diaphragm, which simulates that of perforated ulcer. Therefore, every patient should be studied carefully for evidences of pneumonia or an acute heart condition before a final diagnosis of perforation is made. Whenever there is a definite question concerning the presence or absence of perforation, an x-ray examination of the abdomen for free abdominal air should be conducted. Free air in the upper abdominal region is found in about one-half of the cases of perforated ulcer. The visualization of free air under the diaphragm by an x-ray film is positive proof of a ruptured viscus, but a negative picture does not mean that perforation is not present. A positive x-ray picture is often a valuable aid when perforation has occurred 24 hours or more previously and the diagnosis is doubtful.

Prognosis: If operation is performed in cases of acute perforation before 12 to 16 hours have elapsed, most of them will recover with a remarkably easy convalescence. If the patient is old or suffering from one or a combination of degenerative diseases, the prognosis is not so good. In general, the mortality rate in acute perforation of an ulcer is 25 per cent, but the younger, stronger patients will almost all recover if operated in time.

TREATMENT

The treatment is of course entirely surgical, but a few measures have to be carried out in the period that elapses between the acute perforation and the arrival of the surgeon in the operating room.

1. The patient should be given 0.02 Gm. (⅓ grain) pantopon or 0.016 Gm. (¼ grain) morphine with 0.0008 Gm. ($\frac{1}{75}$ grain) atropine hypodermically at once to relieve the pain.

2. Further collapse may be combated by administering 2 to 5 cc. of adrenal cortex substance intramuscularly.

3. Intravenous solutions may be given while preparations are being made for the operation; 1000 cc. of ten per cent glucose in saline may act as a bulwark to the circulatory system, or 300 cc. of blood plasma may be administered immediately as a preoperative measure.

4. Time should not be lost by going through unnecessary maneuvers; the main thing is to bring the patient to the operating room as quickly as possible, and to have the operation done promptly.

ACUTE INTESTINAL OBSTRUCTION

The following discussion is not given with the thought that there is a medical aspect to the treatment of acute intestinal obstruction, but on the grounds of diagnosis and management preliminary to surgery. Patients with acute intestinal obstruction are frequently seen first by the practitioner and diagnostician and later by the surgeon.

When a patient is seized with colicky pain associated with vomiting, bowel obstruction must always be kept in mind. Of all the conditions responsible for the acute abdominal emergencies, bowel obstruction is most often misdiagnosed. Furthermore, it is the one acute abdominal emergency in which early diagnosis and prompt surgery are associated with favorable results, while delay is apt to end disastrously for the patient. In this emergency, hours count more than in almost any other except the perforations. There was an old axiom in surgery which is as true today as when it was originated; that is, never to let the sun go down on a case of acute intestinal obstruction. In those days as well as now, it was well known that early operation meant early recovery while late operation meant retarded or no recovery.

Etiology: Many classifications of bowel obstruction have been proposed. The simplest and most usable one is the following:

1. Bowel obstruction in infancy and early life, due to intussusception and volvulus.

2. The acute obstruction of middle life, usually involving the small bowel and caused by strangulation of a hernia or obstruction due to old adhesive bands in the abdomen.

3. The bowel obstruction of advanced years, usually found in the large intestine and caused by carcinoma.

Signs and Symptoms: The symptoms and clinical course of acute obstruction of the small bowel vary according to the site of the stricture. In general, pain, vomiting, and distention of the abdomen are the main features. Tenderness may be present, but is not necessarily localized in any particular area. As a rule, there is no rigidity except during the peristaltic rushes. After a varying period of a few to 24 hours, depending upon the degree of obstruction and disorder of blood supply to the intestinal wall, constitutional symptoms may occur. They include rapid pulse, a falling blood pressure, and evidence of oncoming peripheral vascular collapse and shock.

Pain is the most important feature of all because it is always present. Nausea and vomiting almost always occur and may be much more severe than other symptoms. The abdomen is usually distended, unless the stricture is high in the jejunal area. Auscultation over the abdomen may reveal high-pitched tinkling peristaltic sounds which are suggestive of obstruction. Excessive vomiting leads to dehydration and alkalosis. The sodium chloride of the blood falls, and the nonprotein nitrogen, creatinine, and potassium rise. The obstruction of the flow of the bowel contents is not as important as the damage to the intestinal wall. The reason for some patients developing early shock and collapse in bowel obstruction while others do not cannot be explained by the kind of lesion present; one type of intestinal involvement may produce mild symptoms and signs in some individuals and a severe grade in others. Frequently patients become toxic within a few hours when there is a constriction of the jejunum. The pulse becomes rapid, the pain more marked, vomiting severe, and the patient is very restless, pale, cold, and clammy.

Diagnosis: The differential diagnosis of obstruction of the small bowel as stated above is often difficult; however, lack of early and proper diagnosis usually cannot be attributed to inadequate knowledge of the condition but to lack of thoughtfulness concerning the possibility of the presence of this condition. The abrupt onset of pain and vomiting without any other apparent cause should always make one think of acute bowel obstruction. When there is an old operative incision scar upon the abdominal wall, this should further suggest the presence of an obstructive lesion. Acute appendicitis, acute gallbladder disease, perforation of a peptic ulcer, acute pancreatitis, and pelvic diseases in women must all be considered in the differential diagnosis. Mesenteric thrombosis or embolism is rare but simulates obstruction very closely. Other evidence, particularly conditions that may lead to thrombosis or embolism, as advanced age, portal obstruction, or irregular heart, must be taken into consideration.

Acute intestinal obstruction presents certain characteristic features which may be given as follows:

1. After careful history has been taken, palpation of the abdomen may reveal a generalized distention with moderate rigidity. On auscultation of the abdomen, intestinal gurgles are found to be greatly

increased and the rushing of these intestinal sounds gives one the impression that the bowel is making a violent effort to overcome some obstruction. In the earlier periods, these intestinal noises may be continuous and violent. Later on, the bowel seems to tire out and there are periods of quiescence, in which no sounds are heard, alternating with periods of rushing activity. Attention to the stethoscopic examination of the abdomen in these cases is of great diagnostic importance. One must not be thrown off the diagnostic path by the presence of fluid in the abdomen, accumulated as the result of peritoneal irritation, since it may alter the auscultatory findings.

2. Chemical examination of the blood is apt to show an early disturbance of the electrolyte balance and a rise in nonprotein nitrogen. Alkalosis, low blood chlorides, and a high nonprotein nitrogen occur if the obstruction is high in the small bowel.

3. An x-ray examination may be helpful in that the stepladder type of pattern caused by distention of the small bowel above the obstruction is an important diagnostic aid. X-ray examination should be made after the fluid has been removed from the stomach and before an enema is given. If there is a question of differential diagnosis between large and small bowel obstruction, the truth is usually obtained by injecting a small amount of barium per rectum. If there is any doubt, x-ray examination should be repeated in four or five hours. Some say a barium enema is not wise, while others advocate its use.

Chronic bowel obstruction is usually of the large bowel and is caused by carcinoma. However, acute manifestations may come on suddenly because a partial obstruction due to growth may have added to it an inflammatory lesion which causes a sudden swelling of the obstructing mass and practically complete obstruction of the large bowel ensues. In these cases, the patient usually is an older individual and difficulty with the bowels precedes the acute manifestations. Pain is usually not so severe in large bowel obstruction as in the small bowel type, but distention is much greater. The distention may be acute and sudden, or it may be insidious and of mild grade. When a question of large bowel obstruction arises, a barium enema may be given in order to localize the point of the obstructing lesion. The site of the obstruction may be found at times by simple rectal exami-

nation, but more often it is higher in the sigmoid or descending portion of the large bowel. Surgery is called for in these cases.

TREATMENT

1. The treatment of acute intestinal obstruction is frequently surgical, but it must be emphasized that the fluid balance should be maintained by the administration of 2000 cc. of ten per cent glucose in physiological saline solution intravenously every 12 hours. A transfusion may be necessary. The patient should receive nothing by mouth.

2. The lower segments of the small bowel may be unloaded by the use of the Miller-Abbott tube. The patient is sent to the x-ray department for passing the tube through the stomach into the bowel.

3. When strangulation of the bowel is present, operation should be performed within the first few hours after entrance to the hospital. In the presence of obstruction without diagnosis of strangulation, drainage is instituted. If this is unsuccessful in 12 hours and the patient is in good condition, immediate operation is advised.

4. The administration of morphine or pantopon is rarely advisable. The masking of the symptoms following their use may lead the patient or even the physician and especially the patient's relatives into believing the patient's disease has begun to clear up without operation.

Volvulus

Volvulus is strangulation of the intestine due to twists, kinks, or knots. It is caused by twisting of the intestine upon its mesenteric axis, resulting in occlusion of the lumen. Congenital irregularities in the length of the mesentery or of the intestine or an acquired redundancy of the tube promoted by constipation may be factors. Trauma as a consequence of falls, jumps, or any physical shock, as well as any agent that induces overactive peristalsis may produce volvulus. The weight of a fecal mass or tumor pressure from outside the intestine, rough manipulation of tissue during laparotomy, or paresis of the intestine following surgery are all reported to be responsible at one time or another.

Volvulus is seen most frequently in males past middle age. In half the cases the sigmoid flexure is involved. The iliocecal region is the

next commonest site for this malady. The small intestine is involved in a lesser number of cases.

Symptoms and Findings: The symptoms and findings are those of acute intestinal obstruction. Colicky pain is at first restricted to the site of the obstruction, but rapidly spreads over the abdomen. Sudden cessation of pain with continuance of other symptoms is of serious import. Vomiting begins soon after the onset of pain; it is at first entirely reflex, but after a few hours becomes stercoraceous. Abdominal distention is often marked. When the obstruction is high in the tube, the distention is confined to the upper abdomen until late in the course of the disease. Shock of various degrees is frequently noticeable in patients with acute intestinal obstruction. Dehydration results, in part from the continued vomiting and sweating, but probably also from a disturbance of the acid-base regulating mechanism, leading to a reduction in the sodium chloride content of the blood. The urine is usually scanty and commonly contains albumin. Nitrogen retention may be found in the blood. The leukocyte count generally rises during high obstruction and when the intestine or its mesentery is damaged. The bowels usually do not move spontaneously in an acute attack, although the material in the tube distal to the obstruction may be discharged in one or two spontaneous movements. If the obstruction is incomplete, diarrhea may occur. Blood may be passed after strangulation, and peristaltic movements may be visible on the abdominal wall. Hyperactive peristaltic sounds are heard characteristically, although they are not invariably present.

X-rays of the abdomen reveal a distended bowel often with "step ladder" formation. The common clinical picture of congenital volvulus is one of acute obstruction of the second or third portion of the duodenum with bilious vomiting, constipation, and rapid wasting.

Prognosis: Twists, kinks, and knots have been cured spontaneously or by postural treatment and massage, but when the obstruction has been sufficiently acute to cause shock and stercoraceous vomiting, it is doubtful that the patient can recover without surgical treatment. The hope of ultimate cure by surgery diminishes with each hour of delay. Untreated acute obstruction may lead to death within a few hours to ten days.

TREATMENT

The usual treatment of acute obstruction due to volvulus is surgery. Attempts to relieve vomiting and abdominal distention should be instituted by repeated enemata and Wangensteen suction. At times the latter measures accomplish release of the obstruction. Dehydration should be combated by parenteral fluids. Sedation should be administered judiciously and rarely before the diagnosis is definitely made.

Intussusception

Intussusception is the invagination of one portion of the intestine into another. It is seen with the greatest frequency in infancy and is at this age the commonest cause of acute intestinal obstruction. Usually the upper part of the intestine is invaginated into the lower, but the reverse may occur. Invagination may take place high in the intestinal tract. The so-called intussusception of the dying is frequently encountered in autopsies made upon infants; it usually involves but a few inches of the intestine and is probably produced by the death agony.

Etiology: Intussusception appears twice as often in males. The cause for the phenomenon is obscure. In most cases it occurs in children who have apparently been in perfect health.

Pathology: Animal experiments have shown that intussusception is caused by irregular action of the muscular walls of the intestine. As invagination takes place, the mesentery is drawn in with the bowel to allow intussusception to occur; the mesentery must be unduly stretched, long, or lacerated. Invagination does not necessarily produce either obstruction or strangulation, but both are generally present and are the reason for the symptoms. Traction upon the mesentery leads to obstruction of its vessels with consequent congestion, edema, hemorrhage, and even gangrene. Obstruction is chiefly due to swelling, but may be due to dragging of the mesentery, which brings the apex of the tumor against the side of the bowel or bends the intussusception. The invagination as a rule includes all the coats of the intestine. Failure to reduce the intussusception within the first two or three days is due to swelling from edema. Adhesions, too, may prevent reduction, but usually only after several days. Gangrene and consequent sloughing occur much more often in acute than in chronic

cases. Portions of intestine may then be passed. In chronic cases shreds of intestine may be discharged for several weeks.

Symptoms and Findings: The patient is taken suddenly ill with severe abdominal pain and vomiting. The pain is paroxysmal, recurring every few minutes. The vomiting is first of the contents of the stomach, later of bile, and is often projectile. The abdomen is relaxed, and a mass can generally be felt in the epigastrium, in the left iliac fossa, or by rectum. In some cases the mass protrudes from the anus. The description of this mass as "sausage-shaped" is accurate when the invagination is large. During manipulation or during an attack of pain the tumor may become more prominent. By rectal examination the palpable mass resembles the os uteri. The examining finger is usually covered with bloody mucus, whether or not a tumor is palpable. When the tumor protrudes, it is usually a deep purplish color and may be gangrenous. It has been mistaken for prolapse of the anus, polyp, and even hemorrhoids.

There may be one or two loose, fecal stools, after which only blood or blood and mucus are passed. Restlessness is followed by prostration and even collapse with pallor, flaccidity, cold extremities, feeble pulse, and at times a subnormal temperature. Tenesmus is common if the tumor is rectal in location. In some cases, there is absence of peristaltic sounds.

In acute cases, the condition grows rapidly worse. The vomiting and pain continue, and after the second or third day the abdomen becomes tympanitic. Dehydration appears quickly. There is a steady increase in prostration, and toward the end a rapidly rising temperature, which may reach 41.1° C. (106° F.) before death occurs. If the symptoms continue longer, the findings of peritonitis are superimposed.

In chronic intussusception the onset and the manifestations are less dramatic. The obstruction of the lumen is incomplete and the changes in the bowel itself are less pronounced. This type begins with vague intestinal symptoms. Pain, vomiting, and melena are often absent. Progressive loss of weight, constipation, or diarrhea is seen. Only the presence of the tumor leads to recognition of the morbid state.

Prognosis: Spontaneous reduction of intussusception is known. It is possible that some cases of severe colic are really cases of mild

intussusception which undergo spontaneous reduction. Intussusception may be cured spontaneously by sloughing of the invagination and preservation of the continuity of the intestine by adhesions, but such fortunate events are not to be expected. The mortality in untreated cases is close to 100 per cent, while in cases operated on within 24 hours, it is no more than 10 per cent. The prognosis depends more upon early treatment than upon the age of the patient or the degree of intussusception. Late cases are liable to exhibit pronounced toxemia and shock. Delay is less serious in the case of incomplete obstruction, but even these should be subjected to surgery at the earliest possible moment. Recurrence of the condition is rare.

TREATMENT

Laparotomy should be performed without delay when the diagnosis of acute intussusception is made. Traction under anesthesia has brought about reduction without operation, but this procedure is not likely to be successful in unskilled hands. When gangrene or an irreducible mass is present, the involved segment must be resected.

The fluid balance of the patient must be maintained. The quantity of blood lost in the stools is not as a rule great enough to require transfusion. Violent cathartics should be avoided in the postoperative period.

CHAPTER XVI

Acute Abdominal Emergencies

(Continued)

ACUTE PANCREATITIS

Although acute pancreatitis is not a common abdominal catastrophe, it constitutes one of the most difficult and serious diagnostic problems in medicine and surgery, and has one of the highest mortality rates of all acute abdominal emergencies. It is an inflammation of the pancreatic tissues due to infection. The term "acute pancreatitis" is one that formerly implied a very serious and usually fatal condition. The terms "acute hemorrhagic" and "acute necrotic" pancreatitis were looked upon as synonymous with acute pancreatitis. More recently, acute pancreatitis has been differentiated into the simple or so-called interstitial or edematous type, and the necrotic or hemorrhagic form. Obviously, the simple or non-necrotic type is one associated with symptoms and signs that are much milder and more benign than those found in the hemorrhagic form. It must be kept in mind that the difference in the lesion of these two types is a matter of degree only and not of fundamental pathological findings.

Etiology: The cause of acute pancreatitis is closely bound up with gallbladder disease. The most generally held view is that the ampulla of Vater becomes occluded and a flow of bile travels from the common duct into Wirsung's duct of the pancreas. The irritation to the setup in the pancreas may be mild or severe, and the subsequent symptoms and signs are thereby determined. A gallstone or even edema of the ampulla of Vater may be sufficient to cause pancreatitis in certain cases, depending upon the anatomical relationship of the pancreatic and common bile ducts. Investigators have challenged this commonly held explanation of the bile flow into the pancreas as a chief cause. While the argument cannot be settled, it is true that most cases of acute pancreatitis are associated with gallstones, gallbladder disease, infectious process, or some disease of the ampulla of Vater. In many cases there is a history of recent infection, pancreatic injury, alcoholism, overeating, or disease of the abdomen. Obviously

the patient is usually in the upper age group, because the disease is commonly associated with gallbladder trouble. Furthermore, the patient is usually a stout female.

Signs and Symptoms: As acute pancreatitis may be of the mild benign or the severe hemorrhagic forms, it must be emphasized that the mild type may develop into the more severe one within a period of a few hours. The signs and symptoms that occur in the fulminating acute form will be discussed here.

The clinical signs and symptoms of acute hemorrhagic pancreatitis are fairly distinctive, and while they may suggest other acute abdominal emergencies, there are a few features which serve to differentiate this disease from others that simulate it. The onset is usually abrupt and is characterized by severe, agonizing pain across the upper portion of the abdomen which may radiate to the back and shoulders. Vomiting usually develops and the abdomen becomes distended rather early in the course of the disease. The pulse grows rapid and weak, and the patient is pale and appears to be on the verge of collapse. Sometimes actual peripheral vascular collapse or shock develops. As a rule, there is no moderation in the degree of the pain; it is intense from the start and continues to be so. While the clinical features may vary a good deal, severe pain, abdominal rigidity, pallor or cyanosis, and a clamminess of the skin are practically always present. The temperature may be subnormal or slightly elevated, and the leukocyte count is usually 10,000 or more.

From this description, one can readily see that many other acute abdominal emergencies may produce a similar picture, and consequently the differential diagnosis is very difficult. To suspect the presence of this disease is one-half of the diagnosis. Within recent years, several laboratory tests have been devised which are helpful in diagnosis. Particular attention is directed to the tests of pancreatic ferments in the blood and urine. The most popular ones are the serum amylase and the serum lipase tests. While the serum amylase is probably not as precise as the lipase, it seems to be of greater clinical value because its determination requires only one hour and the lipase test takes 24 hours to perform.

Serum Amylase Test: The principle of this test is that the serum containing the amylase is allowed to act on a substrate of a starch suspension which it breaks down into sugar. The amount of sugar

produced in 30 minutes' incubation indicates the quantity of amylase present in the serum. Normally, this amounts to about 20 mg. per cent, and is increased in acute pancreatitis and secreting pancreatic adenomas.

Serum Lipase Test: Lipase in the serum hydrolyzes the neutral fat, olive oil, breaking it down into glycerol and fatty acid. The fatty acid is determined by titration with sodium hydroxide. Comparison of the 24-hour incubated specimen with an inactivated control gives the result in cubic centimeters of twentieth normal sodium hydroxide. The average range in this test is 0.5 to 1.0 cc. up to 1.5 cc., which is the high normal. The increase in serum lipase occurs in the same conditions as increased amylase.

TREATMENT

The treatment of acute pancreatitis is at its best quite unsatisfactory. What is accomplished by surgery in these cases is rather circumscribed. Surgical treatment offers little more than strictly medical treatment; however, one advantage in favor of the surgical approach is that if perforation of a viscus or some other abdominal catastrophe is present, it may be dealt with satisfactorily. In this acute abdominal emergency, as in others, if any uncertainty in the diagnosis arises an abdominal operation must be done so a condition is not overlooked that may be benefited by surgery.

1. Stop all intake by mouth, and administer fluid by rectum.

2. Morphine, 0.016 Gm. (¼ grain), and atropine, 0.0006 Gm. (1/100 grain), may be given frequently enough to control the pain.

3. Peripheral vascular collapse may threaten the patient's life. Therefore, 1000 cc. of ten per cent glucose in saline should be given rather rapidly intravenously at once.

4. If blood plasma is available, 300 cc. should be given as soon as possible.

5. Adrenal cortical substance, 5 cc. intramuscularly, may be repeated several times at two-hour intervals.

6. Large, hot, wet turpentine stupes on the abdomen are warranted not only because of the value of heat, but also because they immobilize the abdomen and tend to ease the abdominal pain.

MESENTERIC THROMBOSIS

When a patient develops acute abdominal pain, the common disorders should be considered first. These are appendicitis, gallstones, pancreatitis, bowel obstruction, and perforation of a peptic ulcer. In women, three additional disorders, acute salpingitis, ruptured ectopic pregnancy, and twisted ovarian cyst, must also be kept in mind. There are, however, other conditions which less frequently produce acute abdominal catastrophes. Among these is occlusion of the mesenteric vessels caused by thrombosis and embolism. It is often considered a fatal disease, though this is not always true because there are mild grades of mesenteric thrombosis which invariably heal. While the mortality rate is placed at approximately 92 per cent, this is too high except for those cases which are characterized by the plugging of the large branch of a mesenteric vessel.

Etiology: The causes of mesenteric thrombosis may be given as follows:

1. Arterial occlusion:
   a. An embolus from a cardiac vegetation.
   b. From an atheromatous plaque.
   c. From a mural thrombus in one of the cardiac chambers.
2. Venous type:
   a. An injury to the abdominal vessels.
   b. A ligation or a crushing of the veins at operation.
   c. Strangulated hernia.
   d. Extension from the portal veins or even from the splenic veins.

