

Dealing with a patient's emotional problems in the intensive care unit is an essential part of good physical care. A patient's psychological response to emotional stress, often affects his physical condition.

It is during times of critical physical problems that a patient's emotional reactions are likely to be acute and overwhelming. Much of his fear is intensified for he is, indeed, seriously ill. Therefore, the nurse in the intensive care unit must be able to respond to signs of emotional distress as well as to signs of physical distress.

Let us consider, for instance, the emergency admission of a patient with acute myocardial infarction. During the first hour of the patient's hospitalization the doctor must make an initial examination, and electrocardiogram will be taken, blood drawn for analysis, probably oxygen will be started, the patient may be placed on a cardiac monitor, and medications given for pain. During all these activities the nurse is expected to admit the patient, care for his belongings, get him settled as comfortably as possible in bed, care for the needs and questions of the family or perhaps even assist in contacting the family if the admission was without their knowledge. The nurse must also communicate with other hospital departments whose services are needed. All of these things are necessary in order to properly care for the patient and all require the nurse's time. But what must the patient be thinking in the midst of all this activity, and often confusion?

We in medicine too quickly take for granted what for the layman is a startling and often horrifying experience. Picture yourself in the role of a patient in the typical intensive care unit. You are immobilized in bed attached to a variety of cables and catheters. You are connected to complicated machines that blink at you, flash at you, or beep at you. Your only thoughts are of the excruciating pain, the inability to breathe, and the ever present fear of death. Explanations, if given, are in medical jargon which are often misunderstood or not understood at all.

The need for emotional support is very evident in a situation such as this. How can the nurse's role in giving emotional support be met?

Immediately upon arrival to the intensive care unit the patient can and should be offered reassurance. For example, while moving the patient from stretcher to bed the nurse's response could be, "Mr. X, we will be doing all the work for you—you just try and relax." This will also let the patient know what is expected of him. Basic explanations as to what will be done for him initially, can be given briefly before the nurse finds herself tied up with her administrative duties. Explanations, such as telling the patient that even though the electrocardiogram is taken with a machine there is no need to

worry about being shocked with electricity, can be very reassuring.

After the preliminary duties of admitting the patient are completed and the nurse has the time to talk with the patient, more detailed explanations can and should be given. Explanations as to what has happened to the patient physically, what his course of treatment will consist of, and why certain restrictions are being placed on him, such as being unable to feed himself, etc., should be given in such a way that the patient will understand them.

In this period the nurse has the opportunity to get to know the patient and to plan for his individual needs. The patient should be given a chance to ventilate his fears and thus relieve some of his anxiety by talking to the nurse.

In order for the nurse to give good nursing care, both physical and emotional, she must have some understanding of how the patient feels and thinks during an illness. Each patient, regardless of age, has fears and anxieties upon being admitted to a hospital. He is more concerned with questions such as "Whats going to happen to me? When will I be able to go home? Will my illness affect my ability to resume my job?"

While it is true that many patients will not actually voice these questions, the nurse should be ever mindful that these fears and anxieties exist and are present in one form or another. It is important, therefore, that the nurse realize that she is not caring for a disease entity, but rather for an individual who is incapacitated by disease and unable to perform his usual functions in life.

What the patient is told should depend on his individual needs. Some patients will make it clear that they prefer to know very little. These patients are using the mechanism of denial to handle their anxiety and need not be flooded with details that they choose not to hear. However, certain basic information should be communicated. The nurse's ability to communicate this information in a calm, matter-of-fact manner can be very reassuring. Other patients may bombard the nurse with detailed questions. For the most part, these questions can be answered directly and truthfully. Such patients feel still in control and therefore less frightened when they know all the facts.

It is hoped that through example this paper has shown that emotional support can be given on a busy intensive care unit.

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PREVENTIVE MEDICINE SECTION

MAJOR GARY WRATTEN AWARD

CAPT George S. Stains, MSC USN, Officer-in-Charge of the Disease Vector Control Center, Alameda, California, received the Major Gary Wratten Award by the Association of Military Surgeons of the United States 75th Annual Meeting, held 20-24 October 1968, Washington, D.C.

CAPT Stains conceived and developed a method of penetrating heavy jungle canopies with pelletized insecticides, an operation not heretofore accomplishable on any significant scale. This equipment has been the principal and usually the only aerial dispersal equipment available in the I Corps area of Vietnam, and has been a major factor in reducing insect-borne diseases in operating troops.