   As far as diagnosis and treatment are concerned, it does not make much difference if the disease is one of the arterial or venous system.

A mesenteric embolus usually follows a thrombus which originates in the left side of the heart or in an arteriosclerotic aorta. A mesenteric artery may also become thrombosed due to arteriosclerosis leading to narrowing and followed by sluggishness of the circulation and finally thrombosis. The veins of the mesenteric system may become plugged because of disease of the veins themselves, suppurative conditions within the abdominal sac, strangulation of hernias, and occasionally trauma. Larson, in a study of 36 cases of mesenteric vascular occlusion in which autopsies were performed, found that a mural cardiac thrombosis was the commonest cause of embolism of the mesenteric artery. Arteritis and arteriosclerosis most

frequently produced thrombosis; venous occlusion most often resulted from septic processes in the gastrointestinal tract, pelvis, or lower abdomen.

Signs and Symptoms: The clinical picture of acute mesenteric thrombosis as it is described in textbooks gives the impression that the average case sets in abruptly with great pain and profound shock, and that death follows within a few days. This may occur, but the usual clinical case in my experience has not followed this pattern. Before discussing the clinical features of mesenteric thrombosis, I should like to emphasize the fact that they depend to a large extent on the completeness of the occlusion, the suddenness of its development, and the degree of anastomotic circulation. When the occlusion is sudden, the onset of pain is abrupt followed by inadequate blood supply, infarction occurs and is identified clinically by the presence of blood in the vomitus. Blood may also be found in the stool, but this is a later manifestation, coming on 24 to 48 hours after onset. In sudden occlusions, the shock may be so great that death occurs within a few hours.

More commonly, however, the disease starts with moderate pain and shock and little or no blood in the stool. In this milder type, the only symptoms during the first 24 to 48 hours may be colicky abdominal pain, nausea and vomiting, tenderness in the abdomen, fever, and rapid pulse rate; these are not positive identification marks of any particular disease. Sometimes the abdominal distention, pain and rigidity, and slight fever are mistaken for evidences of incomplete bowel obstruction. After the first 36 to 48 hours, the pain becomes steadier, the shock more marked, the abdominal tenderness more severe, and the temperature and pulse rate higher. One is led to believe that the patient has an unexplained form of peritonitis. It is true that peritonitis may be a complicating factor. It is not a purpose here to rob mesenteric thrombosis of its dramatic and catastrophic aspect, but more to emphasize the fact that many patients do not have these features.

Thus, the most important features of mesenteric thrombosis are: (a) Sudden pain across the upper abdomen. This pain lacks the localization of other pains associated with special conditions as peptic ulcer and gallstones. (b) Vomiting and distention of the bowel usually occur. (c) Some degree of shock may be present in severe cases,

but it is often absent unless a considerable portion of the bowel is involved. (d) Fever is usually not present in the early stages, but may come on two or three days after onset when bowel gangrene sets in. (e) Although distention is a prominent feature, muscular spasm is usually absent. (f) Peristaltic rushes are absent (Fig. 1).

Diagnosis: The diagnosis of vascular occlusion is always difficult and frequently impossible to make. Early diagnosis is important because other diseases that may be helped by surgical intervention may be recognized and dealt with effectively. Bowel obstruction,

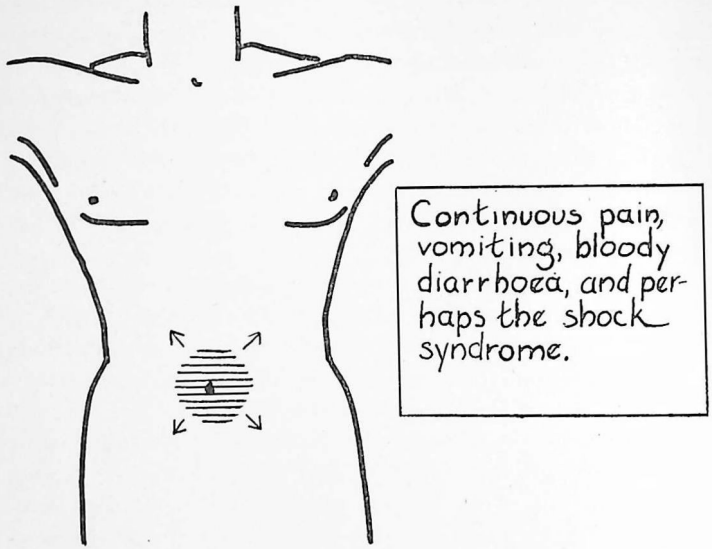


Fig. 1.—Mesenteric thrombosis. Diagram showing area and distribution of pain in acute mesenteric thrombosis.

peritonitis, gallbladder disease, perforating peptic ulcer with peritonitis, and pelvic diseases must all be taken into consideration in differential diagnosis. Mesenteric thrombosis is usually a disease of people past the middle period of life, when arteriosclerosis is common. Embolism, however, may occur in younger persons, especially those with a vegetative endocarditis.

Acute mesenteric thrombosis is often simulated by acute pancreatitis and is almost indistinguishable from acute bowel obstruction. Many times genuine acute bowel obstruction is present in mesenteric

thrombosis. Absence of a high fever and abdominal muscle rigidity are two points in differentiation. Since the differential diagnosis of mesenteric thrombosis is often impossible before operation, the physician's responsibility is to recognize the possibility of mesenteric thrombosis and the need of surgical intervention.

TREATMENT

The treatment of mesenteric thrombosis is surgical rather than medical. When there is acute abdominal pain and bloody diarrhea, an operation should be performed with the hope that an early resection of a small loop of bowel may be sufficient to save the patient's life. However, measures must be carried out to combat shock and sustain the patient in the crisis.

1. Intravenous injections of 1000 cc. of ten per cent glucose in normal saline are helpful, but blood or plasma transfusions are better.
2. An opiate, morphine sulfate, 0.016 Gm. (¼ grain), or pantopon, 0.02 Gm. (⅓ grain), hypodermically, is necessary for pain.
3. Sometimes the administration of oxygen is helpful.

REGIONAL ENTERITIS

Since Crohn and Ginsburg first described this condition in 1932, there has been considerable interest manifested in regional enteritis, but little has been added to our knowledge of this disease. It is a condition which in its acute phase must be differentiated from acute appendicitis and other acute inflammatory lesions of the right lower quadrant.

Etiology: The etiology is unknown. The most promising hope lies in finding an agent that causes obstruction of the mesenteric lymphatics. To date, infection has not been proven an etiologic factor.

Pathology: The gross appearance varies with the stage of the disease. Roughly, the condition is divided into the acute and the chronic phases. In the acute phase, the mesentery is so swollen and edematous that the bowel seems to sink into the mesenteric fat. The bowel itself is thickened, red, lusterless, and covered with plastic exudate. The process is most commonly found in the terminal end of the ileum and often stops abruptly at the ileocecal valve. However, it may exist in any part of the gastrointestinal tract from the duodenum to the rec-

tum. Several segments of the bowel may be involved with intervening areas of normal tissue. In the chronic stage, the muscular layer is markedly thickened and the lumen of the gut is narrowed. The marked redness of the acute phase fades to a purple-brown.

Microscopically, there are chronic inflammatory changes with occasional giant cells.

Signs and Symptoms: The disease is commonest in the young with the predominance in females being two to one. In the acute phase, the symptoms are similar to acute appendicitis with nausea, vomiting, and localization of pain in the right lower quadrant. Tenderness and rigidity are present in this region, and a mass may be palpable. In the chronic stage, the chief symptoms are pain and changes in the bowel habits of the heretofore regular patient. Masses may or may not be palpable.

Diagnosis: In the acute phase, the diagnosis is usually made at the operating table. In the chronic phase, gastrointestinal x-rays carefully done will show areas of the gut in which the lumen is markedly narrowed. This is known as the "string sign." On fluoroscopy, the motility of the barium is carefully watched in the terminal ileum, and any area showing abnormal mobility should be suspected. Boon has advised introducing a Miller-Abbott tube down to the lesion and then administering the barium through it in order to minimize the amount of barium necessary for fluoroscopy. Any case suspected of having regional enteritis should have complete gastrointestinal x-rays, including a barium enema to rule out the possibility of several areas of the gut being involved with intervening normal tissue.

TREATMENT

The accepted form of treatment has been surgical resection of the involved area together with wide sections of normal tissue on either end.

It has been realized, however, that the acute phase may end in spontaneous regression and, therefore, some men advocate conservative treatment in this stage.

There is no certainty that wide resection will prevent the condition from occurring in other segments of the bowel, and, therefore, the prognosis should always be guarded.

ULCERATIVE COLITIS

Ulcerative colitis is a disease of the large intestine characterized by inflammation and ulceration. It may be acute, or chronic with acute exacerbations. Acute ulcerative colitis sets in abruptly, often with sudden pain resembling that of acute appendicitis. The etiology is still undetermined, and there is a question as to whether the disease is a distinct entity. It usually begins in the rectum and moves upward across the transverse colon, often reaching the cecum. The importance of making a diagnosis in the early phase of the disease cannot be stressed enough, since prompt treatment may result in cure, while without treatment the patient will probably pass from the acute stage into the chronic. The disease may be fatal in the acute phase.

Etiology: Many different agents have been proposed as the cause, but no agreement has been reached as to a single etiologic factor. However, it is generally believed that the disease is infectious in origin. Hurst suggested that it was due to an unknown organism which was closely related to the Bacillus dysenteriae, since it was similar to bacillary dysentery. Rankin, Bargen, and Buie believe the disease is of bacterial origin and that the primary exciting factor is the diplostreptococcus. They found that infected teeth, tonsils, and other foci of infection have preceded cases of ulcerative colitis, and that removal of foci of infection may cause a temporary flareup. Allergy may play a definite rôle in etiology, since many cases which have not responded to other forms of treatment have been benefited by management based on this hypothesis. Systemic changes in the body, alone or in conjunction with other factors, may be responsible for ulcerative colitis. Endocrine disturbances, too, have been suggested as causative agents. Infection with gonococci, tubercle bacilli, streptococci, or other organisms may play a rôle in etiology, as well as vitamin or other deficiencies. Mental and nervous disorders also play a part. Ulcerative colitis has followed severe streptococcic infections associated with chronic nephritis, tonsillitis, or acute rheumatic fever.

Signs and Symptoms: Patients with ulcerative colitis as a rule are in the second to fourth decades of life. Symptoms are not always clear-cut. Frequently the onset is abrupt, and nausea, weakness, fever, and a bloodless diarrhea are commonly noted. However, there may be constipation or no change in bowel habits. Often the tongue has

a white furred appearance which disappears as the disease progresses. The acute episode may end fatally in a short time, or it may subside only to flare up again later in milder or more severe attacks until the typical picture of chronic ulcerative colitis is evident.

At times the disease begins in a gradual and progressive manner with mild diarrhea, to which complaint the patient may pay little attention. The diarrhea gradually grows worse, the patient becomes weak, and blood and pus appear in the stools. The patient loses weight as a result of anorexia and diarrhea. This marks the beginning of the chronic stage of ulcerative colitis. Patients with chronic ulcerative colitis present a characteristic history of frequent intractable rectal discharges of pus, blood, and mucus mixed with feces. The character of the stools is dependent on the severity of the disease and the degree of intestinal involvement. Cramps and distress from gas, or pain in definite regions, such as starting in the upper left part of the abdomen and working down to the left thigh or along the course of the large intestine, are common symptoms. The patient has a drawn expression and the complexion is of a peculiar grayish-yellow color.

Premonitory signs of an acute exacerbation include malaise, general exhaustion, fatigue, and a pulling sensation in the abdomen. Aches and pains are felt over the entire body, and small sores may appear in the mouth. The clinical course of the acute form is usually comparatively short and stormy. The disease may be highly toxic and fulminating with a fatal termination in two or three weeks, or the patient may recover in from two to six weeks. On the other hand, the disease may become chronic and continue for months or years, punctuated by periods of remissions and exacerbations.

Diagnosis: The classical picture of ulcerative colitis with fever, malaise, chills, weakness, sweating, and prostration may make diagnosis comparatively easy. However, it must be differentiated from such acute diseases as typhoid fever and amebic or bacillary dysentery. It is important to distinguish it from amebic dysentery by continuous and careful examinations of the stools for ameba and ova. Carcinoma or tuberculosis of the bowel and other granulomatous diseases of the colon must also be considered before the diagnosis of ulcerative colitis is made.

The five main diagnostic aids are:

1. History:
   a. The patient has a diarrhea which causes little distress, but which does not respond to home remedies. A few weeks later a bloody diarrhea develops. This history of blood in the stools, especially in patients between the ages of 20 and 50 years, is important in diagnosis.
   b. Usually pain of the crampy type is felt on both sides of the abdomen. Sometimes it is generalized at first, and then localizes in the left lower quadrant.
   c. Anorexia as well as loss of weight are outstanding features.
   d. Fever of the septic variety points to an active infection.
   e. Exhaustion is out of proportion to the other symptoms.
   f. The patient acquires a muddy-gray pallor.
2. Digital or rectal examination often serves to disclose tender ulcerated areas. About 90 per cent of all cases of ulcerative colitis start in the rectal portion of the large bowel.
3. Proctoscopic examination furnishes conclusive evidence of ulcerative colitis, showing typical ulcerations of the bowel.
4. X-ray examination often shows a characteristic feathery appearance of the bowel. It may reveal the extent of involvement and degree of destruction.
5. Other diagnostic aids include gastric analysis, stool and blood studies, bacteriologic and parasitologic examinations, and observations as to allergy and deficiency states.

The complications of ulcerative colitis include severe and prostrating hemorrhages and multiple abscesses throughout the bowel. Perforation with peritonitis sometimes causes a fatal outcome.

Prognosis: Formerly the prognosis was looked on as very unfavorable because few patients recovered, but within recent years the mortality rate has decreased to about ten per cent. This reduction is probably due to more accurate and prompt diagnosis, since the disease is amenable to treatment if discovered early. Most cases are subject to recurrence, but if the episodes are treated promptly by complete bed rest and other measures the attacks become less severe and eventually cease in the majority of patients.

TREATMENT

1. Complete bed rest is essential until all signs of inflammation disappear.

2. Small blood transfusions of 300 to 400 cc. should be given several times a week.

3. An understanding of the pathological lesions reveals that food with a high residue throws a burden on the involved large bowel. The diet must be of a character that will lessen this load as much as possible. A low residue, high caloric (3000), and high protein diet is advised. The utilization of vitamins is important; yeast or vitamin B tablets and large amounts of vitamin C in divided doses are recommended. It is necessary to educate the patient as to the importance of eating; the tray should be attractive with small portions of food appetizingly prepared.

4. Large doses of calcium, in the form of lactate or gluconate, 2 to 4 Gm. (30 to 60 grains) daily, orally, or calcium chloride, 10 cc. of a five per cent solution, may be injected intravenously slowly. Many observers believe that ulcerative colitis is associated with a defective calcium metabolism.

5. Paregoric may be given in doses of 1.33 to 2.00 cc. (20 to 30 minims) three times a day to control the debilitating diarrhea. Bismuth subnitrate, 1.33 to 2 Gm. (20 to 30 grains) three times a day, may also be of value. Tincture of iodine, 0.33 to 0.53 cc. (5 to 8 minims) in a glass of water on a full stomach, or some iodine preparation, is of aid in 15 to 20 per cent of cases.

6. Dilute hydrochloric acid, 1.33 to 4 cc. (20 to 60 minims) in a glass of water, may be taken with and after meals, to combat the achlorhydria often associated with ulcerative colitis.

7. Anemia, especially the lowered hemoglobin content of the blood, is an outstanding feature to be remedied. Iron and ammonium citrate, 1 Gm. (15 grains) three times daily, should be given. Intramuscular injections of liver extract, 2 to 3 cc. twice weekly, are also valuable therapeutic aids.

8. Bowel irrigations with antiseptic solutions have been recommended. Experience teaches us that physiological saline is as good an irrigating fluid as any.

9. The sulfonamide drugs have been recommended in addition to the general treatment, and satisfactory results have been obtained from their use in some cases. Neoprontosil, 0.33 Gm. (5 grains) t.i.d., has been the drug of choice since it is less liable to produce toxic reactions than the other drugs, and at the same time it is equally effective. However, sulfanilamide has been used with comparatively good

results. Sulfaguanidine, and more recently sulfasuxidine, have been receiving favorable reports in the literature.

10. *Specific Treatment:* The concentrated serum seems to be most effective in controlling the acute phase which frequently clears up rather promptly on administration of injections twice a day for three to six weeks. The dosage varies with the patient and with the severity of the disease. The concentrated serum is usually given intramuscularly. The first dose consists of a few minims; this amount is increased by one minim per dose until 1 or 2 cc. are administered daily. Sometimes the disease is so acute that the patient must be given fairly large-sized doses intravenously. Usually the serum treatment combined with the other therapeutic measures already mentioned brings the disease under control, but this does not mean that treatment is finished. The patient must observe a rigid routine of diet and medication for at least a year after release from the hospital. After several weeks of serum treatment, the administration of vaccine is begun. It may be given twice a week, subsequently once a week, and later the intervals are lengthened until the patient receives a dose of vaccine every month for a number of months. The initial dose is $\frac{1}{10}$ cc. which is increased in increments until the patient is being given $\frac{1}{2}$ cc. as often as necessary. Persistence is the most important part of the treatment. The patient must not discontinue therapy when he feels quite comfortable and the acute phase is under control; early cessation of treatment will probably result in recurrence, which is more difficult to clear up than the initial attack.

11. Surgery is indicated in cases of the fulminating type, perforation, or repeated hemorrhages of the colon, abscess or fistula formation, acute intestinal obstruction, and complicated cases. Patients with intractable symptoms which are not considerably improved after a course of medical treatment are candidates for surgery. Ileostomy with a follow-up colectomy if necessary is the usual surgical procedure employed.

HEMATEMESIS

Hematemesis or vomiting of blood is among the most important medical emergencies encountered, since prompt and adequate management is necessary to save the life of the patient.

Etiology: Acute or chronic peptic ulcer is the commonest cause of hematemesis; approximately one-third of patients have hematemesis during the course of the disease. Peptic ulcer, cirrhosis of the liver, and carcinoma of the stomach are the main causes of profuse hematemesis, but there are many other conditions that may occasionally produce hemorrhage, as jaundice, acute hepatitis, acute gastritis, infectious diseases, and trauma.

Confusion may arise in the diagnosis when blood from the nose or lungs is swallowed and then vomited. A careful history, complete physical examination, and a few simple tests, as studying the specimen for tubercle bacilli, are usually sufficient to determine the cause of hematemesis.

Signs and Symptoms: The blood may be either clotted or fluid, and the color varies though it is usually dark. The color of the blood is dependent on the length of time it has been in the stomach and the amount of acid in the gastric juice. Vomiting of blood causes anemia with its consequences, and there may be slight fever. Sometimes edema develops. Occasionally syncope or convulsions occur. Hematemesis is often the first sign of an acute ulcer. If the patient is first seen in a state of collapse after a severe hemorrhage, he is pale, the pulse is rapid and thready, the blood pressure is reduced, and the skin is cold and clammy.

Diagnosis: Hematemesis must be differentiated from hemoptysis, but this is not usually difficult. The history of previous bleeding from the lung, evidence of tuberculosis or heart disease precede hemoptysis, while in hematemesis a history of cirrhosis of the liver, gastric disturbances, or previous hematemesis is obtained. In hemoptysis the blood is bright red, frothy, and mixed with mucus, and it is ejected after a tickling sensation in the throat; in hematemesis the blood is usually dark in color unless the hemorrhage is profound and has an acid reaction.

If the patient is not seen during the attack, difficulty in diagnosis may arise. Some hysterical patients swallow blood and then eject it, or more often they consume wine, juice of cherries or strawberries, or some red-colored fruit which stains the vomitus so it looks like fresh blood; others take iron, bismuth, and bile which give the blackish color of altered blood. Examination of the vomitus for blood will clear up this confusion.

Prognosis: Prognosis is favorable, though when bleeding is caused by cirrhosis of the liver or if the patient with a peptic ulcer is past 50 years of age, the outlook is grave. When the patient is over 50 years, arteriosclerosis is common and the ulcerous lesion may open into a hardened artery which fails to contract, and hemorrhage may be fatal. In younger individuals, the elasticity and resiliency of the artery are preserved and clotting tends to occur. It should be remembered that a patient who is hemorrhaging may die despite the best of care. This is particularly true when the bleeding is from a ruptured esophageal varix, perforated aneurysm, or from an ulcer which involves the pancreas.

The severity of the hemorrhage and the underlying cause are the chief factors in prognosis. However, other elements are important too, as the ability of the individual to withstand hemorrhage, the general state of health at the time of hemorrhage, and the precision and care used in management. While the blood counts and the reduction in blood volume are indicators of the degree of hemorrhage, it is the pulse rate, blood pressure, and response to transfusions that reveal how well the patient tolerates the loss of blood.

TREATMENT

The main principles in treatment are to keep the patient quiet and to maintain adequate blood volume by means of intravenous fluids and transfusions. In the early stage, the patient should be made comfortable by means of sedation. After the state of collapse subsides and the pulse becomes slower and stronger, usually within an hour, the patient may be moved to a suitable place for treatment. He should not be moved when he is in a state of shock because it may cause immediate death.

1. The patient should be put to bed as soon as possible, with his head lower than his feet. Heat may be supplied to the body in the form of blankets and hot water bottles. Absolute rest is required and is attained by the administration of morphine sulfate, 0.016 Gm. (¼ grain) or more, with atropine sulfate, 0.45 mg. (1/150 grain), hypodermically; nembutal, 0.39 Gm. (6 grains), chloral hydrate, 0.19 Gm. (3 grains), or sodium bromide, 2 Gm. (30 grains), may be given by rectum. The patient with hematemesis usually is terror-stricken; sedation should be repeated as often as necessary to keep

these individuals in the "twilight zone of consciousness." If the hemorrhage is due to cirrhosis of the liver, morphine should be withheld or given in minute doses, because the detoxicating power of the liver may be diminished so that 0.016 Gm. (¼ grain) morphine may be harmful.

2. Nothing should be given by mouth for a day or two, though the mouth may be rinsed out with water from time to time and ice chips given.

3. A blood count must be done and the hemoglobin percentage estimated immediately. These are of value in that they show the degree of hemorrhage, though the blood count cannot always be relied on because it may appear higher than it really is, due to dehydration or hemoconcentration. This is especially true immediately after hemorrhage has occurred and before the blood volume has been restored by transfusions and intravenous fluids.

4. The blood must be typed and a donor secured in case an emergency transfusion is necessary. Blood transfusions are required if the hemorrhage continues. Between 100 and 200 cc. may be given at intervals of one to two hours.

5. An attempt is made to restore the blood volume by administering saline or glucose intravenously, or saline and tap water by rectum. These fluids must be given slowly. The condition of the patient is improved by the intravenous administration of 1000 to 2000 cc. of five per cent glucose in normal saline daily in most cases, but some clinicians believe fluids promote the hemorrhage. However, if the blood volume is maintained, 2,000,000 red blood cells are sufficient to carry on proper oxygenation of the tissue throughout the body, and fluids should not have an ill effect.

6. The blood pressure should be taken immediately and every two hours thereafter until the crisis is over. The pulse rate should also be determined every two hours. A rapid, thready pulse usually means the hemorrhage is continuing, whereas a slower rate indicates that the patient is tolerating the hemorrhage well.

7. Thromboplastin, 20 cc. intravenously, or some like substance may aid coagulation. More rapid clotting of the blood may also be obtained by an intramuscular injection of 10 cc. of 10 to 20 per cent calcium gluconate every four hours for two to four injections.

8. Cathartics and enemas are contraindicated.

9. After the patient has improved sufficiently, a diet routine may be started. There is some controversy as to whether the patient should be fed immediately or not. Recently Meulengracht's treatment has been used whereby the patient is placed on a soft palatable diet immediately. However, it is best to withhold food by mouth for 48 to 72 hours.

10. If the hemorrhage is not controlled in three days by strict and adequate medical measures, the surgeon should be given an opportunity to locate the bleeding vessel and ligate it. The best surgical results are obtained in patients with chronic ulcers, because the ulcer is easy to locate and the diagnosis is more or less confirmed before surgery is undertaken.

11. X-rays should not be taken for several weeks, because barium acts as a foreign body and may precipitate a recurrence of the hemorrhage. It is much more important to stop the hemorrhage than to diagnose the cause.

CHAPTER XVII

The Liver

JAUNDICE

Jaundice is due to an excessive amount of bile pigment in the blood and tissues of the body. Unlike other secretions, bile produces an intense discoloration of the tissues and its presence is promptly recognized.

Etiology: Jaundice, like anemia, is a condition that may be brought about by many different causes. It is a sign found in a variety of diseases caused by abnormal conditions having little or no relation to one another. The chief factors producing jaundice fall into three groups: (1) Excessive hemolysis of the red blood cells as seen in acute or chronic hemolytic jaundice; (2) obstructive lesions in the common bile duct, and (3) damage of the liver cells themselves caused by toxic agents or infections, commonly known as intrahepatic jaundice. McNee recognized these varieties and classified jaundice as follows: (1) Hemolytic; (2) obstructive, and (3) toxic and infective hepatic jaundice.

Signs and Symptoms: An attack of jaundice may be acute or chronic. It may come on abruptly, associated with fever, chills, general malaise and be merely a subsidiary event in the course of a serious and severe disease as acute streptococcal hepatitis, or it may develop so imperceptibly without any other symptoms that the patient is considered more jaundiced than ill. The urine may possess a definite greenish hue due to the presence of bile pigment; the stools may be colorless and described as clay-colored in obstructive jaundice. However, jaundice is usually recognized by the presence of the yellow pigmentation in the sclerae. Other organs may also be involved; for example, the liver may be enlarged and tender, the heart slower than normal, and there may be a tendency toward capillary oozing throughout the body.

DIFFERENTIAL DIAGNOSIS OF JAUNDICE

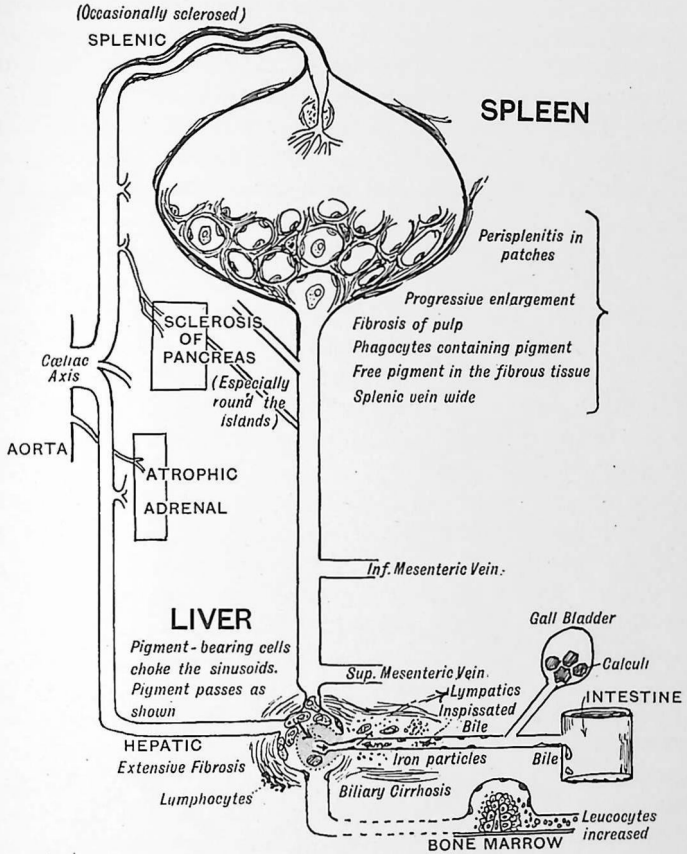
DISEASE	CLINICAL FEATURES						LABORATORY FEATURES						
	Pain	*Weight Loss*	*G. I. Complaint*	*Fever*	*Clay Stool*	*Dark Urine*	*Icterus Index*	*Van den Bergh*	*Bile in Urine*	*Urobilinogen in Urine*	*Urobilinogen in Feces*	*Liver Function*	*Pancreatic Enzymes in Urine and Blood*
Obstructive Jaundice — Gall Stone	++++	0	+++	±	+++	+++	8 to 100 (20 to 60)	Direct	++++	0 to 6 mg. (10 to 100 if there is associated liver damage)	10 to 500 mg.	Normal (unless associated with liver damage)	Normal
Obstructive Jaundice — Cancer	±	++++	++	0	++++	++++	80 to 300	Direct	++++	0.0 to 0.3 mg.	0.0 to 5.0 mg.	Normal (unless late in disease or with metastases)	Increased (early)
Hepatic Jaundice	+++	+	+	+++	0 to +++	0 to +++	10 to 300	Direct or biphasic	+ to +++	8 to 400 mg.	8 to 1200 mg.	Impaired	Normal
Hemolytic Jaundice	0	0	0	0	Green	0	8 to 30	Indirect	0	1 to 3 mg. (depending on liver function)	300 to 3000 mg.	Normal	Normal

Classification:

1. Hemolytic:
   a. Acute:
      (1) Due to acute infections as streptococcal infections, typhoid fever, Weil's disease, and malaria.
      (2) Phosphorus, arsenic, or other poisoning.
   b. Chronic:
      (1) Congenital or familial.
      (2) Acquired.
2. Obstructive:
   a. Gallstones, catarrhal inflammation of the duodenum, ampulla of Vater, and common bile duct.
   b. Carcinoma of the head of the pancreas.
   c. Enlarged lymph nodes pressing the common duct from without, as in carcinoma, leukemia, or Hodgkin's disease.
3. Toxic or infective jaundice (otherwise known as intrahepatic jaundice).
   a. Acute hepatitis, leading sometimes to yellow atrophy and at other times to healing
   b. Multiple abscesses of the liver.
   c. Sclerosis of the liver.
   d. Multiple carcinoma of the liver.

Hemolytic jaundice, also known as hemolytic anemia, follows a rapid destruction of the red blood cells and occurs in the acute or chronic stages. Acute forms are seen in connection with severe infections and sometimes after transfusions when there is a rapid destruction of the blood cells (Fig. 1). Chronic hemolytic jaundice is usually not as serious as the acute type. When a diagnosis of hemolytic jaundice is made, the cause of the destruction of the red blood cells must be determined and removed.

Obstructive jaundice in patients past the middle period of life is usually caused by gallstones in the common duct or by carcinoma of the head of the pancreas compressing the common bile duct. Other conditions may have to be considered, but only after the two commonest causes have been eliminated. Lymph gland enlargement due to carcinoma, leukemia, tuberculosis, or Hodgkin's disease may compress the common duct from without. The diagnosis of obstructive jaundice due to gallstones is made essentially by a history of repeated attacks of colicky pain in the upper abdomen followed by periods of jaundice. Gallstone disease almost always occurs in the middle period of life, especially in women who are stout and who have enjoyed



THE CHIEF CHANGES IN HÆMOLYTIC JAUNDICE

Fig. 1. (Moynihan's "The Spleen and Some of Its Diseases," W. B. Saunders Company.)

good health. Sometimes an x-ray is necessary to identify the gallstones. In carcinoma of the head of the pancreas, there is quite a different story. The patient is usually beyond the middle period of life and has been in failing health for some time; there is an associated loss of weight, appetite, and energy. Jaundice usually comes later and is at first mild and hardly noticeable; then there is an augmentation of the jaundice to a deep yellow type and finally a dark yellow or "black jaundice" develops. Sometimes in the diagnosis of carcinoma of the head of the pancreas, serum amylase and lipase determinations may be helpful but frequently they are not.

Intrahepatic or toxic jaundice involving the liver itself is the commonest type of all. In this category are a number of different kinds of the disease. For example, there is the acute catarrhal jaundice that occurs in youngsters and associated with gastrointestinal upset, some fever, a clay-colored stool, and a mahogany-colored urine. In this simplest of all kinds of jaundice, there may be a very mild hepatitis with an extensive mucous inflammation of the ampulla of Vater or there may be an extensive hepatitis with very little mucous membrane involvement in the duodenum. The lack of precise knowledge as to how much liver involvement exists makes it difficult to give an accurate prognosis in these cases. Sometimes this so-called simple jaundice fails to heal in the usual two- to four-week period, and in place of recovering the patient becomes worse and finally dies with an extensive destruction of the liver. However, acute catarrhal jaundice is usually followed by prompt recovery within a three-week period of time.

Acute hepatitis may follow the taking of drugs, as cinchophen, salvarsan, or such chemical poisons as impure alcohol. When the poisoning is due to arsenic, that metal may be recovered from the urine, hair, or nails. The liver in acute hepatitis is enlarged and painful. The patient is very sick. Fever, vomiting, and sometimes convulsions are present. As the condition becomes worse, vomiting and diarrhea of blood and urinary suppression intervene. If not relieved, the patient becomes more toxic and irrational, passes into a state of muttering delirium, and finally enters the stage of deep coma which is followed by death.

Diagnosis: The diagnosis of jaundice is usually obvious, but some confusion may exist from the poisons of carotinemia, saffronemia, or

ochronosis. Malingerers sometimes take saffron to simulate being jaundiced.

After one has decided that the patient is jaundiced, the method of approach in determining the kind of jaundice becomes the next step. In general, there are three important points: (1) A careful history of the events leading up to the onset of jaundice to determine if poisons, medications, or serious infections may have provoked the attack. The age of the patient is important because youngsters are apt to have a simple catarrhal kind of jaundice, and in the middle period of life gallstones are the commonest cause, while in later periods of life

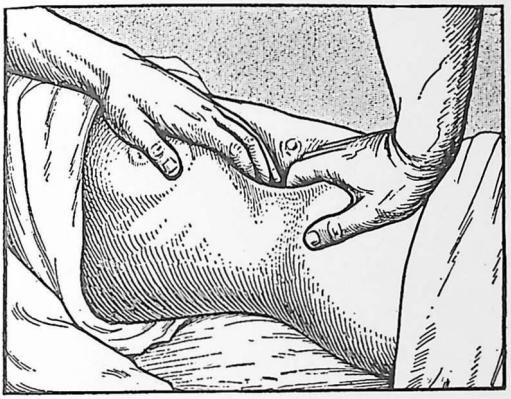


Fig. 2.—Palpation of the lower border of the liver (Gilbert's procedure).

carcinoma of the head of the pancreas must be considered. The associated complaints constitute guide posts in the differential diagnosis of jaundice; for example, a patient beyond the age of 50 years who has been in poor health for some weeks and gradually loses strength, weight, and appetite, followed by a gradually deepening but painless jaundice, is according to the law of averages very likely to have carcinoma of the head of the pancreas.

(2) The examination of the patient: Very often little can be obtained from the physical examination, but there are notable exceptions. The presence of chills and fever in a jaundiced patient may indicate such conditions as acute cholecystitis with acute cholangeitis, epidemic infectious jaundice, or abscesses of the liver following pyelo-

phlebitis. The enlargement of the liver may indicate abscess, biliary cirrhosis, or carcinoma of the liver. Certain poisons, particularly phosphorus, produce a prompt enlargement of the liver with an abrupt onset of jaundice. The physical examination must include careful palpation of the lymph nodes of the body, as generalized carcinomatosis, leukemic leukemia, or syphilis may be associated with involvement of the biliary passages and pressure on the ducts from without, causing jaundice. Rectal examination for carcinoma must be done, as there may be metastases to the liver or the lymph glands around the large bile ducts even before many symptoms are present

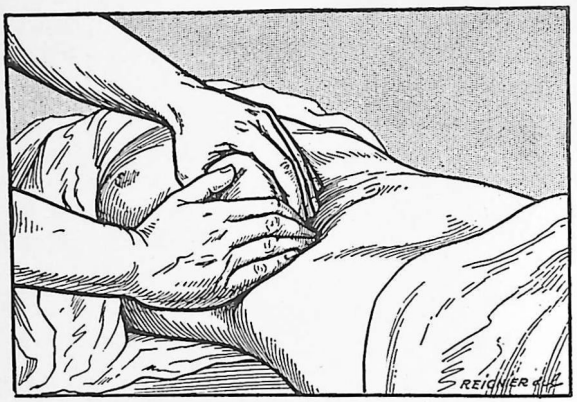


Fig. 3.—Palpation of the lower border of the liver (Mathieu's procedure).

from the rectal involvement itself. Palpation of the abdomen may reveal a distended painless gallbladder in a middle-aged person or an older one that suggests carcinoma of the head of the pancreas. Gallstones seldom cause jaundice and enlarged gallbladder.

As a rule, a precise history and a careful physical examination are all that are required to make a conclusive diagnosis of the cause of jaundice. Sometimes the cause and kind of jaundice are not so obvious; then we must resort to the third phase of investigation, that is, (3) the laboratory aids. (a) As the hemorrhagic tendency in a jaundiced patient is of such outstanding importance to the examining physician, the methods of determining the degree of the threat of hemorrhage will be discussed briefly. The bleeding time and coagulation time of the blood must be estimated. Although normal figures

for these tests do not eliminate from consideration the tendency to hemorrhage, they are helpful. The prothrombin deficiency in the blood may now be determined with considerable accuracy and this is the best index of the hemorrhagic tendency. Vitamin K, being a fat soluble vitamin, is dependent upon bile salts for absorption in the gastrointestinal tract as other fat soluble vitamins are. In an obstructive jaundice, vitamin K may fail to be absorbed. As vitamin K is responsible to some degree for the prothrombin formation, lack of vitamin K may cause bleeding; then, too, the liver may be diseased and incapable of forming prothrombin from the vitamin K (anti-

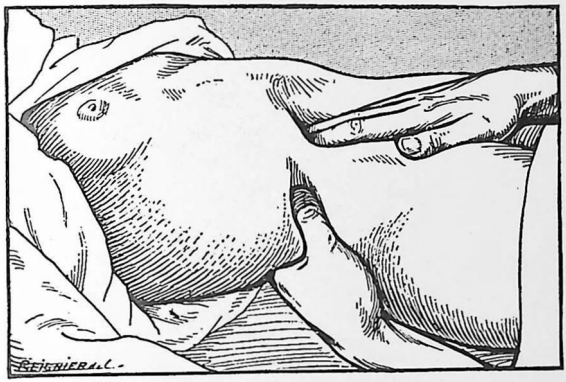


Fig. 4.—Palpation of the lower border of the liver (Glénard's thumb procedure).

hemorrhagic vitamin). The bleeding time and clotting time may be normal and yet prothrombin deficiency in the blood may be present. A normal prothrombin time is from 11 to 12.5 seconds. In jaundice, it may be very greatly reduced and when it is 40 per cent less than normal, the patient is in the danger zone. This is an important determination because it is a guide to the treatment. To overcome the hemorrhagic tendency, several preparations are now available which increase the prothrombin level of the blood to normal. Such preparations are Klotogen and Synkamin. These may be injected intravenously or taken by mouth two or three times a day, depending on the severity of the jaundice.

(b) A plain x-ray plate of the upper abdomen may reveal gallstones or a distended gallbladder. Other x-ray tests include a careful

gastrointestinal examination to eliminate carcinoma of the stomach and other lesions. A dye test of the gallbladder may fail to give aid when jaundice is present, but much information is sometimes obtained from the cholecystogram.

(c) An icterus index is an indicator of the degree of jaundice and tells whether it is becoming more intense or less so before it can be determined in any other way. The Van den Bergh test of the blood was introduced for the purpose of making a differentiation between hemolytic, obstructive, and hepatic types of jaundice. While it does not give as precise information as was hoped for, the test is often a valuable aid in the differential diagnosis of jaundice.

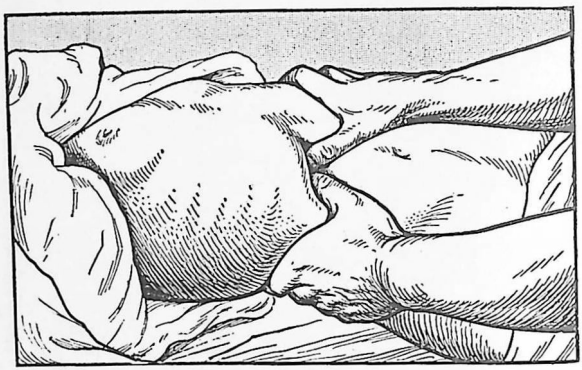


Fig. 5.—Palpation of the lower border of the liver and of the gallbladder by the two-thumb procedure.

(d) A careful examination of the blood, including counts to exclude unusual cases of leukemia or anemia, an estimation of the cholesterol content and if possible quantitative bilirubin determination of the blood, is important. From the blood examination one may also determine the quantity of total protein and albumin globulin ratio.

(e) A urobilinogen test is helpful at times. A positive urobilinogen test of the urine usually indicates jaundice with liver damage, while a negative test points to an obstruction due to carcinoma or stone extrahepatically.

(f) Liver function tests may be carried out in less acute and less obvious cases of jaundice; for example, the intravenous galactose test,

the hippuric acid test, and the phenotetrochlorophthalein test may be very helpful in determining whether the liver damage is an important contributory factor in the presence of jaundice.

TREATMENT

The treatment of the jaundiced patient depends almost entirely on what kind of jaundice the patient has. If it is due to toxin, the elimination of the toxin is the important thing. If due to obstruction, this must be overcome. If due to a lesion in the liver itself, therapeutic measures must be directed at the prevailing condition.

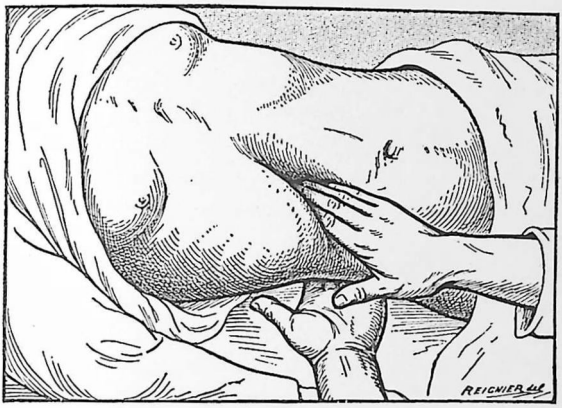


Fig. 6.—Bimanual palpation of the liver. The physician stands at the right of the patient. His left hand, with the thumb free and fingers together, is applied transversely behind the flank, against the last rib. His right hand, pressing in the abdominal wall, hooks about the liver and palpates it. The physician is thus enabled to appreciate the size, consistency, shape, and mobility both of the right lobe of the liver and of the gallbladder (Letulle).

Notwithstanding the cause of jaundice, the following general measures may be helpful:

1. Intravenous glucose, 1000 cc. of ten per cent solution, once or twice a day.
2. Intramuscular injections of vitamin B in doses of 10,000 to 20,000 units every day or two.
3. A high-carbohydrate low-fat diet.
4. Alkalinization with usual measures.
5. Heat applied to the abdomen in the form of hot wet stupes.

6. Bowels are kept active with magnesium preparations, as magnesium oxide, 0.66 to 1 Gm. (10 to 15 grains), three times a day following meals, or milk of magnesia, 15 cc. (½ ounce) daily. Simple saline enemas may give relief.

7. If severe pain is present, morphine sulfate, 0.016 Gm. (¼ grain), and atropine, 0.005 Gm. ($\frac{1}{120}$), or pantopon, 0.022 Gm. (⅓ grain), should be given hypodermically. These drugs may be repeated within an hour if indicated.

8. Calcium chloride, 20 cc. of a five per cent solution given intravenously slowly, may bring relief. Calcium gluconate or calcium lactate, 1 Gm. (15 grains), should be given three to four times daily.

9. Viosterol, 20 drops every two hours until six doses have been given, then 30 to 60 drops three times a day, should be administered.

10. Vitamin K should be given prophylactically, particularly if surgery is contemplated even if the prothrombin content of the blood is normal. An adequate oral dose is 1 to 2 mg. ($\frac{1}{60}$ to $\frac{1}{30}$ grain) daily in addition to 1 Gm. (15 grains) of bile salts. If the prothrombin content of the blood is low, the dose may be increased to as high as 5 mg. ($\frac{1}{12}$ grain) daily plus 2 to 4 mg. ($\frac{1}{30}$ to $\frac{1}{15}$ grain) of bile salts. If oral therapy is not feasible, it may be administered intramuscularly in the dose of 2 to 4 mg. ($\frac{1}{30}$ to $\frac{1}{15}$ grain). A single dose thus administered is effective for several days to a week.