The award, established by the Association in 1967 in memory of Major Gary Wratten, MC USA, who died testing the Medical Unit Self-Contained Transportable (MUST) hospital equipment under operational conditions in Vietnam, is presented for outstanding accomplishment in field military medicine to an individual eligible for membership in the Association. Sponsored by the Garrett Corporation, the award consists of a bronze plaque and an honorarium of $500.—Vector ConSec, PrevMedDiv, BuMed.

SYPHILIS: A SYNOPSIS

A new booklet entitled, "Syphilis: A Synopsis", Public Health Service Publication No. 1660, revised January 1968, has been released by the Venereal Disease Section, National Communicable Disease Center, Atlanta, Georgia.

The new edition is an excellent training and information guide that may be used by Medical Depart-

ment personnel in conjunction with the Venereal Disease Control Program of the Navy.

Copies may be purchased from the Superintendent of Documents, Government Printing Office, Washington, D.C. 20402, at a cost of $2.00 each.—TB-VD ConSec, PrevMedDiv, BuMed.

HEPATITIS OUTBREAK

USDHEW PHS NCDC Morb & Mort Wkly Rep 17(39):359–360, Sept 28, 1968.

Between 1 April and 26 May 1968, an outbreak of infectious hepatitis due to contaminated bakery goods occurred in Michigan. Of 63 cases reported in Ogemaw County, 61 had onset of illness between 28 April and 26 May. None of the 61 patients under 5 years old; 6.6% were 5-9 years old; 67.2% were 10-19 years old; and 26.2% were 20 years or older. The attack rate for males, 8.1 cases per 1,000 population, was nearly twice that for females, 4.5 cases per 1,000 population.

The clustering of cases in a short time period and in a single age group suggested a common source of exposure. Water and milk did not appear to be responsible; however, a series of associations implicated baked goods from a bakery in West Branch. Although most of the patients in Ogemaw County gave a history of having eaten food from this bakery, it was impossible on the basis of these interviews alone to know whether the bakery was the source of the epidemic or simply a popular place. However, interviews with ill persons from adjacent counties and distant areas revealed that although they had infrequent contact with most establishments in Ogemaw County, they consistently had had some contact with the bakery. The probable time of exposure could be narrowed to within the first 2 weeks of April.

Further evidence supporting baked goods as the vehicle was that 1 of the 2 Ogemaw County cases was in a baker's assistant at the bakery. The man saw a physician on 6 April but worked until 11 April, when the diagnosis of infectious hepatitis was made. He did not return to work until 23 April 1968.

At the bakery it was observed that icing was spread on pastry by hand, and glazed items were dipped in the glaze by hand. In contrast, even though dough is shaped by hand into bread and rolls, these are then baked in a 350°-400° oven for 15-45 minutes. Since pastry is not cooked further after hand glazing or icing, these processes are likely points of contamination. Both glaze and icing may be kept for several days and old batches used to start new ones. Bakery products not sold on one day may be sold on the next business day as day-old pastry or frozen for sale in the next 1-2 weeks. Therefore contaminated goods could have been available for consumption over a period of several days or weeks.

Two surveys were conducted during the investigation. In the first, an investigator estimated the age of each bakery patron, hour of sale, kind of products purchased, and amount purchased. The age distribution of the bakery patrons for the day of observation closely resembled the age distribution of reported cases.

In the second survey, questionnaires were used to obtain comparable histories of exposure to possible common vehicles. Interviews were completed for all 61 Ogemaw County patients with onset of illness between 28 April and 25 May. In addition, all persons 10-19 years old in the household of each patient were interviewed. Ninety-two percent of the 41 patients 10-19 years old ate something from the bakery between 1 April and 14 April 1968; only 47% of the 56 household members had eaten bakery goods. Contact with municipal water was high among patients (88%) but was slightly higher among household members (92%).

The high attack rate in high school students appeared to be due to the fact that many pupils at the public high school go regularly to the bakery and buy pastry for lunch. The sex distribution of the cases of hepatitis in Ogemaw County remains unexplained.

During the epidemic, gamma globulin was offered to all residents of the city and the immediately surrounding area and to all school and household contacts. No cases of hepatitis with date of onset after 26 May 1968, have been reported in Ogemaw County.

COCCIDIOIDOMYCOSIS IN LOS ANGELES COUNTY

Los Angeles Co Health Dept Morb & Mort Rep (37):1, Sept 14, 1968.

Coccidioidomycosis begins as a respiratory illness caused by inhalation of spores of the fungus, *Coccidioides immitis*. Those exposed developed: (1) no symptoms; (2) a mild to severe respiratory illness with fever, cough, and /or pneumonia; or (3) least

commonly, a fatal disease following dissemination of the organism thoughout the body. Past infection in all 3 of these forms may be indicated by a positive coccidioidin skin test. As with a positive tuberculin test, this implies previous exposure to the infecting organism. When spread of the organism occurs, many organ systems may be involved. Meningitis, osteomyelitis, skin lesions and lymphadenitis are some manifestations of this dissemination. For unknown reasons serious disease with dissemination is far more common among non-whites.

The disease cannot be transmitted directly from person-to-person or from animals to humans. The most common way infection is known to occur is by inhalation of the fungus which resides in the soil. The organism is most prevalent in arid regions in dry soil and dust. Therefore, infection is most likely to develop in areas where contaminated dust and soil are stirred up.

In California, the San Joaquin Valley, north of Los Angeles County, has long been known as an area with a high prevalence of coccidioidomycosis. In fact, the term, "Valley Fever", was applied to a certain form of the disease before the etiologic agent was discovered. The first cases of this infection in Los Angeles County were reported in 1948. Since that time there have been many outbreaks of coccidioidomycosis in this country. Most of these cases have occurred in the extreme northern and western mountain regions. Documented cases have also been reported from the western part of the San Fernando Valley. Forty-three cases have been reported up to 14 Sept 1968.

Many cases of coccidioidomycosis are not diagnosed, especially in children and adolescents. In these circumstances, the clinical picture often resembles a benign, nonspecific infection or bronchitis. Coccidioidomycosis should be considered in any patient with a lingering, febrile respiratory illness or in a case of pneumonia which does not respond to antibiotics. This is especially true for persons residing in the northern and western portions of Los Angeles. Clinical suspicion is further enhanced by an epidemiologic history of dust exposure in areas endemic for coccidioidomycosis. Diagnosis is supported by conversion of coccidioidin skin test, positive sputum culture, or by a positive complement fixation test. Very high titers of the complement-fixation test are usually indicative of severe infection and dissemination or impending dissemination.

Immunity after recovery from infection is thought to be complete. There appears to be little if any chance of re-infection with subsequent exposure to the fungus. Treatment for the majority of cases is not indicated since the disease is usually self-limited. Possibility of dissemination, with it mortality rate, is a special risk for non-white patients. When disseminated disease is apparent or implied by high or rising complement fixation titers, treatment with Amphotericin B should be considered and carefully instituted.

Preventive measures aimed at dust elimination include watering down soil and road paving. These are of only limited value, however, when one is dealing with such large land areas where the organism is so sporadically found in soil samples. There is now no effective immunizing agent available for coccidioidomycosis. Since total prevention of the disease in Los Angeles County seems improbable, it is important to realize the dangers of intense dust exposure in the arid regions of the northern and western county. A keen awareness of this epidemiologic setting for coccidioidomycosis will promote earlier and more complete recognition of outbreaks. In turn, this may stimulate the employment of applicable control measures.

ARBOVIRAL ENCEPHALITIS— UNITED STATES

USDHEW PHS NCDC Morb & Mort Wkly Rep 17(40):371, Oct 5, 1968.

To date in 1968, a total of 11 confirmed cases of human disease caused by Eastern encephalitis virus have been reported to NCDC. New Jersey, Pennsylvania, Delaware, and Maryland reported this virus in human, equine, or avian populations.

In 9 New Jersey residents with clinical encephalitis and in 1 with aseptic meningitis, Eastern encephalitis etiology was confirmed by serologic testing. Dates of onset were between mid-July and mid-September. Of the encephalitis cases, 4 were less than 15 years old and 4 were over 60 years old. Five deaths occurred, including the 4 elderly patients. In addition to the human cases, 115 equine cases were confirmed in a total of 134 suspect cases in 12 New Jersey counties between 22 Jul and 22 Sept 1968.

A Pennsylvania resident developed a laboratory confirmed case of Eastern encephalitis 1 week after camping in New Jersey. Nine other campers from his group have remained well. In Pennsylvania 19 of 472 sera from wild birds were positive for arboviruses by serologic testing.

In Delaware, approximately 1,500 pheasant deaths occurred in 4 separate flocks in Newcastle and Sussex Counties from July through mid-September. Laboratory confirmation of Eastern encephalitis virus was obtained in 2 of these flocks and also in 5 of 20 suspect equine cases.