11. Calamine lotion with one per cent phenol frequently applied locally may afford some relief for the intense itching.

12. In the event ascites is present, abdominal paracentesis is advisable. This procedure should be followed by administration of diuretics, as salyrgan, 1 cc. (15 minims), given intravenously every other day for three doses, or ammonium chloride, 2 Gm. (30 grains) three times a day may be given.

ACUTE HEPATOCELLULAR DISEASE (YELLOW ATROPHY)

Acute hepatitis is an acute inflammatory or degenerative disease of the liver. The malady is divided according to the degree and severity of the syndrome into a benign type, known as "acute catarrhal jaundice," a type of intermediate severity occasionally caused by metallic poisoning, and the stormy, dramatic syndrome of acute yellow atrophy.

Etiology: The etiology of hepatitis may be chemical, infectious, or metabolic. The known causes of chemical nature are chloroform, phosphorus, trinitrotoluene, arsenic, mercury, cinchophen, carbon tetrachloride, and sulfonamide drugs. The sulfonamide group of drugs has proved a particularly important etiological factor. Carbon tetrachloride may exert its noxious effect through inhalation over a long period of time. Infections which are of etiological importance are the common cold, influenza, syphilis, spirochetosis ictero hemorrhagica, and amebiasis. In cases associated with syphilis, it is often difficult to determine whether syphilitic infection or the arsphenamine therapy has damaged the liver parenchyma. There are cases reported in which the jaundice of the early stage of syphilis developed into acute yellow atrophy without the administration of arsphenamine. Metabolic states at times associated with hepatitis are pregnancy and hyperthyroidism.

Pathology: There is apparently a close relationship among catarrhal jaundice, intermediate or moderately severe hepatitis, acute yellow atrophy, and cirrhosis. The difference is one of severity of injury and of chronicity. The milder cases recover after an illness of weeks or even months, and are classified as catarrhal jaundice. If the jaundice becomes more severe and terminates fatally, acute yellow atrophy is recognized.

The basis of catarrhal jaundice may be mucoid obstruction of the opening of the common bile duct or toxic necrosis of the liver or cholangeitis. Biopsy shows cloudy swelling of the parenchymal cells and compression and inflammation of the small bile ducts and of the gallbladder. Necrosis of the liver cells is produced by the toxins involved, chemical or bacterial. The bacteria of bacterial toxins are seldom found in the liver. The poisons of disordered metabolism form an important group. These poisons are carried to the liver to be destroyed and the liver cells often perish in the attempt. In Weil's disease, the liver merely shows cloudy swelling, but it contains large numbers of spirochetes. There may be associated necrosis of the renal tubules.

The liver in acute yellow atrophy is atrophic and yellow. It may be half its normal size. At first the organ is bright yellow; later it becomes red as the necrotic cells disappear. The usual appearance at autopsy is a mottling of red and yellow areas. The kidneys are

apparently acted upon by the same toxin which destroys the liver, and the epithelium of convoluted tubules may show marked necrosis. The urea excreted is greatly diminished as it is no longer formed by the liver. The amino acids are correspondingly increased, as the normal de-aminization which occurs in the liver is stopped. The end picture of acute yellow atrophy with recovery is one of hyperplastic nodules of liver cells separated by an abundant connective tissue containing large numbers of bile ducts.

Signs and Symptoms: The onset may be insidious. The symptoms are varied. For several days slight jaundice, malaise, anorexia, nausea, occasionally vomiting and constipation or diarrhea are seen. Fever of 37.8° to 38.3° C. (100° to 101° F.) is seen in some patients. The jaundice then deepens, the stools become acholic, and the urine tinged with bile. Mental sluggishness, pruritus, and general lassitude are characteristic of this period. There may be bradycardia. The liver may be enlarged and tender. The gallbladder and spleen are sometimes palpable. As jaundice becomes more marked, the digestive disturbances may become less severe, although they frequently persist if untreated.

Drug intoxication with hepatitis may be accompanied by the symptoms of the effect of the drug on other organs or systems. Should the patient live two or three days, evidence of hepatic damage appears, as does enlargement and tenderness of the liver and at times of the spleen. Anorexia, epigastric distress, nausea, and vomiting are associated. Jaundice is frequently present.

Acute yellow atrophy remains benign for a period of days or weeks. The second stage, however, is abrupt in onset. Severe headache, restlessness, delirium, vomiting, convulsions, transient paralysis, and dilatation of the pupils are indicative of marked toxemia and irritation of the nervous system. The jaundice becomes deeper; the liver begins to diminish in size; hemorrhages may occur into the skin or from mucous surfaces. Abortion may take place. The temperature usually remains low, but may rise suddenly before death. The disease almost always proves fatal in a few days after onset of the severe symptoms, and usually after the development of coma and stertorous breathing.

Laboratory Aids: Recent investigators have agreed that a decrease in the amount of prothrombin in the plasma is the most probable

explanation of the hemorrhagic tendency in jaundice. The maintenance of a normal prothrombin value is determined by the presence in the food of an adequate supply of vitamin K and in the bowel of sufficient bile for absorption of vitamin K. The prothrombin content of the blood is decreased after experimental hepatic injury and in some cases of cirrhosis and severe hepatitis.

Slight elevation of the serum phosphatase may be of value as a means of indicating early liver damage in cases under treatment with neoarsphenamine. Syphilis *per se* does not elevate the blood plasma phosphatase. Early detection of an arsenical hepatitis is essential if severe grades of inflammation are to be avoided. The serum Van den Bergh reaction is direct or biphasic. The icterus index varies widely. As a rule, the higher the icterus index, the more severe the disease and the greater the possibility of transition to acute yellow atrophy.

Liver function tests are of questionable value in acute hepatitis, but the galactose tolerance test is useful in the diagnosis of recent diffuse hepatocellular injury. Bile is present in the urine. Its presence in the stool is variable.

At the outset of catarrhal jaundice, the urobilinogen of the urine is elevated. As the jaundice deepens, the amount rapidly decreases because bile is now largely excluded from the bowel and little urobilinogen is being formed and absorbed into the portal circulation. During this period, the feces urobilinogen is markedly reduced. The reappearance of an increased amount of urobilinogen in the urine is often the first evidence of improvement. The amount in the feces increases very rapidly. Persistent elevation of the urine urobilinogen, in spite of the disappearance of jaundice, should warn that liver damage still exists and that recurrence of jaundice may take place. This has been noted in cases of acute catarrhal jaundice which smoulder and then flare into acute yellow atrophy. In toxic jaundice, duodenal drainage should reveal bile in at least small amounts, in contrast to its absence in cases of neoplastic obstructive jaundice.

The leukocyte count is normal or decreased. A macrocytic anemia may occur in the more severe and prolonged cases. In the severe and terminal cases, nitrogen retention with uremia may complicate the cholemic picture already present.

Prognosis: Prognosis in acute yellow atrophy is grave, and that of all forms of hepatitis is guarded.

TREATMENT

1. Bed rest is essential in all cases of hepatitis until convalescence is well established.

2. Fluids should be forced.

3. The diet should be high in carbohydrate, moderate in protein, and low in fat. At least half the carbohydrate should be given as glucose. Intravenous ten per cent glucose is advisable in quantities from 500 to 1000 cc. daily, even though the patient does not vomit.

4. Hot abdominal stupes contribute relief from pain. If further sedation is required, a combination of barbiturates, salicylates, and codeine is effective. The more potent opiates are not tolerated well where liver damage is present.

5. Vitamin B in large doses, 10,000 to 20,000 units, intramuscularly is recommended.

6. Insulin in small doses has been advocated.

7. Duodenal drainage with 50 per cent magnesium sulfate solution is advised on a fasting stomach every four or five days. Magnesium sulfate, 15 to 30 cc. (½ to 1 ounce), may be given by mouth daily for catharsis if necessary.

8. Sodium thiosulfate in doses of 0.5 Gm. (7½ grains) intravenously two or three times daily is useful in rendering heavy metals insoluble and so retarding or preventing their absorption. Sodium formaldehyde sulfoxylate in doses of 10 Gm. (150 grains) intravenously daily is thought by some clinicians more effective in preventing the absorption of such metals.

9. Bile salts occasionally relieve digestive distress.

10. Ferrous salts may be necessary to combat the anemia. Antipruritics vary in their efficacy and may be left to individual selection.

CHAPTER XVIII

Acute Infections

FEVER, PERSISTENT AND OBSCURE

Occasionally fever constitutes the only evidence of disorder until later on when the disease has run almost its entire course. It is readily granted that the term "obscure fever" is a relative one, for what may be obscure fever in one locality may be quickly explained in another where more careful work is done. The term "obscure fever" should be reserved for the cases of long-continued fever in which careful and skillful examinations have been performed and yet the fever remains unexplained.

Etiology: After painstaking history and physical examination have been completed and the usual laboratory tests made, a certain number of cases will remain undiagnosed. The following diseases are the commonest causes of a persistent unexplained fever: (1) Tuberculosis; (2) subacute bacterial endocarditis; (3) carcinoma of internal organs; (4) thrombophlebitis; (5) rheumatic infection, and (6) a hidden septic focus. Typhoid fever, undulant fever, syphilis, and malaria may confuse one for a while, but the special tests clear up the diagnosis.

Diagnosis: Before a diagnosis of obscure fever is made, the history should be carefully studied, and a searching physical examination must be done. The aches and pains mentioned by the patient should be considered, as well as his habits and occupation. The character of the fever and mode of onset are often of aid in arriving at the diagnosis and determining the cause.

The approach to the special studies is outlined as follows:

1. Blood culture.
2. Throat, sputum, urine, and stool cultures.
3. X-rays of the chest.
4. Agglutination studies.
5. Rectal examination, especially if malignant disease is suspected.
6. Erythrocyte sedimentation test.
7. Radiography of the alimentary canal.

The blood, throat, sputum, urine, and stool cultures often reveal the causative organism as the streptococcus, staphylococcus, or tubercle bacilli. Tuberculosis should always be suspected; an x-ray examination showing a shadow at the apex of one lung with the associated symptoms of cough and loss of weight points toward tuberculosis unless another diagnosis can be positively made. The Widal test usually discloses typhoid, and the agglutination tests for tularemia, undulant fever, typhus, and Rocky Mountain spotted fever are equally revealing.

Failure to recognize the cause of the fever may be attributed to the atypical onset and course of the disease; the disease may not be well known or it may not come to mind because of its rareness in the locality; characteristic symptoms may not be present or they may be present for too short a period of time, or examinations may be inaccurate or carelessly done.

Concealed suppurative processes, as empyema, abscess in the mediastinum, perinephritic abscess, pararectal collection of pus, may be difficult to diagnose. The exploratory needle employed to make diagnostic chest taps is the instrument that has explained more unexplained fevers than any other. Notwithstanding x-ray and other examinations, percussion of the chest occasionally suggests the presence of loculated pus and the diagnostic tap reveals it. After a painstaking examination has been made, tuberculosis, subacute bacterial endocarditis, and thrombophlebitis should be considered. An early carcinoma of a parenchymatous organ, as the kidney, liver, or spleen, may escape diagnosis until late in the course of the disease.

CHICKENPOX (VARICELLA)

Chickenpox is an acute communicable disease characterized by eruptions in various stages of evolution.

Etiology: The infectious agent is a filterable virus; although it is entirely distinct from the virus of smallpox, nevertheless it has some relationship to the virus of herpes zoster. The disease is usually a childhood illness leaving a lifelong immunity, but adults who have not contracted this illness in childhood remain susceptible. The causative agent is air-borne and may also be spread by droplet infection.

Pathology: The superficial layers of the skin are involved though in exceptional cases there may be involvement of the corium. Since the outer layer of epithelium is implicated, pock marks or cicatricial changes are exceptional, unless secondarily infected. The pathological changes are limited to the skin and mucous membranes.

Symptomatology: The incubation period varies from 4 to 21 days, but it is exactly 14 days in most cases. Rarely is the disease ushered in with a convulsion. It usually starts with fever for approximately 24 hours with a continuance of the fever throughout the eruptive stage. The eruption starts on the face and torso. It has a tendency to exaggerate the number of lesions on the covered parts of the body, while the number on the extremities is less. The lesions hastily go through a transition of the macular to the papular stage and rather rapidly fill with a transparent, and exceptionally a translucent, fluid. The lesions are conglomerative or heterogeneous in character, *i. e.,* a given area will present lesions in the papular, vesicular, and desiccating stages. After approximately three to five days of fever and eruption, a normal temperature and a desiccation period of seven to ten days follows. The lesions are usually discrete. Very rarely will a malignant type (varicella gangrenosa necrotica) occur.

Complications: Chickenpox may be complicated by secondary infections of the skin, resulting in abscesses, furuncles, or erysipelas. The lesions may be malignant by their position in the larynx, cornea of the eye, or within the urethra. Occasionally encephalitis may be a complication.

Differential Diagnosis: Smallpox with its three- to five-day prodromal period and subsequent eruption is the most important disease in differentiation. Secondary pustular syphilis with its positive history and serological examination are readily ruled out. Secondarily infected scabies are easily recognized by their lack of eruption on the face and the intense pruritus at night. Pustular dermatoses, dermatitis herpetiformis, and impetigo are sometimes confused.

TREATMENT

1. Institutional vaccination for this disease has been tried but is not of practical usage. Pooled convalescent serum given intramuscularly in 10 cc. dosage during the first five days after exposure will generally either result in complete protection or so alter the infection

that there will be very few vesicles and practically no febrile reaction. Chickenpox is a reportable and placardable disease.

2. The patient should rest in bed until the lesions are past the acute stage and the temperature is normal for a few days.

3. Weak potassium permanganate tub soakings act as an antiseptic and alleviate the itching of the lesions. The crusts should be removed with ointment, as ointment of ammoniated mercury, only after complete desiccation has occurred.

4. In the presence of fever, a light diet is given.

5. The only danger in the disease is secondary infection of the lesions. To prevent this special attention to general cleanliness is imperative.

WHOOPING COUGH (PERTUSSIS)

Whooping cough is an acute communicable disease involving the upper respiratory tract and characterized by spasmodic attacks of coughing, terminating with an inspiratory whoop.

Etiology: The most likely cause of whooping cough is the Bordet-Gengou bacillus, although the virus has been commented upon as a symbiotic cause of infection. Bacteriologically, the bacillus has been demonstrated as being essential to the occurrence of the disease.

Pathology: The blood picture in most cases presents a most marked leukocytosis with a differential picture of high lymphocytes. The trachea, bronchi, and bronchioles are greatly inflamed during the early or catarrhal stage of the disease. At first the mucus secreted is not very thick, but later it becomes semiviscid and stringy, and accumulates. Some authorities believe this accumulation irritates the mucosa and causes coughing, which is spasmodic in character because the material is thick and difficult to expel. Others believe the paroxysms are due to the toxic effects of the organisms on the central nervous system. The tracheobronchial glands are usually enlarged and remain so for a few weeks after the disease is over.

Signs and Symptoms: The incubation period is from 14 to 28 days. Whooping cough may be divided into three phases:

Phase 1: The onset is usually insidious with cough accompanied by a catarrhal condition of the upper respiratory tract. The fever curve at the start may be of a low type. During this phase the patient may have a series of coughing spells which are usually nonproductive.

These coughing spasms are particularly troublesome during the night and early morning hours. The organisms may be found on potato agar culture plates. During the terminal part of this stage, lasting anywhere from one to two weeks, the coughing spells increase in severity and the transition to the second phase begins.

Phase 2: The paroxysmal stage. The second phase lasts approximately two to six weeks. During this time, a series of coughs accompanied by inspiratory whoops are audible. These spasms may be readily provoked by any irritation of the patient. An effort syndrome, such as fast walking, running, climbing up or down stairs, will precipitate a paroxysm. In infants, sensorium disturbances will provoke the characteristic whoop. These spasms are quite numerous during the day but seem more prolonged during the sleeping hours. The irritation set up in the pharynx by the coughing spells may invite edema and considerable stagnant mucoid material. In these cases, a moist character to the cough is noticed and it is usually terminated with an expulsion of this mucoid material, either by expectoration or vomiting. Gradually the number of spells during the day and night start to subside and the third phase begins.

Phase 3: This is the receding or convalescent stage, lasting from two to four weeks. Infrequently this stage prolongs itself or has an interim of quiescence, and then is repeated long after the expected time for recovery has passed. During this period, the number of whoops diminishes and the severity is decreased. In fact, toward the terminal stage of this phase, the spasms are only brought about by provoking or irritation or self-induction on the part of the patient.

Complications: The severe paroxysms may invoke an epistaxis or a cerebral accident. Occasionally ruptured blood vessels in the conjunctiva over the eye may occur. Especially encephalitis has been noted in the height of whooping cough. The danger in whooping cough is the secondary invaders causing a pyogenic pneumonia. Bronchopneumonia and atelectasis causing lung collapse, occasionally empyema, have been mentioned. Due to the intense strain in coughing, herniations in the abdominal wall may occur.

Diagnosis: Diagnosis may be difficult during the initial stage. though cough plate cultures are helpful. An early lymphocytic leukocytosis points to whooping cough. Influenza and bronchitis are

most often confused with pertussis, but can usually be eliminated from diagnosis when all symptoms are considered.

Prognosis: The mortality rate in children under four varies from 10 to 20 per cent. It is higher during the winter months when bronchopneumonia is common, and in midsummer when intestinal disturbances are frequent. The general rule is—the younger the child, the more serious the prognosis. If the initial stage is prolonged, the paroxysmal phase is not so severe.

TREATMENT

The patient should be isolated, particularly if there are other young children in the house, for a period of three weeks after the whoop begins.

1. Bed rest during the catarrhal stage and for a short time during the paroxysmal stage is indicated for children under four years of age. This is done to prevent severe complications. The patient's head should be elevated with two or more pillows which are equipped with rubber protectors. However, if the child is afebrile and the attack is mild, it may be most convenient to allow him to remain out of bed. Plenty of fresh air and natural sunlight are important. Care should be taken to see that the patient is warmly dressed, out of drafts, and properly isolated.

2. Proper nutrition should be maintained. It may be best to give a child frequent small semisolid feedings, rather than three regular meals. Glucose or sugar may be added to the diet to combat acidosis from vomiting. If vomiting occurs, the patient should be fed again about ten minutes after the paroxysm ends. Improper feeding may result in persistent vomiting, wasting, and lowering of resistance.

3. If vomiting is severe, gastric lavage with sodium bicarbonate, 3.1 Gm. (46.5 grains) to the pint, once or twice daily, combined with small rectal or drip saline infusions containing five per cent glucose is helpful. In these cases, plain water, sugar water, or a small amount of fruit juice should be given cautiously orally.

4. For the poorly nourished patient, transfusions of citrated blood, 50 to 150 cc. being given according to the age of the patient, may be a lifesaving measure. Intramuscular injections of whole blood are frequently helpful in quantities of 20 to 30 cc. Five per cent glu-

dose solution may also be administered intravenously in 50 to 100 cc. amounts.

5. Drug treatment is symptomatic and usually a simple expectorant mixture as

℞ Antipyrine ..... 0.533 Gm. (8 gr.)
Ammonium chloride ..... 2.66 Gm. (40 gr.)
Syr. Ilinonis .....30 Gm. (1 oz.)
Aqua dest. q. s.....60 Gm. (2 oz.)
Sig.: Teaspoonful every three hours.

is all that is necessary. Other drugs which may be of use are

a. Antispasmodics:
(1) Belladonna seems to be the drug of choice. It is given in increasing doses, beginning with 0.2 cc. (3 minims) three times a day, increasing one minim per dose per day until signs of toxicity appear.
(2) Ephedrine, 0.008 to 0.016 Gm. (1/8 to 1/4 grain), two times a day should be used with caution.
(3) Other drugs which have been recommended are eumydrine, four to ten drops of a 0.1 per cent solution, three times a day, and benzylbenzoate, 0.66 to 4 cc. (10 to 60 minims), daily.

b. Sedatives: Much sedation is contraindicated, since it usually prevents expectoration of mucus. Bromides, chloral, codeine, ether, or luminal may be used.
(1) Bromides, usually the ammonium salt, 0.133 Gm. (2 grains), with tincture of belladonna, 0.2 cc. (3 minims), and chloral hydrate, 0.133 Gm. (2 grains), are frequently given.
(2) Luminal is probably the drug of choice. It is prescribed in tablet or powder form in doses of 0.004 Gm. (1/16 grain) for an infant and 0.008 to 0.016 Gm. (1/8 to 1/4 grain) for older children, three or four times a day. If vomiting is severe, it may be prepared in special ampoules for injection.
(3) Ether in oil by rectum, one part ether to three parts oil, may be effective providing severe bronchitis or bronchopneumonia are not present.

c. Expectorants: Wine of ipecac, 0.133 cc. (2 minims); ammonium chloride, 0.133 Gm. (2 grains), or potassium iodide, 0.133 Gm. (2 grains), or a combination of the latter two have been recommended.

d. Vitamin C (ascorbic acid) seems to antagonize the growth of B. pertussis and inactivates its toxin. It is given in tablet form by mouth in doses of 200 mg. daily for the first week, 150 mg. daily for the second week, and 100 mg. daily for the third week. Half this dose is sufficient for children under one year of age.

6. *Specific Treatment:*
   a. Vaccines: In general, vaccines during the acute infection seem to be of little value. In most cases, children are not ill enough to warrant this procedure. If treatment can be started early in the catarrhal stage before the paroxysms develop, antigen, 0.2 cc., may be given as the initial dose to an infant, increasing the amount 0.2 cc. daily up to 1.0 cc., providing no reaction occurs.
   b. Sera: Hyperimmune serum has proved itself most beneficial in the treatment of sharp cases of whooping cough.
   c. Chemotherapy: While the sulfonamides have no direct effect on whooping cough, most complications of the disease respond very well to the drugs.
   d. Other measures:
      (1) The severity of the cough may be relieved by one or two x-ray exposures of one-quarter to three-quarters of a pastille dose applied to the back through a suitable filter.
      (2) Inhalations of seven per cent carbon dioxide in air or oxygen, or a mixture of helium and oxygen, may have a good effect.