Eastern encephalitis virus activity was confirmed in 5 wild bird flocks, 1 horse, and 5 ponies in Wicomico and Worcester Counties, Maryland.

California encephalitis virus activity has been reported from 6 states in 1968. Arkansas and Iowa each reported 1 confirmed case, while Kentucky reported 2. Wisconsin and Minnesota 3 each, and Ohio 4 cases; 24 additional cases 8 from Wisconsin and 16 from Ohio, were suspect on clinical grounds and single serum specimen titers. Of the 10 patients in Trigg and Calloway Counties, Kentucky, previously reported as suspect cases of California encephalitis viral disease, only 2 confirmations were made; paired sera on the other 8 patients were negative.

Since the beginning of this summer 4 confirmed human cases of Western encephalitis have been reported from 3 states. Two of these were from Texas, which also reported 2 suspect cases. Colorado and Wisconsin each recorded 1 confirmed case.

To date, the only confirmed cases of human disease caused by St. Louis encephalitis virus have occurred in southeastern Illinois. In addition to the 16 clinical cases of encephalitis or aseptic meningitis previously reported from Saline County and vicinity, 23 suspect cases have now been investigated. Further laboratory studies on paired sera are in progress.

TRICHINOSIS—UNITED STATES 1967

USDHEW PHS NCDC Morb & Mort Wkly Rep 17(31):289, 296, Aug 3, 1968.

In 1967, 67 cases represent approximately ½ of the 115 cases reported in 1966 and ⅓ of the 199 cases reported in 1965. This decline evident the past two years, has occurred despite an intensification of surveillance of trichinosis throughout the country. During the past 21 years, reported incidence of trichinosis has varied from 200 to 500 cases per year. In 1967, for the first time, no deaths attributable to trichinosis were reported. No large outbreaks occurred in 1967, and the largest clusters reported were 2 separate episodes involving 2 families, each with 3 cases.

The 67 cases were reported from 24 states. New York reported the highest incidence with 15, 12 from New York City. An analysis of the geographic distribution of trichinosis for the past 8 years (1960-1967) revealed that the New England and Middle Atlantic states reported the highest mean attack rates; the South Atlantic, East South Central, and West South Central states the lowest. The extent to which the lowest mean represent true differences in incidence or variations in recognition and reporting is unknown.

In 53 of the 67 cases, pork products were incriminated as the source of infection, Table 1. Sausage was implicated in 18 cases and "hamburger" in 5 cases. Of 53 cases, 35 cases consumed the suspect meat in homes, 16 in restaurants, and 2 at markets where the meat was sold. The source of meat was determined in 44 cases, and had purchased the implicated meat from commercial sources, and none were due to farm grown, home processed pork. Of the 67 persons with trichinosis, 29 reported that the meat had been cooked or partially cooked, 21 consumed raw meat, and the preparation of meat was unknown in 17 cases.

The diagnosis of trichinosis was based on a combination of historical information, clinical manifestations, muscle biopsies, and skin and serologic tests. The mean incubation period in the 67 cases was 9 days, and the mean period between date of onset and time of diagnosis was 23 days. Elevated eosinophil counts (greater than 5%) were reported in 50 cases. Periorbital edema was reported in 45 cases. In 35 cases, the patients had both elevated eosinophil counts and periorbital edema. Hospital discharge summaries were obtained for 18 confirmed cases.

Sera were collected from 52 of the 67 patients. The diagnosis was confirmed by various serologic

TABLE 1. *Source of Infection for Cases of Trichinosis—1967*

Food	Cases
Pork products:	
Fresh sausage	12
Salami (sausage)	3
Chops	3
Cured "Italian" sausage	2
Chopped pork	2
Frankfurters	2
Cured "Polish" sausage	1
Bacon	1
Pork steak	1
Pork roast	1
Unspecified	25
Subtotal	53
Non-pork products:	
Hamburger	5
Unknown	9
Total	67

tests in 49 cases. Muscle biopsy was performed in 29 cases, of which 20 were positive. There were 19 cases that demonstrated both a positive serologic test and a positive muscle biopsy. There were 9 cases with negative biopsies but positive serologic tests, and 2 cases with negative serologic tests but positive biopsies.

CLOSTRIDIUM BOTULINUM TYPE B DUE TO HOME-COOKED CHICKEN

USDHEW PHS NCDC Morb & Mort Wkly Rep 17(38):348, Sept 21, 1968.

An elderly couple, each 78 years old, developed botulism after eating leftover chicken. The chicken had been frozen until 16 July when it was stewed in a broth containing rice. It was described as "tasty" when served the same day. Leftovers were placed in a covered, plastic container and stored in a cellarway where the temperature was later recorded at 75°F. It was warmed and served at lunch the next day when it was noted to taste "moldy." At noon on 18 July the chicken was again heated and served; the wife ate more than the husband who complained that it tasted "slimmy." A doctor was seen by the couple about 7:30 a.m. on 20 July because of visual and bulbar symptoms and impending respiratory failure. The wife's symptoms were more severe than the husband's; they were both hospitalized and treated with *Clostridium botulinum* type AB antitoxin. She died about 24 hours later; he made an uneventful recovery.

Laboratory examination showed *C. botulinum* type B toxin in the serum from both the husband and wife and in the leftover chicken. The wife's serum contained 20 mouse LD_{50} doses/ml and the husband's, 10-20 mouse LD_{50} doses/ml. In addition, *Clostridium botulinum* type B was isolated from the chicken.

Editorial Note: Botulism resulting from the ingestion of poultry is quite rare in the United States. Of 640 reported outbreaks which occurred from 1899-1967 only one, also type B, was attributed to poultry. This is in agreement with the low incidence of *Clostridium botulinum* spores in raw meats in the United States and Canada. Nevertheless, *C. botulinum* spores might well contaminate raw poultry, and it is possible that the heat resistant spores could survive normal cooking. In this outbreak storage of the leftover chicken in broth at room temperature undoubtedly permitted spores to germinate. This made possible the production of toxin; reheating on 2 subsequent days was obviously inadequate to inactivate all the toxin present.

KNOW YOUR WORLD

Did You Know?

That in 1967, 60 human cases of listeriosis were reported from 24 states?

Ten of the 60 cases (16.7%) were fatal. Of the 50 cases, 34 were males and 16 females. More cases occurred in infants less than 1 year old than in any other age group. Infecting serotypes were identified in 38 of the 60 cases and most frequently identified was *Listeria monocytogenes* type lb. Listeriosis is not a reportable disease; voluntarily reports are made to the NCDC. There is limited information on the pathogenesis, epidemiology, clinical manifestations, laboratory diagnosis and reservoirs of this disease. Interested laboratories and public health departments are encouraged to contribute complete case histories, cultures for serotyping, and sera for serologic diagnosis to the National Communicable Disease Center, Chief, Bacterial Serology Unit, Laboratory Program, Atlanta, Georgia 30333.[1]

That in the winter 1967-1968, a major epidemic of A_2 influenza occurred in the United States?

Forty-six states reported outbreaks of influenza-like illness. The extent of the outbreaks of influenza was much greater in the eastern part of the country. Excess mortality occurred in January 1968 for the country as a whole and for 8 of the 9 geographic divisions. Excess mortality appeared 4-5 weeks after the onset of outbreaks.[2]

That preliminary experiments carried out in Washington, D.C. show that polluted air in cities used for drying milk during the hot weather, affects the flavor of powdered milk?

The immediate causative agent seems to be traces of ozone. Possibly the sunlight action and heat from automobile exhaust fumes result in the conversion of some of the combustion products of ozone. After

the hot weather was over in Washington, D.C., satisfactory dried milks were again produced. Intentional contamination of air with ozone concentration as low as 30 to 50 parts per billion during cool weather was sufficient to produce off-flavors in dried milk.[3]

That through 3 Oct 1968, 48,760 cases of smallpox were notified to the WHO?

This is a decrease of 51% from the 99,548 cases notified in 1967, for the same period. Delayed reports from countries in Southeast Asia may add to this total more than 5,000 cases. Notable increases occurred in the Democratic Republic of the Congo, Burundi, Kenya, Malawi and Mozambique. Cases in eastern and southern Africa for the past 10 years have shown a steady decline, with a record low for 1967. Ethiopia, Mozambique, South Africa, Southern Rhodesia are among the countries with active or about to commence erradication programs.

Between March-June 1968, 102 cases of smallpox occurred in Sudan, the source being the neighboring Gambela Provine, Ethiopia. Intensive immunization program and investigation, (1,123,276 persons) has terminated the outbreak 2 months after onset of disease.[4]

That during the past 15 months, 9 cases with 3 deaths from diphtheria have occurred in Vancouver?

Clinical diphtheria has been a rare disease in British Columbia for many years. Seventeen healthy carriers were discovered following investigation of contacts of these cases.[5]

That water quality standards designed to protect fish from harmful effects of industrial wastes may protect the fish but are inadequate to save their food supply—organisms that serve directly or indirectly as fish food?