7. *Prevention:* Vaccine injections have been followed by good results. Usually 8 cc. of vaccine are used, each cubic centimeter containing ten billion killed organisms. It is given in increasing amounts at weekly intervals for three weeks, the first dose being 1 cc. in each arm, and 1.5 cc. in each arm on the other two visits.

SMALLPOX (VARIOLA)

Smallpox is an acute communicable disease characterized by a prodromal period of three to five days, followed by an eruption and uniform stages of evolution.

Etiology: The disease occurs throughout the world, especially during the winter months. People of all ages are attacked, but it is most serious and fatal in young children. Infants before and after birth are susceptible. Negroes are affected more often than white people, and the disease is more severe and fatal in the colored group.

The cause of the disease is a filterable virus, but the specific agent is not certain. Guarnieri described certain inclusion bodies found in the cells which he called *Cytoryctes variolae*. A protozoan or bacterial etiology has also been suggested. The virus can be demonstrated in the fluid of the lesions, in the lesions, and the crusts.

Smallpox is transmitted directly in most cases, particularly by the droplet method. However, contact with the patient, scabs, scales, or

fluid from the lesions is a common means of communication. Whether the disease is air-borne is a question, though it is probable that any virus disease may be transmitted in this way for a very short distance.

Pathology: The most extensive changes are found in the skin and mucous membranes, since the eruption affects both. The lesions complete the evolution of a macular, papular, vesicular, and pustular phase, and terminate with crust formation. In the pustular stage, umbilication occurs. When the lesions heal, a central pit or depression remains, extending into the corium of the skin. The severity of the depression will propose the terminal cicatricial changes and may result in pit marks. The parenchymal organs present cloudy swelling and occasionally focal necrosis. A lymphoidal hyperplasia takes place throughout the body.

Signs and Symptoms: The incubation period is from 10 to 18 days, but is usually 12 days. The prodromal period of three to five days usually presents the picture simulating an influenzal infection. Chills, insomnia, headache, myositis are the commonest symptoms. The myositis may be quite intense and exaggerated as a low back pain. Usually recovery after this period is followed by the presentation of the eruptive stage. The eruptions are centrifugal in distribution, occurring first on the face and then on the extremities. A paucity of eruption is usually noted on the torso proper. The eruptions pass through a transition of macular, papular, rapid vesicular to pustular stages taking approximately seven to nine days to reach the height of their evolution. The lesions are usually quite discrete with a halo about them. Approximately seven to nine days of desiccation and terminal crustation occur before the completion of the course of the disease. Fever is quite characteristic of the prodromal period and a secondary rise occurs during the height of the pustular period.

Complications: Secondary infection may cause a streptococcemia, abscesses, furunculosis, areas of gangrene, and erysipelas. Pneumonia and encephalitis are not uncommon sequelae.

Diagnosis: Chickenpox may be readily differentiated by the eruption occurring in the febrile stage and the centripetal distribution of the lesions; pustular syphilis by its history, chronicity and serological examination. Other skin diseases, as measles, rubella, lichen urticatus, dermatitis venenata and medicamentosa, erythema multiforme,

scabies, pityriasis, and impetigo have their characteristic history and findings.

TREATMENT

Vaccination and re-vaccination are fool-proof measures in eradicating smallpox. Emergency vaccinations may be done with intradermal chorioallantoic chick embryo vaccine. Otherwise vaccination should be done within one year after birth, repeated at the pubescent and again at the adolescent stages of life.

Specific immuno-transfusions, colloidal gold, and chemotherapy have been found wanting after the disease has occurred. Symptomatic care is indicated. The patient should be isolated and quarantined. Vaccination of all contacts should be rigidly enforced. It is preferable that the patient be moved to an isolation hospital for care with subsequent fumigation and cleansing of his living quarters. The patient must be kept under strict quarantine until all crusts have separated, particularly those on the palms of the hands and soles of the feet.

The symptomatic care may be outlined as follows:

1. Rest in bed with plenty of fresh air.
2. The diet during the febrile stage should be limited to liquids, as milk, buttermilk, eggnogs, and broths. After the initial fever, nourishing solid food, as meat, eggs, and the more easily digested vegetables should be given in preparation for the stage of suppuration. During the secondary fever, diet is again limited to liquids.
3. Joint pains may be relieved by hot fomentations.
4. The patient should receive plenty of water and fruit juices.
5. Headache, which is one of the common complaints of these patients, should be treated by the administration of phenacetin, 0.33 Gm. (5 grains), three or four times a day, or acetylsalicylic acid, 0.66 Gm. (10 grains) three times a day, and occasionally, codeine sulfate, 0.033 to 0.066 Gm. (½ to 1 grain) as needed.
6. Tepid sponges, cold packs, or sponge baths are efficacious in the febrile states. Weak potassium permanganate tub soakings are soothing and will alleviate most subjective complaints.
7. Delirium is treated by the use of sedatives, such as chloral hydrate, 1 to 2 Gm. (15 to 30 grains) per rectum, or morphine sulfate, 0.033 Gm. (½ grain) subcutaneously.

8. Conjunctivitis requires irrigation of eyes three to four times daily, using normal saline solution or boric acid solution, and anointing the lids at night with an ointment of yellow oxide of mercury 0.033 to 30 Gm. (½ grain to 1 oz.).

9. Annoying throat conditions may be alleviated by the use of cooling drinks. The mouth should be kept clean by frequent washings; potassium permanganate solution, 1:4000, is probably most effective. If inflammation of the tongue is severe, it usually yields to painting with glycerite of tannic acid, but incision may sometimes be required.

10. Morphine, 0.011 Gm. (⅙ grain) hypodermically, is probably the most certain medication for relief of pain, which is sometimes extremely severe. Acetylsalicylic acid, 1 Gm. (15 grains), three times a day, is very effective in some cases.

11. The crusts should not be removed, but should be permitted to be soaked off, or ointments, as bicarbonate of soda, 8 Gm. (2 drams) and petrolatum 30 cc. (1 oz.), applied during the terminal stages.

DIPHTHERIA

Diphtheria is an acute communicable disease, usually characterized by involvement of the mucous membranes of the respiratory tract or system with the production of a pseudomembrane and symptoms due to toxemia.

Etiology: Diphtheria is commonest in children under the age of ten during the late fall and winter months. It occurs the world over, and is usually endemic in large cities but often becomes epidemic.

The disease is caused by the Klebs-Loeffler bacillus which does not penetrate the mucosa. The organism grows best on Loeffler's medium and is identified on staining with Loeffler's methylene blue. Other media which identify the organisms more rapidly are impregnated swab sticks with either sterile horse serum or a potassium tellurite medium.

Diphtheria is most often transmitted by carriers through active or convalescent cases, these being the most positive sources. The mode of spread is through the air or by direct contact *via* the droplet method or from freshly soiled articles. Epidemics have been caused by contaminated food and milk. The portal of entry is through

the nose, throat, or other mucous membrane or by direct inoculation through open wounds. The economic status is considered an important factor in the incidence, and lack of proper food, poor heating, and overcrowded living conditions play their part. Susceptibility to the disease varies; infants up to six to nine months rarely contract diphtheria, and many healthy adults have the organism in their throats without having the disease.

Pathology: The organism usually remains at the point of focal infection and is rarely recovered from the blood stream. The organisms, Klebs-Loeffler bacilli, proliferate readily within the selective tissue infected, liberating a toxin which is absorbed and distributed by way of the blood and lymphatic systems. The by-products of the organism, the toxoid, toxin, and toxon, affect first the local tissue and subsequently the parenchymal organs. These organs are all involved in diphtheria, but the most marked changes of a fatty degeneration occur in the musculature of the heart. This fatty degeneration displaces the normal cellular arrangements with a terminal edema and interstitial fibrosis. Fatty degeneration may also occur in the central and peripheral nervous system.

Signs and Symptoms: The incubation period is from two to seven days. The commonest site of involvement is the nasopharynx. The onset is insidious with a complaint of general malaise, slight fever, and difficulty in swallowing. Anatomically, the portals of entrance might be divided into nasopharyngeal, mesopharyngeal, laryngeal, or involvement of all of the passages in the upper respiratory system. The mesopharynx is the most commonly involved. At the onset a thin film may occur over the tonsils, assuming later a more gelatinous appearance, being white or gray in color. The depth of the color change in the pseudomembrane is subject to the enmeshing of polymorphonuclear leukocytes, fibrin deposits, organisms, and erythrocytes. The membrane may progress upward, forward, and/or downward, resulting in the clinical types noted. Throughout the period, absorption of toxins occurs. Occasionally a symbiotic infection (usually streptococcic in origin) occurs with the Klebs-Loeffler bacillus and results in a marked involvement of the area affected and a severe lymphadenitis. This lymphadenitis is termed a bull neck. The size of the pseudomembrane does not determine the severity of the toxemia.

Complications: Early myocardial changes are most important in the morbidity-mortality rate of this disease. Evidence of a tachycardia, bradycardia, syncope, nausea and vomiting, and hypertension are usually related to the myocardial damage. Palatinal paralysis, ocular disturbances (ciliary muscle), peripheral neuritis, and absence of knee jerks are evidences of central nervous system involvement. Pneumonia and respiratory paralysis are of a serious character. The difficulty in respiration due to atresia or partial stenosis of the larynx is most significant. There is a mechanical obstruction due to the existence of and extension of the membrane into the trachea and bronchi. It may cause suffocation and a fatigue syndrome.

Diagnosis: Follicular tonsillitis has a sudden onset, high fever, severe pain in the throat and hard glands, and is self-limited within approximately 72 hours. Acute streptococcic anginas are characterized by marked hyperemia over the mesopharynx with positive cultures to support the diagnosis. Vincent's angina is insidious in onset, of an ulceromembranous character and has evidence of alveolar or oral sepsis. Positive smears verify the diagnosis. Scarlet fever is characterized by the triad of a sore throat, glossitis and punctiform rash. Syphilitic angina is chronic and supported by a history and positive serological reaction. Laryngeal diphtheria must be differentiated from foreign bodies, acute catarrhal laryngitis (croup), retropharyngeal abscess, laryngismus stridulus, enlarged thymus, congenitally relaxed larynx and diverticulum.

Prognosis: The prognosis is directly related to the day of onset of the disease and the rapidity or latency of the treatment with the specific antitoxin. The severity of the complications without proper management quite often cause an exitus. Rarely is the disease self-limited with a recovery independent of specific treatment. The complications infrequently leave residual damages, especially to the nervous system.

TREATMENT

1. **Prophylaxis:** The disease may be placed in the same category as that of variola, *i. e.,* extinction by active immunization. Subsequent susceptibility should be determined by the Schick test, and if positive a repetition of the course of immunization should be carried out at once.

2. **Active Treatment:** Isolation should be enforced; quarantine is not essential. Specific antitoxin should be administered intramuscularly in large doses—20,000 to 60,000 units as early as possible. Cultures must always be taken, but regardless of the culture report, if a case clinically suggests this disease, antitoxin must be given. If the patient is susceptible to the foreign protein of the serum, serum tolerance should be induced prior to the giving of the large doses required for the disease.

3. Absolute rest should be recommended in every case for a minimum of four weeks and gradual rehabilitation allowed to take place.

4. During the acute stage a liquid diet is preferable and should contain adequate carbohydrates, sufficient vitamins, especially B and C, and a minimum of proteins. Overfeeding should be avoided in order to prevent vomiting. Difficulty in feeding, which may arise owing to paralysis of pharyngeal muscles, can be overcome by feeding through a nasal catheter. After the acute stage is passed, the diet may be increased to include stewed fruits, soft boiled eggs, gelatin, light puddings, gruel, and well-cooked cereals.

5. For relief of the dyspnea, turpentine stupes applied to the neck and upper chest have proved of benefit. As an emergency measure, it is beneficial to rub the chest with camphorated oil, followed by application of hot flannels.

6. If evidence of cardiac involvement is noted, ten per cent glucose in daily doses of 250 to 500 cc. should be administered intravenously in all cases. Morphine sulfate, 0.004 to 0.006 Gm. ($\frac{1}{16}$ to $\frac{1}{10}$ grain), is administered subcutaneously as needed to secure rest and quiet. The cardiac stimulants are of little value, but caffeine sodium benzoate, 0.133 to 0.33 Gm. (2 to 5 grains), subcutaneously, is of value in vasomotor collapse. No drastic catharsis, no bathroom privileges, and no large meals are to be given during convalescence and with cardiac involvement the period of absolute bed rest is increased.

7. In severe laryngeal involvement, intubation or tracheotomy must be resorted to.

MUMPS (EPIDEMIC PAROTITIS)

Mumps is an acute communicable disease characterized by an inflammation of the salivary glands, most commonly of the parotid

Etiology: The disease is caused by a filterable virus which has been recovered from the saliva and also from the blood of infected individuals. The portal of entry is most commonly through the mouth by the droplet method, though articles contaminated by saliva or air-borne infection must be considered.

Pathology: The involved glands are red, swollen, and moist. Mononuclear infiltration occurs around the blood vessels and the ducts. The latter may be dilated and obstructed with retained saliva. The adjacent lymph nodes are swollen and congested, but suppuration of the glands rarely if ever occurs.

Signs and Symptoms: The incubation period is from 14 to 21 days. The onset is usually insidious, though in some instances it may be quite acute. It is characterized by chills and fever, the latter more frequently exaggerated than a low curve. Pain on the side involved is noted as a subjective complaint with difficulty in mastication and deglutition. Objectively, the mucous membranes of the mouth and pharynx are slightly injected and edematous. Edema may be noted about Steno's duct. Observable swelling occurs between the ascending ramus of the mandible and the mastoid process. It usually assumes a grotesque appearance. The opposite side may become involved about two or three days after the initial infection has been noticed. The swelling approaches its highest stage in three to five days, and a similar amount of time elapses before the swelling subsides. Palpation elicits pain over the swollen gland and a rather doughy, elastic character to the skin. Infrequently the submaxillary or sublingual glands may be involved.

Complications: Complications occur most frequently in patients beyond the pubescent years, and hence are more serious in nature. Mastodynia or mastitis is complained of. Gastrointestinal upset and jaundice with intense pain in the epigastrium are evidence of hepatitis or pancreatitis. Occasionally convulsion, stupor, and neck rigidity with a spinal fluid finding of a high lymphocytic cell count are evidence of encephalomeningitis. During the course of convalescence, chill, marked pyrexia, and pain in the scrotum are evidence of an epidydimoörchitis. The possibility of sterility makes this a serious complication. Oöphoritis expressed in terms of extreme pain in either lower quadrant or bilaterally in the female may also result in sterility.

Diagnosis: The disease must be distinguished from:

1. Anaphylactic reactions due to neurogenic factors.
2. Infections, *i. e.*, tuberculosis, undulant fever, tularemia, syphilis, and pneumonia.
3. Von Mikulicz's disease, ruled out by blood smears, ordinary cervical lymphadenitis, and suppurative parotitis following dental caries or trauma.
4. Tumefactions, usually of long standing, of a benign or malignant character.
5. Foreign bodies, inspissated mucous plugs, cicatrices, and calculi.
6. Emphysema, as occurring in musicians or children blowing air into the ducts; usually transient in character.

TREATMENT

Mumps is a reportable and placardable disease. The treatment is particularly symptomatic, but where complications are suspected, 20 to 60 cc. of convalescent mumps serum has proved of value. Relief of pain is most frequently brought about by warm applications, dry or moist, to the glands involved. Bed rest is essential for these cases to prevent complications. Adults particularly must be told about the potential complications and warned to avoid overactivity.

Occasionally, when glandular swelling is at its height, and the patient is restless and uncomfortable with a moderately high fever, phenacetin, 0.2 Gm. (3 grains) and caffeine citrate, 0.033 Gm. (½ grain), administered in a capsule and repeated in three hours will be found useful as an emergency remedy.

SCARLET FEVER (SCARLATINA)

Scarlet fever is an acute communicable disease, usually characterized by a sore throat, glossitis, and a punctiform rash.

Etiology: Scarlet fever is caused by a variety of strains of Hemolytic streptococci. It is generally spread by direct contact, especially through throat, nasal, and ear secretions; it may also be communicated by clothing, toys, and other articles, by a third person or through infected milk. As in diphtheria, the portal of entry is through the respiratory passages. Localization of the primary infection is most frequently in the throat or nasopharynx, but the organism may

enter the body at other sites and in these cases the local symptoms in the throat and nasopharynx are often mild. The total number of cases in a community seems dependent on the size of the population, probably because in large cities there are more carriers. An individual usually becomes immune after an attack of scarlet fever, but some people experience recurrences which may be explained by the fact that so many strains of the Hemolytic streptococci cause the disease.

Pathology: The rash is due to an erythrogenic toxin causing a vascular irritation. The toxemia causes cloudy swelling in the parenchymal organs, as in most acute infectious diseases. In the septic cases, there is an accompanying bacteremia and resistant foci of infection in the parenchymal organs. In the heart, the commonest lesion causes a focal accumulation of cells, *i. e.,* mostly lymphocytes, histiocytes, and plasma cells. Histologically, similar lesions occur in the kidneys. The degree of tissue reaction is most severe in those cases that die after the tenth day. The reactions are most conspicuous in patients with bacteremia.

Signs and Symptoms: The incubation period is from two to seven days. The onset is usually sudden with a complaint of sore throat, nausea and vomiting, headache, and fever. The throat shows evidence of marked injection and edema. Occasionally exudate is present on the tonsils. The tongue will be coated at the start and subsequently desiccates from the tip backward, presenting a red appearance on the fourth day with the red, glistening papillae present. This has been spoken of as the raspberry tongue of scarlet fever but is best termed "the glossitis" of the disease.

The rash appears from 10 to 36 hours after the onset of symptoms. It is a densely scattered, erythematous, punctate rash which may appear confluent. It is noted first on the upper chest and back, and then rapidly spreads over the body and extremities. The color may vary from pale pink to deep scarlet, and disappears on pressure, leaving a white mark on a background of scarlet. The skin is hot and dry, and may be edematous. The face is usually flushed, without rash, except for the area around the mouth which remains white. There is a leukocytosis of from 10,000 to 18,000, and a trace of albumin is found in the urine.

As the fever increases, the throat symptoms become more severe; the fever usually reaches its height in 24 hours, remains there for four or five days, and then gradually falls by lysis as the rash fades. Desquamation begins about the sixth day when the temperature falls and eruption disappears. The type of desquamation depends on the texture of the skin. It may peel off in tiny powdery scales from parts of the body where the skin is sensitive, while tough flakes or even slabs may come off the palms of the hands and soles of the feet. Desquamation does not always occur, especially not in patients treated early with scarlet fever antitoxin or convalescent serum.

In the septic type, a profuse nasal discharge is present almost from onset. Throat symptoms are very severe and there may be difficulty in swallowing. Cervical adenopathy may be marked with extensive brawny induration of the neck occasionally. Patches on the tonsils and throat suggest diphtheria. Despite the unfavorable appearance of the patient, prognosis is much more hopeful than in the toxic cases. The fever reaches an unusual height of 40° to 41.1° C. (104° to 106° F.) in the latter, the pulse is rapid as are the respirations, and the patient may be irrational. Death often occurs before the rash appears.

Complications: The complications of scarlet fever may result from the bacterial invasion or they may be due to the erythrogenic toxin. The bacterial invasion may cause peritonsillar abscess, sinusitis, otitis media, and mastoiditis. Rarely bacteremia results in endocarditis and onychias and paronychias of the fingers and toes. The toxin may cause lymphadenitis, perleche, arthritis, synovitis, and nephritis.

Diagnosis: Measles can be readily differentiated from scarlet fever by its upper respiratory infection with its rash occurring on the face and body. The rash is of a maculopapular character. Rubella has a postcervical adenitis and a rash, much larger in size than the scarlatiniform rash, which is present on the face and body. Exanthem subitum has two or three days of high fever followed by a transitory infantum eruption. In erythema infectiosum (fifth disease) there is a marked morbilliform rash on the face and extremities with extremely marked pyrexia. The rash of scarlet fever can be proved in differentiation from the scarlatiniform erythema with the Schultz-Charlton test. Human convalescent serum may be used intradermally in verifying the blanching test.

TREATMENT

1. **Prophylaxis:** A Dick test will reveal susceptibility to scarlet fever. Active immunization with the Dick toxin is recommended to develop immunity. Although prolonged in its treatment, investigative evidence shows that intracutaneous injections of 750, 3000, and 11,000 skin test doses at two-week intervals give very satisfactory results.

2. **General Treatment:**
   - *a.* Rest in bed is imperative throughout the acute stage of the disease and until complications, if present, disappear. Usually children should be kept in bed for about 18 days and adults for two weeks.
   - *b.* Adequate amounts of fluid should be given; in mild cases, the patients can usually take enough by mouth.
   - *c.* Diet should be fluid and nutritious during the first week, if the throat is intensely inflamed, followed by a soft or full diet. In general, the diet does not have much influence on the outcome of the disease.
   - *d.* Gargles are not usually indicated. An antiseptic mouth wash, if properly used, may be employed, but it is not advocated for small children.
   - *e.* Cold applications in cervical adenitis are of value.
   - *f.* For the toxic conditions with marked cyanosis caffeine sodium benzoate, 0.2 to 0.33 Gm. (3 to 5 grains), in frequently repeated doses is of some value.
   - *g.* When mild nephritis develops the patient should be kept in bed on a low-protein, salt-free diet. The indication for immediate treatment is the development of uremia. Removal of blood (250 cc. in five-year old children, 300 cc. in ten-year-old children, and 500 cc. in adults), followed by an equal injection of physiological saline solution, usually brings the patient out of a state of coma and relieves the convulsions. At times it may be necessary to repeat this treatment.
   - *h.* All surgical and medical complications are to be treated symptomatically. In the event of a bacteremia, meningitis, or inaccessible surgical point, chemotherapy is to supplement specific therapy.

3. **Specific Treatment:**
   - *a.* Dick antitoxin of 300,000 neutralizing doses is recommended in sharp cases of scarlet fever.
   - *b.* Human convalescent scarlet fever serum is preferable because no allergic reaction occurs. If available, human convalescent serum may be given in 20 to 80 cc. doses intravenously with no untoward reaction. The therapeutic value may be noted within 24 hours after usage.