A study by investigators of the Natural Academy of Sciences, Philadelphia and the University of Kansas raises the possibility that these vital organisms may be even *more sensitive than fish to pollution.* The study is reported in "Progressive Fish Culturists," July 1968, Department of Interior's Fish and Wildlife Service.[6]

That in Bulgaria silicosis accounted for 91% of long-term loss of working capacity due to occupational disease in 1966?

The number of new cases per year fell from 91.4 per 1,000 workers in 1956 to 7.1 per 1,000 in 1966. In Great Britain, annual deaths from silicosis rose from 382 in 1945 to 776 in 1957 and then declined to 616 in 1965, although still well above the 1945 level. Due to present-day preventive measures the number of new cases per year in both countries has fallen considerably.[7]

That when the Swedish transportation system was switched from left-hand to right-hand drive, a ban was put on the use of private automobiles for a period of 29 hours?

Air sampling by the Swedish Board of Health while the ban was in effect showed that the sulfur dioxide content decreased by half and carbon monoxide, which sometimes measures 300 particles per million, could not be detected. A visual test using paper tapes to collect dirt out of the air varied between 3 and 10 on a scale of 25, where the normal average had been 14. There are demands in Stockholm now for regularly scheduled traffic bans to give the population a chance to breathe fresh air.[8]

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EDITOR'S SECTION

CRITICAL NEED FOR NONSURGICAL EYES

Dr. Lorenz E. Zimmerman, Chief, Ophthalmic Pathology Branch, Armed Forces Institute of Pathology (AFIP), has asked all ophthalmologists and pathologists to help alleviate "the profound shortage" of eyes obtained postmortem. This is especially so in cases in which the patient has been followed by the ophthalmologist and the clinical findings are well documented; as well as those in which the patients have been on long term drug therapy. He said the inadequacy is seriously hamper-

ing the study of a variety of ocular complications occasionally observed when certain drugs are used over long periods. The AFIP is particularly interested in drugs, such as chloroquine and phenothiazines, that are known to cause retinal damage after they have been administered in large doses over a long period of time; as well as steroids and antimetabolites. In addition, the study of postmortem eyes will help document pathologically many nonsurgical conditions that have been followed for years. Our knowledge of the ophthalmic pathology of many medical diseases has been hampered through the years by the lack of eyes to study microscopically. Generally speaking most of the eyes received at the AFIP and at other ophthalmic pathology laboratories have been obtained by surgical enucleation. Consequently there is an appalling lack of information concerning the pathology and pathogenesis of such important conditions as senile macular degeneration, optic neuritis, myopia, . . . etc. If our knowledge of the effect of medical diseases on the eye is to advance we must make a concentrated effort at once to provide this pathological material.

Ophthalmologists are encouraged to develop a thorough program of indoctrination among their medical confreres about the importance of obtaining eyes postmortem, not only to be used as donor material, but also for pathologic studies and clinicopathologic correlations. There is a definite need to improve the understanding of the general population regarding the removal of eyes as part of a complete autopsy. In several communities the enucleation of eyes postmortem is already routine portion of the autopsy. All clinicians should urge their hospital pathologists to include examination of the eyes as an integral part of their autopsy procedures. All physicians should seek permission for routine postmortem removal of the eyes. We should all do our part today so that the ophthalmic care of patients can be improved tomorrow. Let us not procrastinate! Let us act at once!—Training Branch, BuMed.

NEW ASSISTANT TO THE DIRECTOR MSC DIVISION FOR MEDICAL ALLIED SCIENCES OFFICERS

Captain William G. Cumming, Jr., MSC USN, has been assigned collateral duty as the Assistant to the Director, Medical Service Corps Division, Bureau of Medicine and Surgery for Medical Allied Sciences Officers (BuMed Code 35B). Captain Cumming will assist and advise the Chief of the Medical Service Corps in all matters relating to the recruiting, assignment, and career planning of Medical Allied Sciences officers and provide a contact point within the Bureau to assist and advise officers of this section. Captain Cumming's telephone extension in BuMed is 64349. —MSC Div, BuMed.

USNR PHYSICIANS HELP 1,575 KIDS GO TO CAMP

Naval Reserve physicians volunteered their time and talents so that San Diego, California youngsters could enjoy the great outdoors this past summer.

The doctors, who have civilian practices in the San Diego area, conducted the physical examinations at night during July and August at the Naval Hospital, San Diego. The Mayor's Youth Opportunity Program committee had requested assistance from the Commandant, Eleventh Naval District and CAPT H. L. McCoy, MC USNR, the commanding officer of Naval Reserve Medical Company 11-6 volunteered his unit.

CDR G. R. Ferrell, MC USNR, executive officer of Naval Reserve Medical Company 11-6, organized the Navy's part of the program after RADM H. D. Warden, MC USN, commanding officer of the Naval Hospital, offered the facilities at the Hospital Corps School. He scheduled the physicals for July and August.

The physicals were accomplished in four evening sessions. The youngsters were transported to the Hopital Corps School by their parents, by social or welfare organizations, or by commercial buses. Eleven doctors, four nurses, and two Medical Service Corps officers took part in conducting the 1,575 physical examinations.

These four sessions were in addition to the regularly scheduled drill periods of the company. The present commanding officer of the unit, CAPT D. R. Carmichael, MC USNR, said, "we are glad we could provide a community service, and at the same time help some San Diego youths."—Reserve Div, BuMed.

LATENT INHERITED DISEASE

F. S. Rosen, Amer J Med Sci 256(2):67–68, Aug 1968.

The frontiers of preventive medicine are rapidly expanding beyond the traditional concerns with the infectious scourges of man. The hazards of the urban environment and the threat to natural resources have already received widespread public attention as the dialogue on water and air pollution quickens. The automobile, cigarettes, asbestos, and numerous others of civilized man's accoutrements

are indicted as a health menace to the individual. More recently, another vista of preventive medicine has been opened in the detection and preventive therapy of latent inherited disease. The exuberant public response to massive screening of newborn infants for phenylketonuria (PKU) has resulted in legislation in more than 40 states of the Union where such testing is now compulsory. There is now good reason to question the wisdom and the enthusiasm which has led to what may perhaps be premature enactment of medical progress into legal formats. Sober counsel and evaluation are now needed before the PKU precedent is applied to other problems. As Bessman recently pointed out, "the laymen who have been carrying on the amazing campaign that saw to the passage of 25 state laws in 18 months . . . can only be reassured of their rectitude."[1]

The very process of screening the blood of enormous numbers of newborn infants for phenylalanine levels has turned up a previously unrecognized and innocent finding—benign hyperphenylalaninemia. Treatment of such children with a phenylalanine deficient diet may be potentially hazardous. In those less populous states where the number of cases found is bound to be small and where the technology and skills for proper follow-up of new cases are wanting, the risk of doing harm by dietary restriction is real. Obviously, more pilot projects and careful analysis of follow-up data were needed prior to this legislative binge.

The example of Wilson's disease adroitly poses the dilemma of presymptomatic diagnosis and treatment. Evidence that penicillamine therapy effectively reverses the hepatic and neurologic symptoms of the disease is now secure. Although the therapy is not without serious consequences, particularly due to the high allergenicity of the compound, its benefits outweigh the most dire idiosyncracies of patient response to its administration. Is it not perfectly logical therefore to administer penicillamine to the presymptomatic patient in order to promote copper excretion and avoid the ravages of the disease? At this point, the science of the biostatistician and the conscience of the physician confronted with an individual case come into sharp conflict. There is no foolproof test for the diagnosis of Wilson's disease because the precise nature of the defect in copper metabolism in this disease is not known. Highly presumptive evidence for the presymptomatic state can be gathered from the measurements of serum ceruloplasmin, liver copper content, and copper excretion. On those bases, penicillamine administration to presymptomatic siblings of known cases has thus far been successful although statistical analysis tells us that the sampling of such patients and the length of follow-up are not yet adequate.[2] Without an exquisitely precise test for diagnosis and until data on the treatment of presymptomatic siblings are beyond question, it would be injudicious to embark on a compulsory screening program, enacted into law, and court the hazards of a life-long commitment to therapy in the sporadic cases which would be found in such a screening program. No body of knowledge is so perfect and no therapy is so benign as to warrant a repetition of the PKU legislation. The value of massive screening per se has proved to be a vehicle for expanding medical progress. It must continue without the onus of legislation.

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Address requests for reprints to Children's Medical Center, Harvard University, Boston, Massachusetts.

CURRENT RESEARCH IN CHRONIC AIRWAYS OBSTRUCTION

Recent research into the causes and progressive nature of emphysema and other chronic lung diseases is the subject of a new 400-page publication just released by the National Center for Chronic Disease Control, Public Health Service.