4. **Miscellaneous:** Scarlet fever is a reportable and quarantinable disease. The average period of quarantine is from three to six weeks.

CHAPTER XIX

Acute Infections

(Continued)

MEASLES

Measles is an acute communicable disease characterized by an upper respiratory infection with an exanthem and an enanthem.

Etiology: Measles is caused by a filterable virus which enters the system through the nasopharynx. It is one of the most readily transmissible of exanthemata, being particularly of an air-borne character. The period of incubation is from 10 to 18 days, most commonly 14 days.

Pathology: The pathological changes are primarily confined to the mucous membranes and skin. The mucous membranes of the nasopharynx and nasopharyngeal tract and, infrequently, the gastrointestinal tract are inflamed and a cellulitis is noted.

Signs and Symptoms: The onset is usually ushered in by cough, fever, and nasopharyngeal effusion. The catarrhal phenomena are a progressive upward and downward involvement of the mucous membrane resulting in conjunctivitis with epiphora, photophobia, and a laryngotracheobronchial irritation. This prodromal period may last from three to seven days during which time an enanthem is present in the mesopharynx and Koplik spots are noted on the aural mucous membrane. Following the prodromal period, a slight drop in temperature may be noted succeeded by a maculopapular eruption beginning on the face. This polymorphous crescentic eruption progresses downward over the neck, body, and extremities. It assumes a bright red color and reaches its height in three to five days, taking an equal amount of time to recede. This eruption may be discrete or confluent and rarely is of a hemorrhagic type. Occasionally desquamation may be noted at the point of eruption.

Complications: Aural sepsis occurs most frequently, followed by adenitis. Otitis media occurs in 17 per cent of cases, and bronchopneumonia in 13½ per cent. Encephalitis and encephalomyelitis have been recognized as sequelae to the disease.

Diagnosis: Measles may be confused with rubella. The latter has its characteristic postcervical adenopathy, and the lesions are smaller and transient in their appearance. Scarlet fever presents its characteristic triad of sore throat, glossitis, and pin-point rash. Serum sickness usually has a positive history of a toxo-allergen. There is invariably the angioneurotic edema and accompanying pruritus. The rose spots of typhoid fever appear on the trunk and abdomen, and the Widal test is quite conclusive.

Prognosis: Measles is important because of its so-called status morbillosus. The serious age group is between two and five years. Deaths are usually due to the acute pulmonary edema in the eruptive stage or to the complicating sepsis and encephalitis during convalescence.

TREATMENT

1. **Prophylaxis:** Prevention should not be considered in that only passive immunity may result and subsequent exposure will again require the same measures as on the initial attempt to prevent this disease. Modification is the desired procedure, especially if the individual has recently convalesced from serious illness or operation. Modification may be brought about by whole blood injections from serologically negative individuals (usually parental blood). Convalescent measles serum has a high opsonification and is preferable; it is given in 10 to 20 cc. doses intramuscularly. Normal serum may also be used as well as immune globulin. The latter, a placental extract, should be given early in the incubation period. If given late, little effect is noted.

2. **Isolation:** Measles is a reportable and placardable disease. Therefore, all patients should be placed under isolation as required by most laws for a period of 14 days.

3. **General Treatment:** There is no specific serum for the treatment of measles. The sulfonamides have not been successful in virus infections. Rest in bed; hydrotherapy, internal and external; no catharsis, and symptomatic control of the cardinal symptoms are indicated.

The eyes may be protected from strong light and should be bathed frequently with physiological saline or boric acid solution, and the eyelids should be kept free from crust formation by anointing them with vaseline.

Frequent instillations of albolene into the nose relieve the discomfort from rhinitis.

Oral hygiene should be particularly noted and early treatment of the perleche should be carried out. Severe laryngitis or distressing cough may be ameliorated by steam inhalations with menthol or compound tincture of benzoin added.

Cough may be controlled with small doses of codeine, 0.004 to 0.016 Gm. (1/16 to 1/4), hypodermically.

Alcohol sponges or tepid baths may be used to lower the temperature and quiet the patient.

The indications for sulfonamides are in the event of any evidence of secondary infections of the streptococcus and other bacteria that respond to this therapy.

GERMAN MEASLES (RUBELLA)

German measles is an acute communicable disease characterized by a postcervical adenitis and a fine maculopapular rash.

Etiology: The causative agent of rubella is a virus. It occurs in greatest numbers in the second and third decade of life because it assumes an epidemic proportion in from five- to ten-year periods. The disease leaves a lifelong immunity.

Symptomatology: The disease may be ushered in with a moderate upper respiratory disturbance. These mild catarrhal symptoms are accompanied by a low-grade fever curve. The individual is usually cognizant of a lymphadenitis located in the postauricular, postcervical, and occipital regions. These glands are small, tender, and readily palpable. The rash occurs on the face and has a mottled appearance, and subsequently is noted on the body in the form of a discrete, reddish-orange color, slightly larger than the punctiform rash of scarlet fever but smaller than the morbilliform rash of measles. The rash lasts from 12 to 48 hours at the longest. The glandular involvement persists from two to ten days after the rash has disappeared and is quite characteristic of the disease.

Complications: Complications are rarely encountered. A few cases of encephalitis have been reported, but there is a question as to the number.

Prognosis: Fatalities have not been reported except as the result of concurrent infections or when the rubella was a coincidental communicable disease superimposed upon some severe infection.

TREATMENT

German measles is a reportable and placardable disease, but is considered the mildest of all contagious illnesses. The treatment is particularly symptomatic and is of interest chiefly in its differentiation from the other communicable diseases.

The skin may be protected by anointing daily with carbolized vaseline (carbolic acid, 0.33 cc. — 5 minims — to vaseline, 30 cc. (1 ounce), or oil of eucalyptus and olive oil, equal parts of each.

During the three or four days of active symptoms in this disease, quinine sulfate, 0.133 or 0.2 Gm. (2 or 3 grains), to a teaspoonful of chocolate syrup may be used.

ERYSIPELAS

Erysipelas is a self-limited acute erythematous inflammation of the skin, caused by the *Streptococcus hemolyticus* and accompanied by a severe constitutional reaction. The lesion is characteristically a red swollen area with sharply demarcated and elevated border with small, flamelike pseudopodia extending beyond the border.

Etiology: The causative organism is a hemolytic streptococcus of no constant strain. The organism enters the skin at the site of a wound, fissure, or abrasion. Often there is no recognizable channel. Erysipelas is commoner in women than men and occurs most frequently in individuals between the ages of 35 and 55 years, but does occur in early infancy and old age. Persons who have recently undergone an operation and women in the puerperium are the most frequent victims of the disease. Undernourished and debilitated individuals are also more susceptible. The disease occurs in every part of the world but is usually more frequent and more severe in temperate climates.

Pathology: Sections through the infected area show marked congestion of the capillaries, edema, areas of skin necrosis, and lymph spaces crowded with streptococci. The distribution of the streptococci is peculiar for they are found exclusively in the lymphatic vessels in greatest numbers at the margins of the inflamed areas; they

are absent in the central portion and are seldom found in the contents of the blebs. Leukocytes are found scattered throughout the area and mononuclear cells are present in great numbers in the corium and lymphatics. A powerful toxin is produced by the organisms and the viscera undergo changes which are common to acute infections, *i. e.*, cloudy swelling and splenomegaly.

Signs and Symptoms: The incubation period is about three days, but varies from two to eight. The onset is sudden with a rise of temperature, malaise, headache, sometimes vomiting, and not infrequently delirium.

Local Reaction: The local lesion begins most often on the face, especially about the nostril or the inner canthus of the eye. The first sign may be a red area extending from the nostril or the inner canthus of the eye across the bridge of the nose. The area is hard, tense, shiny, and tender with a well-defined edge, which is usually irregular and bright red. The process spreads rapidly, the marginal areas retaining the features noted, but the center tends to fade. Small, red pseudopodia may be seen at the periphery marking the extension of the process in the lymphatics. Extension is always by continuity. Small vesicles or blebs may appear. Desquamation of a flaky type occurs as the process fades out. Great alteration appears in the facial features as the process extends rapidly on the cheek and over the bridge of the nose to the opposite side, giving the "butterfly" appearance. The eyelids become markedly swollen, red, and glistening, and the eyes cannot be opened; there is rarely involvement of the cornea. The lesion seems to stop at the hair line and at the ramus of the jaw. However, occasionally it extends down the neck and over the chest. The regional lymph nodes are involved and enlarged.

Systemic Reaction: The fever is high early in the course of the disease and rises to 38.3° to 40° C. (101° to 104° F.). A feeling of weariness, anorexia, slight headache, and chilly sensations increase quickly. The face is flushed and the eyes are bright. The skin is hot and dry, with periods of drenching sweat, the tongue is coated, and the lips are parched.

The blood usually shows a leukocytosis of 12,000 to 20,000 with an increased percentage of polymorphonuclear leukocytes. The spleen is seldom palpable. The urine shows a febrile albuminuria and often contains urobilin. Relapses and recrudescences occur.

Complications: Abscess of the eyelids, postauricular, preauricular, and cervical lymph glands, and acute sinusitis are frequent. Pharyngeal abscess may also occur. Gangrene of the skin is a rare sequel. Pneumonia may be a terminal event. Among the localizations are otitis media, mastoiditis, pericarditis, endocarditis, empyema, and arthritis.

Diagnosis: The diagnosis can usually be made at a glance. In the acute staphylococcal infections the skin feels harder and the margins are not definitely demarcated and the lesion spreads more slowly. The systemic symptoms are lacking. The method of spread and the absence of constitutional symptoms differentiate acute eczema and the allergic dermatitides.

TREATMENT

1. Isolate the patient.
2. Fluids, up to 4000 cc. daily, should be administered.
3. A high caloric and high vitamin (particularly A and D) diet should be given.
4. Codeine sulfate, 0.033 Gm. (½ grain), and acetphenetidin, 0.2 Gm. (3 grains), every four hours are usually sufficient to allay pain and induce sleep.
5. The bowels should be regulated; an enema may be given every other day, and a mild laxative, as mineral oil, 30 cc. (1 ounce), daily.
6. Hot or cold compresses may give comfort.
7. Abscesses should be incised.
8. Sulfanilamide is effective and is the drug of choice. The initial dose is 4 Gm. (60 grains), with an equal amount of sodium bicarbonate. Then 1 Gm. (15 grains) is given every four hours with sodium bicarbonate in equal amount, until the optimal blood level is reached. The drug may then be reduced to 1 Gm. (15 grains) four times a day and should be continued until the temperature has been normal for 24 hours.
9. Multiple small transfusions, 50 to 100 cc., should be given in severe toxemia.
10. Antiserum and antitoxin may be administered.
11. X-ray and ultraviolet therapy have been advantageous in some instances.

TYPHOID FEVER

Typhoid fever is an acute specific infectious communicable disease caused by the Bacillus typhosus and characterized by blood stream invasion, high and continued fever, slow pulse, enlarged spleen, rose-colored rash, and diarrhea. It is a disease of insidious onset which runs a prolonged course of about 21 days, usually ending by lysis.

Etiology: Typhoid fever is essentially a disease of youth and early adulthood, generally occurring between the ages of 15 and 25 years. Rarely is it seen in infancy or in patients past 50 years of age. It occurs in both sexes and is most prevalent during the summer and early autumn months. While it has worldwide distribution, its incidence has decreased in recent years, owing to the improvement of sanitary conditions and prophylactic immunization. In general, the main sources of the disease are contaminated water, ice or milk, and infected food. Soil contaminated by defective drains and the like may pollute the water, and at the same time vegetables from this soil which are eaten uncooked may cause the disease. Often the disease is contracted while individuals are on their vacations and have access to milk or water which is not pure. Swimming in polluted streams may cause typhoid fever. Other causes include "typhoid carriers," contact with soiled linen or the stools of typhoid patients, and consumption of food contaminated by flies or shellfish from infected water. People may be exposed to the disease, but remain immune to it. Usually an attack of the disease results in immunity; in those cases where a second attack occurs, another strain of typhoid organism is the cause or a massive dose of the same organism which caused the previous attack.

Signs and Symptoms: The incubation period is from 7 to 14 days. Usually there are no symptoms during this time, though there may be a slight fever at night. The onset is slow, the most prevalent early symptoms being headache, epistaxis, and a general feeling of weakness which is not serious enough to necessitate neglect of the patient's work. As time goes on, the malaise becomes more pronounced, the temperature begins to rise, the appetite is poor, and the body aches. The picture is one of mild, progressively increasing intoxication. During the first week of the disease, the temperature

continues to rise until it attains a height of 39° to 40.5° C. (102° to 105° F.); the pulse rate is increased but not in proportion to the degree of fever. At the end of the first week, a mild degree of bronchitis, enlargement of the spleen, bradycardia, leukopenia, and the characteristic rose spots are present. The latter are small pink macules which disappear on pressure; they appear in crops usually and while they are most often found over the abdomen and lumbar region, they may be noted on other parts of the body. They are probably due to dilatation of the capillaries, and small quantities of typhoid bacilli are often found on section. The urine is of a dark color with high specific gravity, albumin, and a few casts. The patient is weak, pale, and looks sick; with the onset of diarrhea and related symptoms, a state of exhaustion prevails.

Manifestations become progressively worse during the second week; the patient is often delirious and may die during this stage. During the third week, the symptoms become more profound, the heart is rapid and weak, the lungs are congested, the abdomen distended, and it is during this period that perforation and hemorrhage may occur. In almost all cases of typhoid fever, the stools of the patient contain blood after the first week. At this time, death may occur from intestinal hemorrhage, epistaxis, or pneumonia, or in cases which are not very severe, recovery may begin by lysis. In the latter cases, the temperature gradually returns to normal and other symptoms disappear. During this period, there may be a relapse which is usually mild though it may be severe enough to cause death.

Pathology: The bacteria enter the body through the gastrointestinal tract from the ingestion of contaminated food or water. It is possible that many of these bacteria are destroyed in the stomach, but at the same time it must be said that ulcers of the mucosa and submucosa of the stomach and esophagus are frequently found. The lymphoid tissues of Peyer's patches and the solitary lymph follicles are most commonly invaded by the bacteria. The lymphoid tissue of the lower part of the ileum is inflamed. Catarrh throughout the bowel is the commonest finding. The long axis of the ulcers parallels the long axis of the bowel. The spleen is usually enlarged. Cloudy swelling of the liver and small areas of focal necrosis are seen. Bronchitis is commonly present, and there may be pneumonia. The myocardium becomes flabby. The kidneys show cloudy swelling.

Complications: The commonest complications are perforation and hemorrhage, and these may cause death. Perforation is due to rupture of a necrotic Peyer's patch which in turn is caused by a distended bowel or peristalsis. The typical picture of shock is evident when perforation occurs. Hemorrhage may occur from the nose or bowel, and is the result of rupture or necrosis of a blood vessel in a necrotic area. While occult blood may be found in the stools of many typhoid patients, such slow bleeding is not serious. Severe hemorrhage is evidenced by chills, marked pallor, rapid pulse, and absence of abdominal pain; the patient lies very quietly and may show evidence of air hunger. Other complications include bronchitis and pneumonia, thrombosis, acute nephritis, cardiac failure, neuritis, and cholecystitis.

Diagnosis: Since typhoid fever is so infrequently seen, diagnosis may cause some difficulty. Formerly, diagnosis was made from clinical evidence, but now laboratory methods aid somewhat. The typhoid organism can be isolated from the blood during the first week of the disease, and it may be found in the urine and feces thereafter. Blood agglutination by the Widal test indicates the presence of typhoid antibodies. Agglutination with a dilution of the patient's serum in a strength of 1:50 or 1:100 is considered positive. The value of this test has been somewhat diminished since the advent of prophylactic injections of typhoid vaccine.

Diseases which may simulate typhoid fever include malaria, miliary tuberculosis, subacute bacterial endocarditis, typhus fever, trichinosis, and undulant fever. The marked daily variation in temperature in malaria should help in diagnosis, as well as examination of blood smears. In miliary tuberculosis, the pulse-temperature ratio is lacking, a family history of tuberculosis is usually present, and chest plates, blood studies, and stool cultures may help in differentiation. In bacterial endocarditis, the fever is seldom as severe nor as continuous, chills are more frequent, petechiae appear in the conjunctivae, and the presence of dyspnea, heart murmurs, joint pains, and red cells in the urine point to this diagnosis. A positive Weil-Felix reaction, numerous skin lesions, and an abrupt onset aid in the diagnosis of typhus fever. In trichinosis, there is leukocytosis, eosinophilia, and muscular tenderness.

Prognosis: Mortality averages from about 6 to 20 per cent or higher. However, this comparatively high rate may be explained by the fact that the disease is not frequently encountered and one or two deaths in a year when there are few cases increases the mortality rate. The febrile period usually ends at the beginning of the fifth week though it may continue for more than six weeks. The duration of this period has little effect on the mortality.

TREATMENT

1. Absolute rest in bed and isolation with good nursing care are necessary.

2. Diet is very important. The diet should contain at least 2500 Calories a day with a minimal amount of residue. Carbohydrates should form the major portion since they are easily digested. However, at least 1 Gm. of protein per kilogram of body weight is given with some fats. Only fluids, semisolids, and soft foods should be included. Milk, cream, butter, eggs, well-cooked cereals, sugar or glucose, fruit juices, chicken broth, and mashed potato may make up the major portion of the diet. Anything that might cause perforation should be prohibited. Stools should be inspected and if undigested curd is found it is a sign that too much milk is being given or that the function of the gastrointestinal tract is impaired. At least 3000 cc. of fluids must be taken daily. If necessary, they may be given parenterally.

The diet should be supplemented by vitamins. It is now believed that many of the complications and sequelae of typhoid fever formerly thought due to toxemia are in reality due to vitamin deficiencies.

Vitamins A and D may be supplied in halibut liver oil and 1 cc. should be taken daily.

Vitamin B complex may be administered in the form of brewer's yeast, 30 Gm. (1 ounce) daily. If this cannot be taken, the individual factors of the complex may be given separately. Thiamin hydrochloride is given in doses of 2 to 10 mg. daily by mouth, or may be administered in solution, 20 to 50 mg. intravenously or intramuscularly daily. The dose of riboflavin is 1.8 mg. for a caloric intake of 3000 Calories. Nicotinic acid is not advised as it increases peristaltic activ-

ity. Liver extract, 1 to 2 cc. intramuscularly daily, may be given and it supplies the B factors other than thiamin.

The daily requirement of cevitamic acid in typhoid is 120 mg. and it may be more. This may be taken orally in amounts of 200 to 500 mg. in 24 hours. Citrus fruit juices also supply this vitamin. If it is found by laboratory test that the blood level is below 0.5 mg. per cent or a 24-hour urinary excretion level is below 30 mg., then this vitamin should be given parenterally in daily doses of 500 mg.

3. A high temperature may be relieved by sponge baths. If the temperature is 39.5° C. (103° F.) or more, these baths should be given every four hours. Ice bags may be applied to the head and abdomen. Alcohol rubs three or four times daily are of great benefit and keep the skin in good condition.

4. A new horse serum is claimed to produce good results.

5. Blood serum from typhoid carriers or transfusion of whole blood in amounts of 50 to 100 cc. daily or every other day may be of value.

6. Sulfanilamide seems to have little or no effect on this disease; sulfaguanidine has been tried without much success.

7. If intestinal hemorrhages occur, stop all food and fluid by mouth; withhold for a period of 24 hours or until evidence that bleeding has ceased appears. Ice chips may be given and the lips moistened frequently with a mixture of lemon juice, glycerin, and water. Ice bags may be applied to the abdomen; the foot of the bed should be elevated, and morphine sulfate, 0.011 to 0.016 Gm. (⅙ to ¼ grain) hypodermically, should be given. A hypodermic injection of 100 units of parathyroid extract is of value in helping to increase the coagulability of the blood. Calcium gluconate, 10 cc. of a ten per cent solution, intravenously at four- or five-hour intervals is thought to be of value. If possible, 500 cc. of citrated blood should be given. Five hundred cubic centimeters of plasma may be given in lieu of this and hydration should be kept up by intravenous fluids, 2000 to 3000 cc. of five per cent glucose in normal saline solution.

8. If constipation or flatulence is troublesome, a low enema may be given.

9. If perforation occurs, immediate surgery is necessary. Cases operated on within 24 hours recover much more frequently than those operated on later.

10. Prophylaxis depends on:
    a. Early recognition of the disease.
    b. Isolation technic.
    c. Disinfection of stools and urine.
    d. Careful observation of food and water supplies.
    e. Vaccination.
    f. A patient who has recovered from the clinical phase of typhoid fever must have three negative cultures of the stool, taken at three-day intervals, before being released from isolation.
    g. Carriers: Recently, iodophthalein has been reported by Saphir and Howell as effective in the treatment of typhoid-paratyphoid carriers. Four doses of 4 Gm. (60 grains) each of iodophthalein were administered orally at weekly intervals, and during a seven months' period of observation the stools remained free from paratyphoid A organisms.

    Vaccine therapy may be tried in an attempt to cure the typhoid carrier and at times surgery may be advised.

MENINGITIS

Meningitis is an inflammation of the membranes of the brain or spinal cord, occurring most often in children. Inflammatory lesions involving the meninges of the brain and spinal cord, whether purulent, tuberculous, or serous, present characteristic clinical signs and symptoms. There is a group of meningitides caused by pus-producing organisms of which the meningococcus is outstanding; others, as the staphylococcus, streptococcus, pneumococcus, and gonococcus may cause the same kind of purulent infection. Rather than take up the individual forms produced by various pyogenic organisms, the meningococcic type of meningitis will be considered. While other forms of purulent meningitis may not follow exactly the bacteriological, pathological, and clinical patterns of the meningococcic type, they are quite similar from the diagnostic and therapeutic aspects. Naturally, from the prognostic angle they may be different. Tuberculous, syphilitic, serous, traumatic, and other less common forms of meningitis will not be considered in detail here. What is said in this chapter regarding the diagnosis and treatment of meningococcic meningitis may be applied to all of the purulent forms.