"Current Research in Chronic Airways Obstruction" (Public Health Service Publication No. 1717) contains 30 papers presented at the 9th Aspen Emphysema Conference, held in Aspen, Colorado, June 9 to 12, 1966.

Beginning in 1958, a group of 100 national and international experts in chest medicine, physiology, biochemistry, and other medical specialties have assembled in Aspen each June to discuss research projects in chronic lung disease and their clinical experience in caring for patients.

The Chronic Respiratory Diseases Control Program, sponsor of the last three conferences and of the 11th conference held June 12 to 15, this year, is the publisher of the current volume of studies.

A limited number of single copies of "Current Research in Chronic Airways Obstruction" are available from the Public Inquiries Branch of the Public Health Service, Washington, D.C. The publication may be purchased from the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402, for $2.00 each or $150 per hundred.—National Center for Chronic Disease Control, Arlington, Va.

NEW ARTIFICIAL LUNG

Long term maintenance of blood-oxygen levels in newborn infants suffering from respiratory distress syndrome may soon become a practical clinical reality with a new artificial lung developed by scientists in the National Heart Institute, a component of the National Institutes of Health.

The NHI scientists, and collaborating scientists in Boston, Chicago, and Baltimore report their use of the highly efficient and disposable membrane lung to safely maintain adequate blood oxygen levels in newborn lambs during continuous use for periods of up to 4 days (96 hours).

These findings have just been published in the *Transactions of the American Society for Artificial Internal Organs,* by Drs. Theodor Kolobow and Warren M. Zapol of the NHI's Laboratory of Technical Development, Joseph E. Pierce, NHI Laboratory of Kidney and Electrolyte Metabolism, Ambrose F. Keeley, Boston City Hospital, Robert L. Replogle, University of Chicago Medical School, and J. Alex Haller, Johns Hopkins University School of Medicine.

Heretofore, prolonged blood-oxygenation with an artificial lung has been limited in duration to less than 12 hours in newborn laboratory animals, and has been accompanied by severe damage to lungs, blood cells and blood proteins, as well as the formation of dangerous blood clots and air bubbles in the blood.

The cylindrical, pint-sized lung, called the "spiral coil membrane lung," contains a thin (5/1000 inch) silicone rubber membrane formed into a flat tube or envelope that is wound about a central spool. The envelope is fitted with oxygen inlet and outlet ports. Blood enters one end of the lung's cylindrical housing, flows between layers of the spirally-wound silicone envelope and, still flowing parallel to the cylinder's axis, exits at the other end. As in other membrane lungs, blood oxygen and carbon dioxide exchange occurs by diffusion across a membrane. However, unlike most membrane lungs, the spiral coil lung is suction-actuated, i.e., oxygen is pulled through the lung by the intermittent application of a slight vacuum to the oxygen outlet port.

The new lung owes most of its safety advantages as well as its high oxygenating efficiency to this gentle, cyclic application of negative pressure, as it prevents oxygen bubbles from entering the blood (gas emboli) should pin hole leaks occur in the membrane, and the pulsatile motion it imparts to the membrane greatly increases blood oxygenation by eliminating the "stagnant" boundary layer of oxygen-saturated blood immediately adjacent to the membrane. Thus, more blood is brought into contact with the membrane where oxygenation occurs. Finally, the low perfusion pressure and pulsatile motion, along with normal arterial blood pressure, act to propel blood through the lung and eliminate the need for a separate blood pump with its attendant damage to fragile blood components.

Performance of the spiral coil lung was studied during prolonged use in 8 newborn lambs (from 1 to 8 days old), each connected to an externally located spiral coil lung by means of plastic tubing inserted into an artery and a vein in the neck. Lambs were chosen for these studies because they weigh about the same as newborn infants. In these studies, oxygenating efficiency of the artificial lungs were determined daily during brief periods of oxygen lack when the lambs were subjected to an atmosphere containing only 7 percent oxygen.

The NHI and collaborating scientists report that the artificial lungs performed well during continuous operation in the animals for periods of from 21 to 96 hours, and that no consistently abnormal gross or microscopic changes occurred in the 6 survivors.

From this excellent performance of the spiral coil lung, and the overall benign affects of its prolonged use in animals, the scientists feel that its use should be considered as a method of treating respiratory distress in the newborn infant or adult. The spiral coil lung can oxygenate up to 450 cc. of blood (nearly a pint) per minute, yet has a total priming volume of only 45 cc.—National Institutes of Health, NHI, Bethesda, Maryland.

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