Etiology: Acute meningococcic meningitis is the commonest and most important form, caused by the *Meningococcus intracellularis.* While this organism may be found in the secretions of the nasopharynx of normal individuals, it is not until the disease sets in that

it is present in any great number. This diplococcus is a gram-negative type, found intracellularly. Why certain individuals are more apt to develop the disease than others is a question that remains unanswered. The disease may occur sporadically and attack persons in vigorous health. In institutions, the germ may be carried from one individual to another, and an epidemic may break out.

Pathology: The disease is usually characterized by a systemic involvement with a positive blood stream culture before evidence of meningeal irritation appears. The pia arachnoid over the base of the brain and spinal cord becomes involved, with the production of a thick purulent exudate. This consists of fibrin and polymorphonuclear leukocytes which have the meningococci within them. Sometimes the inflammatory process is widespread over the entire surface of the brain and spinal cord; again it is more circumscribed.

Signs and Symptoms: The disease sets in abruptly and therefore must be differentiated from other infectious diseases that begin suddenly, as pneumonia, tetanus, and streptococcal septicemia. For a day or two before the appearance of the characteristic rigidity of the neck, the patient usually feels irritable. Headache and fever are present. Sometimes the onset is so sudden that the first evidence noted is stupor, delirium, or even coma. A brief inspection of the patient reveals stupor or semistupor which is not commonly seen in other acute infectious diseases. The contrast between this clinical picture and that of the patient with pneumonia is sharp. The latter is apt to be alert, stimulated, bright, and usually has the typical anxious expression so characteristically lacking in acute meningitis. Most patients with other infectious diseases are practically never so stuporous in the first few days of the disease. Fever of 39° to 39.5° C. (102° to 103° F.) is a common finding, and the blood leukocyte count usually ranges above 15,000 per cmm. The patient may have scattered petechial hemorrhages, especially over the ventral surface of the body. These purpuric spots have been responsible for the name "spotted fever" applied at times to this disease. The so-called "tache cérébrale" may be seen on stroking the abdomen.

Diagnosis: The importance of a prompt and accurate diagnosis cannot be overemphasized, especially at this time when specific chemotherapy is so effective. The chief point in recognition consists in thinking of the possibility of acute meningitis. When called to see a

patient with an acute infection, it is always a good habit to test the neck for rigidity and the legs for Kernig's sign. The diagnosis is clinched by examination of the spinal fluid which should be done immediately. The pressure is usually above 200 mm. of water. The fluid is turbid or even frankly purulent in advanced stages of the disease. There is a great increase in the number of polymorphonuclear leukocytes; 2000 or more cells per cmm. may be present. The sugar content of the spinal fluid is commonly reduced to less than 20 mg. per cent. The type of organism causing the meningitis can usually be readily determined, though the etiological diagnosis is no longer so important since the treatment of all forms of pyogenic meningitis is much the same.

TREATMENT

1. While the mortality rate in untreated meningococcal meningitis is about 85 per cent, there has been a gradual decline since 1908 when Flexner reported his first series treated with specific antiserum. While early administration of serum has met with some success, this method of management of meningitis has not been highly satisfactory.

2. Since the introduction of the sulfonamide group of drugs, the mortality rate of meningitis has been greatly reduced. The effect of these chemotherapeutic agents has often been dramatic. Subsidence of symptoms with sterilization of the blood and spinal fluid has frequently been noted within 24 to 36 hours. While relapses have occurred after the use of antimeningococcus serum, practically none occurs after treatment with the sulfonamide drugs.

Sulfanilamide, sulfapyridine, and sulfathiazole have all been used with fair success in the treatment of meningitis, but sulfadiazine seems to be the drug of choice. This drug is given in the following way: 4 Gm. (60 grains) orally as soon as the diagnosis is made, followed by 1 Gm. (15 grains) every four hours until the fever, signs, and symptoms have been controlled for 36 hours. Sodium sulfadiazine in physiologic saline solution may be given intravenously to patients who cannot take the drug by mouth. Three to 6 Gm. (45 to 90 grains) of the drug may be given daily in this way. Reports in the literature reveal that meningococcic meningitis responds satisfactorily to sulfadiazine in over 90 per cent of cases.

The same precautions that have been sounded in the use of the other sulfonamide drugs must be recognized in the treatment with sulfadiazine. The drug may cause vomiting and its sodium salt may have to be given intravenously in some cases. The blood count must be watched for the development of agranulocytosis. The urine must be studied for evidence of renal insufficiency. These unfavorable reactions, however, are less likely to occur with sulfadiazine than with sulfanilamide, sulfapyridine, or sulfathiazole. As sulfadiazine is more readily absorbed than some of the other drugs of this group, it is possible to obtain a satisfactory blood level of from 10 to 15 mg. per cent within eight hours. If the blood level fails to rise above 3 mg. per cent within this time, one should not hesitate to give 3 to 5 Gm. (45 to 75 grains) of sodium sulfadiazine intravenously at once and to continue giving it every day until the disease is controlled.

3. Penicillin is used in the following manner: 10,000 to 20,000 units in 10 cc. of sterile isotonic saline solution is injected intraspinally after 10 cc. or more of spinal fluid is withdrawn. The dose is repeated at ten-hour intervals for from three to five doses, and then one dose in 24 hours is given until recovery is assured. The number of intraspinal injections needed depends upon the condition of the patient. Usually, about 100,000 units are required to control the disease. Simultaneously, intramuscular injections of 10,000 units of penicillin is given every three hours and continued until there is definite improvement. The usual period of intramuscular therapy is from three to seven days, and the total amount given varies from 180,000 to 500,000 units. Even more successful results follow combined sulfonamide and penicillin therapy than follow therapy with either drug alone.

4. It is preferable that the patient be hospitalized.

5. Fluids should be pushed. A liberal diet, high in Calories and vitamins, should be given as soon as the vomiting has subsided. Forced feeding may be necessary when a tendency to chronicity develops.

6. In some instances catheterization may be necessary for a short period. The urinary output should be watched closely and means other than catheterization used to secure relaxation of the bladder sphincter.

7. A cleansing enema should be given daily.

8. For the relief of the severe headache, sodium bromide, 0.66 to 1 Gm. (10 to 15 grains) three times a day, may be given, but in the early stage of the disease the narcotics, morphine sulfate, 0.011 to to 0.016 Gm. (⅙ to ¼ grain), or pantopon 0.011 to 0.022 Gm. (⅙ to ⅓ grain), are necessary for the relief of pain and restlessness. These depressants should be used with caution, however, as pneumonia may ensue.

9. In pulseless, fulminating cases, epinephrine, 0.6 to 1.22 cc. (10 to 18 minims) intramuscularly or intravenously, every four hours according to the pulse, may be tried as an emergency measure.

ACUTE EPIDEMIC ENCEPHALITIS

This is an acute infectious disease, the cause of which is unknown, characterized clinically by nervous system disturbances.

Signs and Symptoms: Generalized involvement of peripheral nerves, lethargy, meningeal symptoms, stupor, and coma are the main features. All cases do not run true to this pattern. Sometimes in place of lethargy, there is violence, and in place of stupor and coma there are irrationality and jactitation.

Encephalitis may appear sporadically or there may be epidemics of it. The disease is rare in children and in older people; it occurs most commonly in young adults under the age of 40. The onset as a rule is acute and there is fever, headache, general malaise, vomiting, and other variable features that characterize the early period of any acute infectious disease. During the first day or two, the condition may be confused with influenza or ordinary upper respiratory infections. After the first few days, the fever rises higher, the patient becomes irrational, lethargic, or noisy, and finally certain characteristic evidences of brain involvement make their appearance. There may be twitchings or choreiform movements of the arms and legs; double vision and paralysis of certain muscles of the eyeball may appear. Sometimes there are mild clonic movements, particularly involving the abdominal muscles. The persistence of these unusual manifestations quickly indicate that the patient has something more than the "flu."

The examination of the patient may reveal rigidity of the neck, paralysis of some of the cranial nerves, periodic attacks of dyspnea or apnea, and a generalized rigor of the muscles of the legs and arms.

Poliomyelitis, meningitis, cerebral thrombosis or hemorrhage, uremia, and rupture of a mycotic aneurysm of vessels of the brain must all be considered. A spinal puncture may show practically no evidence of disease. An increase of the glucose content above 90 mg. per cent is suggestive of encephalitis, while in pyogenic forms of meningitis, the glucose content is well under 50 mg. per cent. Sometimes there is an increase of the cell count but not always.

Prognosis: The outlook for a patient with the various kinds of acute encephalitis is not good. There is a mortality rate of about 20 to 30 per cent. Sudden bradycardia or an acute respiratory paralysis may quickly terminate the patient's life. When these patients recover, the recovery is apt to be more apparent than real in some cases, for a number of years later the individual may come down with a post-encephalitic Parkinson's syndrome.

Pathological Anatomy: The brain is usually hyperemic and tiny hemorrhages occur in the meninges and in the brain, particularly in the area of the basal ganglia. Vascular congestion with perivascular lymphatic infiltration with edema are characteristic. Sometimes small necrotic patches are found. Hydrocephalus, generalized edema of the brain, petechial hemorrhages, tiny areas of necrosis, congestion, and lymphocytic infiltration are the main features found at autopsy.

TREATMENT

The treatment may be classed into general and special measures. The general measures consist in protecting the patient from intercurrent infection and injury, keeping up nutrition, watching for distention of the bowels from obstipation, and carefully preventing overdistention of the urinary bladder and urinary tract infections.

Special Measures: Repeated lumbar punctures and intravenous administration of hypertonic glucose, 50 cc. of a 20 per cent solution, daily or twice daily, are used to control high spinal fluid pressure if it exists. The sulfonamides appear to be of no value in encephalitis. The specific antiserums seem to have little effect. The reported results of the therapeutic antiserums are conflicting so one may assume that their value is strictly limited. Finally, in the management of a patient suspected of encephalitis of the acute epidemic type, isolation measures for the protection of those around the patient must be carried out.

In the chronic stage, attention should be given to the eradication of any foci of infection, paying particular attention to the sinuses. Massage and hydrotherapy are useful. Drugs may relieve the symptoms but do not arrest the progress of the disease. Hyoscine hydrobromide is given by mouth, beginning with a dose of 0.0003 Gm. (1/200 grain) three times a day. This dose must be increased as the patient develops a tolerance for it. Many patients require 0.0013 Gm. (1/50 grain) three or four times a day. Tincture of stramonium may be given in a dose of 0.66 cc. (10 minims) three times daily and increased either by 0.066 cc. (1 minim) a day or by 0.33 cc. (5 minims) per dose per week until a maximum dose of 8 cc. (120 minims) three times a day is reached. The unpleasant symptoms which develop, such as drying of the throat, blurring of vision, and mental confusion may make the treatment of questionable value. When discontinuing the drug, it should be done gradually.

POLIOMYELITIS

Acute poliomyelitis (Heine-Medin disease) is an acute infectious contagious disease characterized typically by symptoms referable to changes in the anterior horn cells of the central nervous system.

Etiology: The specific etiology of poliomyelitis is a filterable virus. Its portal of entry is still debated. The larger school believes that the virus enters the central nervous system directly from the nasopharynx, particularly by the olfactory nerve. The disease has been recently classified simply into: (1) The abortive type, which is not diagnosed except by elaborate experimental study; (2) the nonparalytic type; (3) the lower motor neurone type, both spinal and bulbar; (4) the encephalitic type—rare, and (5) the ataxic type—very rare. Mixed types may occur. The disease has been considered one of childhood, but recently greater incidence has been reported in the older age groups. The ratio of males to females is 3 to 2. Negroes appear to be less susceptible than white people. Recognizable cases occur largely in the temperate zone. The disease is most prevalent during spells of hot dry weather but may appear at any time of the year. One attack of the disease appears to confer lasting immunity.

Pathology: Congestion and edema are present in the entire nervous system, more marked in the cord and brain stem than in the brain

proper. Most of the pathological changes are found in man in the lumbar segments of the spinal cord; the cervical region is affected next in order of frequency. The first notable changes are in the vessels of the anterior horn which become congested, distended, and surrounded by small cell infiltrations. The gray matter is particularly affected, but the meninges and white matter are also involved. The nerve cells may die quickly with little alteration of cell outline but with swelling of the nucleus, coagulation of Nissl bodies, and gradual disintegration of the cytoplasm of the cells, or there may be necrosis of the nucleus, disappearance of the Nissl body, and evidence of active phagocytosis of nerve cells. Degenerative changes can be traced into the anterior roots. Later the motor nerve trunks show decrease in size and number of their fibers. The anterior horn as a whole becomes sclerosed and shrunken. Muscles become pale and flabby; atrophy is early and marked. Extensive hyperplasia of lymphoid tissues is described.

Signs and Symptoms: The incubation period varies from 6 to 18 days. The initial symptoms are quite the same in all types of the disease except the abortive, and they may be quite as severe in the nonparalytic as in the paralytic form. The onset is usually abrupt. Early symptoms are headache, fever, vomiting, constipation or diarrhea, and frequently congestion of the throat. The temperature usually is from 37.8° to 39.5° C. (100° to 103° F.) without characteristic curve. Usually the fever lasts not more than ten days and generally falls by lysis. The pulse is rapid in proportion to the fever. A more rapid pulse suggests early bulbar involvement. Hyperesthesia is often seen early. It is usually more marked along the spine and over the large nerve trunks and is demonstrated by somewhat deep pressure. Diminution of sensation almost never occurs. There is often pain in the neck, back, extremities, or abdomen. The abdominal pain may resemble that of the surgical belly. The duration of pain is usually short, but occasionally the necrotic pains may be long-standing. Drowsiness alternating with irritability when disturbed is common. Delirium is rare. Twitchings of groups of muscles are occasionally seen early. Ataxia is rare; convulsions are infrequent. Evidence of meningeal irritation occurring early is stiffness of neck and back, and often a positive Kernig and Babinski sign. Reflex changes are important. Early the deep reflexes are exaggerated and equal. A posi-

tive Babinski or ankle clonus may be present temporarily. The deep reflexes may become unequal, diminished, or lost. Superficial reflexes are present unless the underlying muscles are paralyzed. The pupils are not affected. There may be difficulty in voiding urine.

If paralysis occurs, it is practically always flaccid and most often develops on the second or third day. The paralysis usually reaches its maximum almost immediately, but additional paralysis may develop over a period of several hours to as many days. Any group or any combination of groups of muscles may be affected. The degree of involvement varies from weakness to complete loss of power. Death is practically always due to respiratory failure associated with increasing paralysis of muscles of respiration.

Diagnosis: In the majority of cases, the spinal fluid is increased in amount and shows an increased cell count to as high as several hundred. Mononuclear cells predominate as a rule, although at times predominance of the polymorphonuclear cells is seen. The protein is usually slightly increased. The sugar is normal or high. The blood count is not characteristic.

Prognosis: The seriousness of the disease can be overrated. There are many abortive cases. A large percentage of cases are diagnosed that develop no paralysis at all. Many of those patients who develop paralysis recover with little or no disability if adequate care is given. There is little danger of behavior disturbances and of mental deterioration.

TREATMENT

1. Poliomyelitis is a quarantinable disease, the minimum period of quarantine being three weeks. During the course of an epidemic it is advisable that all cases of indefinite illness in children under five years of age, especially if fever, diarrhea, cough, and vomiting are present, should be treated as positive cases of infantile paralysis.

2. Bed rest and all the fine points of nursing technic are essential in the acute stage.

3. The infection should be controlled at the port of entry by means of argyrol, 25 per cent, or hydrogen peroxide applied with a postnasal spray.

4. Convalescent serum has been used but the results have not been convincing.

5. During the acute phase the bowels should move at least twice

a day. Enemas may be necessary; a very satisfactory one consists of giving 120 cc. (4 ounces) of warm olive oil, to be retained one hour or more, then followed by 1000 cc. (one quart) of soapy water. If this method fails, follow by an enema of magnesium sulfate, 60 cc. (2 ounces), glycerin, 10 cc. (2 ounces), and warm water enough to make 500 cc. (one pint).

6. The diet should consist of milk, plain, diluted, or modified; broths; modified cereals if much gas is present, and fruit juices. The patient should drink plenty of water and, if refused, warm saline solution should be given rectally. Vitamin C, 25 to 50 mg. twice a day, and B_1, 10,000 units daily, are recommended. Their efficiency is problematical but they can do no harm. If there is difficulty in swallowing, feeding must be forced by stomach tube.

7. When fever is high, sponge baths or cool enemas should be given. Ice cap may be applied to the head. Lumbar puncture is frequently of value when there are signs of meningeal irritation and may be done repeatedly. Increased intraspinal pressure may also be relieved by hypertonic glucose solution, 50 cc. of a 50 per cent solution intravenously once or twice daily.

8. In the polyneuritic type, a suppository of opium, 0.033 Gm. (½ grain), extract of belladonna, 0.008 Gm. (⅛ grain), and sodium salicylate, 0.33 Gm. (5 grains), should be administered every three hours until pain is relieved.

9. If stupor is present, a hot mustard pack should be applied. The patient should drink water or grape juice while in the pack and should be rubbed dry after the pack.

10. Perivascular drainage continues to be advocated occasionally but apparently the virus cannot be washed out.

11. A respirator should be on hand at all times to be used in the event of respiratory paralysis.

12. Orthopedic care, as pads, splints, or casts, is given as support to weakened or paralyzed groups of muscles.

13. To date it has been emphasized that weakened muscles be protected from attempts at motion. However, the Kenny treatment of a firm mattress supported by bedboards, hot foments to the affected muscles, passive movements through the range of motion possible without pain, and muscle training is receiving wide publicity; its value may be proved.

TETANUS

Tetanus (lockjaw) is a specific infectious disease caused by the *Bacillus tetani*, which produces a powerful toxin. It is characterized by intermittent painful tonic spasms of the muscles. Although it is commoner in tropical countries, it occurs in the United States, especially along the Eastern seaboard during the summer months.

Etiology: Tetanus usually follows an injury. Lacerated wounds of the hands or feet caused by contaminated nails or splinters, and gunshot or shrapnel penetrations are the most frequent causes of the disease. A high incidence is due to burns incurred in 4th of July accidents. Occasionally the B. tetani enters the body during operation on the rectum or perineum. Any laceration of the skin or tissues may be the source of infection, and consequently careful first aid treatment should be given any punctured wound. Probably the most dangerous wounds are those received in cultivated fields, street and road accidents, about animal barns, and those in which foreign bodies or sequestra are left.

The B. tetani is a drumstick-shaped organism with a terminal spore. It is slender, slightly motile in the vegetative form, and usually grows singly. It is most often described as an obligatory anaerobe which is gram-positive in its staining properties, and grows at but 37.5° C. in a slightly alkaline medium devoid of oxygen. It produces an exotoxin which is especially harmful because of its affinity for the central nervous system.

Signs and Symptoms: The incubation period varies from one day to three or four weeks, depending on the length of time required for the toxins to travel along the nerves to the centers. It may be prolonged if antitoxin is given to prevent tetanus. Symptoms are absent during this period and the wound in which inoculation has occurred may be forgotten.

The first indications of infection usually consist of headache and general depression. Active symptoms may begin with stiffness in the mandibular joint on opening or closing the mouth, difficulty in swallowing or chewing, restlessness, irritability, and frequent yawning. Sometimes chills or rigors occur, and the muscles nearest the wound may show spasticity. Stiffness of the neck, arms, or legs; headache; fever, and chills may be observed. These signs appear a few days after the injury, and if they are recognized as the premonitory signs

of tetanus, therapy may be instituted immediately and the patient will have a better chance for recovery.

Later, the neck becomes rigid. Tonic spasm of the masseter muscles causes trismus or lockjaw, and the mouth becomes distorted in a "sardonic grin." As a result of involvement of the facial muscles, the mouth cannot be opened and efforts to do so cause great pain. Gradually the process involves all the muscles in the body. The abdominal and lumbar muscles reveal boardlike rigidity. The back may be so stiff that the patient rests on his head and heels during a spasm. The entire trunk and limbs may be rigid.

The most characteristic features of general tetanus are rigid locking of the jaws and painful convulsions which may be precipitated by jarring or handling of the patient or any irritation. These spasms occur with increasing frequency and can be precipitated by the slightest stimulus. They may be local or general in character, and may be momentary or last for a few minutes, but relaxation is not complete between attacks. During these spasms, the patient usually perspires profusely. When death occurs during a paroxysm, it is due to exhaustion, suffocation, or heart failure.

The terminal stage of the disease develops during the second week. Unfortunately, the patient remains mentally alert until death. The pain grows more intense and convulsions are more frequent; urinary retention, high fever, sweating, and exhaustion usually precede death.

Diagnosis: Careful history and examinations will usually differentiate tetanus from diseases with which it might be confused. A history of injury plus a B. tetani culture from pus or tissue of the wound are very important in diagnosis. Rabies, strychnine poisoning, tetany, hysteria, and meningitis may make the diagnosis questionable. Rabies follows a dog bite. A history of having taken the drug or its recovery from the intestinal contents are necessary for the diagnosis of strychnine poisoning. The muscles of the jaw are seldom involved in this poisoning, and there is complete relaxation between spasms. In tetany, the involvement of the hands with fingers outstretched and the thumb turned under the palm, the absence of rigidity of the jaws and lumbar muscles, and the peculiarity of the position of the patient distinguishes it from tetanus. A lumbar puncture is valuable if meningitis is suspected. At all times, a culture of B. tetani found in the tissues at the portal of entry clinches the diagnosis of tetanus. Impac-

tion of an infected third molar tooth may present symptoms suggestive of tetanus, but swelling of the face and pain on pressure over this tooth and the second molar make the diagnosis comparatively easy.

Prognosis: Recovery occurs in about 45 per cent of cases. Age, site of wound, length of the incubation period, and the abruptness of the period of onset all play a part in prognosis. Tetanus in the very young and in older patients is usually fatal. If the infected wound is on the face or neck or if the symptoms are severe, the disease is likely to be fatal. If the period between inoculation and the first symptom is more than ten days, prognosis is good, but if it is less than a week, prognosis is bad. However, the nature of onset is important too. If onset is insidious or more than four days, chances for recovery are very good, while if it is abrupt or less than two days, the disease will undoubtedly be fatal no matter what treatment is used.

TREATMENT

1. Prophylactic:
   - *a.* Thorough cleansing of the wound is necessary.
   - *b.* If infection is suspected, 5000 to 10,000 units of antitoxin should be given intramuscularly or subcutaneously.
   - *c.* One cc. of tetanus toxoid may be given deeply subcutaneously, and followed in six weeks by another injection of the same amount. This treatment is preferable to the antitoxin because it actively immunizes the patient against tetanus and causes little discomfort.

2. Curative: There have been many programs advocated in treating tetanus. The following regime appears to be the best one for most cases. To a large extent it is the method reported by Vener and Bower.
   - *a.* A serum test for sensitivity is done.
   - *b.* The patient should be kept in a quiet darkened room to soothe the irritated nervous system.
   - *c.* Chloral hydrate is given orally, or, if the patient is unable to swallow, a retention enema of this drug with the same amount of calcium bromide is given. The dose varies from 0.33 to 2 Gm. (10 to 30 grains), dependent on the size and age of the patient. This dose may be repeated if necessary.
   - *d.* An hour later administration of antitoxin should begin. Twenty thousand units are injected completely around the wound. If possible, this area should be anesthetized previously.
   - *e.* One hour later 60,000 units of antitoxin should be injected intramuscularly at the proximal extremity of the part involved so as to control the progress of the toxin. Then the focus should be incised widely or excised thoroughly, care being taken to keep within the

circle formed by the antitoxin injections. All foreign material should be removed from the wound and hot compresses of potassium permanganate should be applied.

f. Two or three hours later cisternal puncture should be done, removing about 10 cc. of fluid, and injecting slowly by gravity 20,000 units of antitoxin heated to body temperature. This procedure causes the temperature to rise, but in six or eight hours it recedes without undue effects.

g. When the temperature has receded to 39° C. (102° F.) 0.33 cc. (5 minims) of epinephrine should be given hypodermically, followed in five minutes by the slow intravenous injection of 40,000 units of antitoxin diluted in 300 to 500 cc. of physiologic solution of sodium chloride. Epinephrine hypodermically should be repeated in the middle period of the antitoxin injection and following it. If the antitoxin is kept at room temperature for 24 hours before using and heated in a lukewarm water bath just before injection, serum reactions are less likely to occur.

h. Two hours after completion of the above injection 1 Gm. (15 grains) of methenamine should be given intravenously.

i. About an hour later another 20,000 units of antitoxin should be given intravenously in 300 to 500 cc. of physiologic solution of sodium chloride. Precautions against serum sensitivity and anaphylactic shock must be taken. If the patient has had any untoward reactions from the first injection the second is withheld. About 12 hours later the final 40,000 units of antitoxin is given deeply intramuscularly and proximal to the site of the previous injection. This dose is increased to 60,000 units if the intravenous injection has been omitted. About ten hours after this injection methenamine is given as before.

j. The total dose of 200,000 units of antitoxin has now been given. The ordinary prophylactic dose of 1500 cc. should be given every four or five days for four doses to maintain the serum desensitization of the patient.

k. Sodium amytal, 0.4 to 0.6 Gm. (6 to 9 grains), by mouth or rectum should be given to control spasms.

l. In severe cases or those in which the prognosis is bad 0.1 Gm. (1.5 grain) of avertin per kilogram of body weight should be injected rectally and repeated every four to six hours if spasms recur.

m. If the patient perspires profusely and dehydration occurs sodium chloride should be replaced. Since the muscular exertion of the patient is great he must be well fed. If he is unable to take anything by mouth, it is wise under anesthesia to pass a fine stomach tube through the nose so food may be given. The very act of swallowing may be dangerous because it may initiate a spasm.

n. Oxygen should be administered if cyanosis is present.

o. Pneumonia should be guarded against.

CHAPTER XX

Acute Infections

(Continued)

PSITTACOSIS

Psittacosis is an acute infectious disease of man resulting from contact with parrots or laboratory animals infected with the virus of psittacosis. The disease is characterized by severe toxemia with a peculiar bronchopneumonia and symptoms suggestive of typhoid fever.

Etiology: Many organisms have been reported as causes of psittacosis. However, the disease has been proven to be due to a filtrable virus since the etiologic agent may be passed through Chamberland and Seitz filters.

Pathology: The changes found at autopsy are those of a general septicemia with a peculiar inflammatory picture in the lungs. The lungs are usually uniformly congested and swollen, and are red to dark purple and boggy. Purulent material may be exuded from the bronchi. There may be lobular or lobar consolidation. Microscopically various stages are described: (1) A hemorrhagic vesicular pneumonia with proliferation and desquamation of the alveolar walls; (2) an increase in engorgement with much serous exudate containing few leukocytes; (3) development of a fibrinous exudate containing many small round cells as well as large multinucleated cells. There is a variable degree of bronchitis. Perivascular infiltration in the brain as well as serous meningitis have been described. The organs of the body show cloudy swelling as a result of severe toxemia.

Signs and Symptoms: The disease may occur at any age or in either sex. The incubation period varies from 5 to 21 days. The illness usually begins with fever, chilly sensations, and general malaise. There may be a photophobia and frequently a splitting headache. In spite of the fact that the patient has a temperature of 39.5° to 40° C. (103° to 104° F.) for the first few days, he may feel quite well and the pulse is usually relatively slow. During the early stages of the disease, there are usually morning remissions of the fever. Anorexia, vomiting, sore throat, and herpes may appear quite early. In

from three to seven days, findings of pulmonary involvement are usually present.

As a rule, the physical findings manifest themselves in the bases of the lungs first. Only a few râles may be heard at first, but later signs of consolidation, patchy in character, may appear. The patients rarely show the marked increase in respirations or the cyanosis so often associated with other types of pneumonia. There may be a persistent cough but the production of sputum is usually minimal. In many cases, the patient appears quite well about the eighth day only to have a continuation of the pneumonic process with resultant toxicity and fever for several more days. During this period, small, pink, oval, papular skin lesions may appear on the trunk. These lesions fade on pressure and develop a white halo on rubbing. Typically the disease lasts from 10 to 14 days with the fever ending by lysis. Fulminating cases may occur with the development of a typhoid state, delirium, diplopia, hallucinations, and stupor. The urine often shows albumin with no other findings. Relative leukopenia with a shift to the left is common. There is usually no marked leukocytosis or lymphocytosis. Recovery from the disease is slow, the cough and lung findings disappearing gradually. The patient may remain in a weakened condition for weeks. The commonest complication is phlebitis of the femoral vein. Parotitis and ulcerative stomatitis occur rarely.

Diagnosis: The diagnosis is suggested by a history of contact with parrots or parakeets. Clinically, the disease simulates influenza or typhoid more closely than any other infectious disease. The acute onset with severe headache and malaise may cause one to entertain a diagnosis of influenza. Hacking cough associated with a relative bradycardia frequently brings typhoid to the clinician's mind. The diagnosis may be clinched by injecting mice with sputum from the patient and demonstrating the intracellular coccobacillary bodies in the spleen or liver after the mouse dies. Blood serum may be sent to the Williams Hooper Foundation in San Francisco where the specific complement fixation test is done. This test becomes positive as early as the sixth day of the disease. It should be repeated during the course of the disease, and if the antibody titer rises, this is almost pathognomonic for psittacosis. The antibodies are present in the serum for more than a year in some of the convalescent cases. A posi-

tive Wassermann may give positive complement fixation reaction for psittacosis. Nonspecific fevers never caused elevating titers nor titers above 1 to 8 in my experience.

Prognosis: Psittacosis is a serious infection. Various observers have reported mortality rates from 8 to 45 per cent. The most important factor in prognosis is age. The disease is a very serious threat to life in older individuals. The disease lasts from two to three weeks. If patients are going to die, they usually do so during the second week; they become extremely toxic with extensive pulmonary involvement, and expire.

TREATMENT

The treatment of psittacosis is mainly symptomatic and palliative. Meyers differentiates between two antibodies produced by the virus of psittacosis: (1) The complement fixing antibody which is utilized in the diagnostic test and appears early in the disease, and (2) a virus neutralizing antibody appearing later in the disease. Serums high in this virus neutralizing antibody may be effective in the treatment of psittacosis. One case is cited in which a crisis is produced by immune serum with a high titer of virus neutralizing antibodies. Meyers has also prepared hyperimmune goat serum. Hinshaw of the Mayo Clinic reports two cases treated with sulfapyridine, both of which recovered. The general treatment of psittacosis may be outlined as follows:

1. The patient should be isolated and in surroundings as quiet as possible, as excitement tends to make the headache and delirium worse.

2. A full diet can and should be given with the exception of stimulating and irritating foods. Large amounts of fluids may be given.

3. Acetylsalicylic acid, 0.66 Gm. (10 grains) four times a day, or phenacetin, 0.33 Gm. (5 grains) three times a day, should be given in an attempt to relieve the headache, which is usually the chief concern of the patient. Narcotics, as morphine sulfate, 0.008 to 0.016 Gm. (⅛ to ¼ grain), hypodermically, may have to be resorted to, but should be given only in exceptional cases.

4. Tepid baths or alcohol sponge baths may be necessary to reduce the fever.

5. The distressing cough is ordinarily not relieved by the usual mixtures, and codeine sulfate, 0.016 to 0.033 Gm. (¼ to ½ grain), may be administered. With laryngitis as a complication, warm steam inhalations with compound tincture of benzoin added to the water are of benefit.

6. The perichondritis in the nose may be relieved by application of zinc oxide ointment or yellow vaseline.

7. Luckie feels that massive doses of leukocytic extract, 5 cc. given hypodermically or intramuscularly, every four hours day and night, are indicated and influence the disease remarkably.

Convalescence requires careful consideration, as relapses are common and phlebitis may and is likely to develop. If the case has been severe, the patient should live quietly for 30 days after the temperature drops, and resume exercise and labor very slowly.

TULAREMIA

Tularemia is an acute specific infectious disease caused by the Bacterium tularense. It occurs in animals, especially the rabbit and rodents, and in human beings.

Etiology: The Bacterium tularense is a short, rod-shaped, nonmotile, gram-negative bacillus. Man acquires tularemia by direct contact with animals, particularly rabbits or squirrels, or through blood-sucking insects infected through these animals. Wild rabbits are chiefly responsible for the disease in human beings. Infection is most often acquired through handling, skinning, or preparing the animals for cooking.

There are four main types of the disease, which are usually dependent on the manner in which the disease is contracted: (1) The ulceroglandular, which is the commonest; (2) glandular; (3) oculoglandular, and (4) typhoid or intestinal forms. The typhoid type, which is the rarest, is difficult to diagnose because there is no primary lesion or glandular involvement to be seen, and because it resembles gastrointestinal disease.

Signs and Symptoms: The period of incubation is usually one to five days. Onset is sudden with headache, fever, chills, and general aching. This is followed by loss of weight, prostration, glandular symptoms, vomiting, sweating, and weakness. The lesion of ulceroglandular tularemia is quite characteristic; there is a painful papule

at the site of the infection which usually breaks in a day or two, releasing a necrotic sore. The lesion is a small ulcer with a raised edge. The regional lymph nodes are painful and usually enlarged. Hyperglycemia is usually present, but there is an absence of leukocytosis. The primary ulcers may so closely simulate an ordinary abscess that they may be cut open and drained in error. This makes a bad matter worse, and often spells disaster for the patient.

The glandular type is like that described above except there is no primary lesion. In the oculoglandular form, the lesion is on the lower eyelid with involvement of the lymph nodes, pain, and swelling. The typhoid type results from eating rabbit meat that has not been cooked properly. There is an absence of the primary lesion and regional lymph node involvement, but there is severe epigastric pain, vomiting, diarrhea, and enlargement of the anterior cervical lymph nodes. Typhoid tularemia is sometimes mistaken for undulant fever.

Diagnosis: Diagnosis may be clinched by a history of dressing or eating wild rabbits, isolation and identification of the bacillus, localized lesion, glandular swelling, and agglutination of the patient's serum with *Pasteurella tularensis.* Diagnosis should be made clinically first, as the agglutination is not usually positive for two or three weeks and often longer. It may be confirmed by culture from inoculated guinea pigs or by an intradermal test with a specific antiserum.

Prognosis: Most uncomplicated cases of tularemia recover, though convalescence is a prolonged process; often a year elapses before the patient feels like himself. Cases of death from tularemia have been reported as due to glandular enlargements, rapidly developing septicemia, and focal necroses in the liver, spleen, lymph nodes, bone marrow, and lungs. Meningitis and pulmonary complications usually end fatally.

TREATMENT

1. The patient should be put to bed and suppurating lymph nodes drained.

2. Ice bags or hot water bottles applied to the painful lymph nodes usually relieve the pain.

3. Treatment is usually symptomatic, though there is a specific treatment for the disease. Foshay's serum, 15 cc. twice daily on alternating days, has proved to be quite successful in bringing about symptomatic relief and cutting the death rate.

4. Sulfanilamide, 1 Gm. (15 grains) four times daily, has been given with some success. Powers and Powers achieved favorable results with the combined treatment of sulfanilamide and antiserum.

5. Sodium salicylate, 1.2 Gm. (18 grains) dissolved in 30 cc. of water given intravenously twice daily seems to be beneficial.

6. Other remedies include:

a. Bismuth sodium tartrate, 2 cc. of a three per cent solution.

b. Quinine sulfate, 0.33 Gm. (5 grains), three times a day for two weeks.

c. Metaphen intravenously in dilution of 1:1000 in doses of 10 cc. every other day for three injections, or in severe cases 10 cc. daily for four days and repeated on alternate days for three more injections.

d. Prontylin in 10 cc. doses four times daily until cyanosis begins, and then repeated a week later.

7. Preventive measures are important and may be listed as follows:

a. Rabbit hunters and eaters should avoid rabbits that are easy to catch; they are probably diseased.

b. When dressing wild game the hands should be protected, especially if there are open lesions or cracks on the hands.

c. Wild game must be thoroughly cooked.

d. Ulcerative lesions developing on the hands or face after the person has handled wild game should suggest tularemia, and treatment should be instituted immediately.

BRUCELLOSIS

Brucellosis is a focal or systemic infection usually caused by the ingestion of raw milk containing Brucella, though there are other avenues of infection, as the skin, mucous membranes, or the gastrointestinal tract. It is principally a disease of young adult males who work on farms, in packing houses, or butcher shops. The most important factor in the control of the disease is the pasteurization of all dairy products, especially milk. Although man contracts the disease from animals, so far as is known it is not transmitted from man to man. Brucellosis is uncommon in the United States, though quite a number of cases have been seen in Texas, Iowa, and other midwestern States.

Signs and Symptoms: Brucellosis is difficult to describe because it presents so many symptoms and signs common to other infectious diseases. Typhoid fever, tuberculosis, acute rheumatic fever, acute endo-

carditis, tularemia, and influenza are commonly confused with brucellosis.

Just as the incubation period ranges from 2 to 10 or 12 weeks, so too do the clinicial signs vary in character and severity. The onset may be sudden or insidious with acute upper respiratory symptoms, and the disease usually continues for about three months. Fever, weakness, and drenching sweats are the outstanding clinical features. A multiplicity of other symptoms seen in any infection may develop.

Spondylitis is probably the commonest complicating disorder of the bones and joints referable to undulant fever. Most authors agree that spondylitis as a complication of undulant fever is most likely to occur several months after the onset of the febrile state, but cases of brucellosis have been reported in which localization in the spinal column developed as early as three weeks and as late as one year after the original infection. The patient may even appear to have recovered from the systemic disease only to become affected by the spinal complication at some later date.

Diagnosis: The examination of the patient as a rule fails to reveal any evidence of disease commensurate with the fever and other symptoms. Frequently the patient feels unusually well, notwithstanding the fact that the fever may be 39.5° C. (103° F.). The differential diagnosis is difficult because so many other conditions may produce a similarity of symptoms. After tuberculosis, syphilis, endocarditis, malaria, and typhoid fever have been eliminated as causes of the fever, special laboratory procedures must be used to make the diagnosis of brucellosis. The diagnosis is clinched if one can grow the organism from the blood and identify it. In acute brucellosis, agglutination tests and skin tests are helpful, but not so in the more chronic cases. A positive agglutination test does not mean the patient is suffering from brucellosis at the time the test is positive. These tests too may be negative in some persons who have an active disease.

Leukopenia occurs in most patients, and the lymphocytosis with a high ratio of immature lymphocytes is common. Other laboratory aids, as the sedimentation rate and erythrocyte count, are of less importance. Although some patients die of the disease, fatalities are rare. Sometimes intercurrent conditions as pneumonia, tuberculosis, and other infections are responsible for the death of the patient. While fatalities are rare, morbidity is prolonged and constitutes one

of the most unfavorable features of the disease; the disease may last from six weeks to several months.

TREATMENT

The treatment may be classed into the symptomatic or general, and the special therapeutic agents.

1. Symptomatic treatment requires that the patient be kept in bed and that the caloric requirements of the body be furnished by an adequate diet. The other simple methods used to relieve distressing symptoms and to make a patient comfortable are employed.

2. The special agents are serum, vaccines, and brucellin.

   a. Antibrucella serum has given very favorable results, especially in the acute cases. If the diagnosis is positively made, about 20 cc. of serum is given intravenously each day on three successive days, and the clinical response is usually quite dramatic.

   In very severe cases 90 to 120 cc. may be given in unit doses of 30 cc. during 48 to 72 hours. Daily doses of 10 cc. each may be given intramuscularly or subcutaneously until 20 or 30 cc. have been administered. Serum therapy is not indicated in chronic cases of more than eight months' duration unless sudden severe exacerbations occur.

   b. Vaccine therapy has been followed by more indefinite results than serum therapy. Within recent years better preparations have been used and some of the former difficulties have been overcome to some extent. Experience and good judgment are the essential requisites in determining the proper dosage. Usually a test is performed for hypersensitiveness to the vaccine—0.05 cc. of a 1:10 dilution of the vaccine is injected into the deep subcutaneous tissues or the muscle. If there are no reactions a second such dose may be given three days later. The dosage is then increased by 0.25 cc. at intervals of three days until a total of 1 cc. is given. Five to eight injections of 1 cc. each may then be administered at three-day intervals. If a severe reaction occurs during the course of treatment, the following dose should be reduced to one-half that which caused the reaction, and the succeeding doses may be gradually increased. A series of four to six or more sharp systemic febrile reactions, usually accompanied by a transient exacerbation of symptoms, is the goal to strive for. Only extreme local or general reactions should be avoided.

   c. Brucellin is obtained from the brucella cells grown in liver broth. The bacteria-free active agent is obtained from the liver broth filtrate. The patient is tested out for sensitivity by giving an intradermal injection of 0.1 cc. of brucellin and, if the patient is nonsensitive, 1 cc. is given hypodermically at three-day intervals until the morning and evening

temperatures between the intervals of injections tend to become subnormal. Here too the object of therapy is to produce a series of four or more febrile systemic reactions.

d. Treatment of brucellosis could hardly be passed over without mention of the sulfonamides. Experience has shown that no sulfonamide has given very satisfactory results. Neoarsphenamine, mercurochrome, acriflavine, metaphen, gentian violet, and other substances have been employed in the care of these patients, but their value must be regarded as undetermined until more work is done. Injections of foreign protein substances as typhoid vaccine and sterile skimmed milk have been used with some degree of success. Artificial fever therapy in the management of these cases has been quite effective. The usual course of therapy is six fever sessions, each of three hours' duration, at a rectal temperature level of 40.5° C. (105° F.), given during a period of two weeks. Especially good results have been obtained in patients who did not respond to vaccine therapy.

RABIES (HYDROPHOBIA)

Rabies is an acute infectious disease of warm-blooded animals, especially dogs. It is characterized by terminal paralysis, convulsive seizures, and a fatal outcome which is often preceded by coma.

Etiology: Human beings acquire the disease when they are bitten by a rabid animal or when a human abrasion is licked by the animal. The etiologic agent of rabies is questionable; it is most often referred to as a virus, yet it may be a protozoan organism with cell inclusion bodies. Negri found that certain rounded eosinophil bodies occupy the interior of the nerve cells in most cases, but it is not known if these cause the disease or are merely the result of it. The virus of rabies is filtrable and is contained especially in the saliva; it spreads up the peripheral nerves to the central nervous system.

Signs and Symptoms: The incubation period varies from two weeks to two months, depending usually on the proximity of the site of infection to the central nervous system. The average incubation time is about six weeks. When the patient first shows signs of the disease, there is irritation around the scar of the bite as well as severe pain. The early symptoms are associated with the central nervous system and are those of severe encephalitis. The patient complains of headache, difficulty in swallowing, and loss of appetite. He is irritable, sensitive, and unable to sleep. Usually a slight rise in pulse and temperature is noted. Several days later, the stage of excitement

sets in and the patient becomes restless, excitable, and has maniacal tendencies. He experiences reflex paroxysms of pain, and when he attempts to swallow, he is conscious of painful spasms of the muscles of deglutition and respiration. There is frothing at the mouth and vomiting, most often of a bloody saliva. The fever rises to 38.3° to 39.5° C. (101° to 103° F.); the pulse increases in rate with each convulsion. Shrieks of terror and wideopen mouth are characteristic of the pharyngeal spasm. Patients are unable to swallow and efforts to do so result in pain and often convulsions.

At times the patient seems to be perfectly normal, and then again goes into a maniacal attack. After two or three days of this, the patient passes into a stage of exhaustion or a paralytic stage; he is quiet and the convulsions cease. He becomes unconscious, often going into coma, and the temperature rises to about 41.6° C. (107° F.), pulse is rapid, the heart becomes weaker, and finally death occurs.

There is hyperemia and perivascular round cell infiltration of the central nervous system, and congestion of the pharynx, esophagus, and stomach. Typical and diagnostic Negri bodies are present especially in the ganglion cells of cerebral and cerebellar cortex.

Diagnosis: When an animal is suspected of being rabid, he should be killed and his brain studied for Negri bodies. This finding is diagnostic. In doubtful cases, the saliva of the dog should be injected into the brain of a rabbit; the latter will promptly die of rabies if the dog is rabid. The disease must be differentiated from tetanus, hysteria, and focal epilepsy.

TREATMENT

Since death is inevitable, treatment is purely palliative, the object being to insure rest, and control pain and convulsions.

1. The patient should be isolated in a darkened, quiet room and given sedatives as needed. The ordinary sedatives have very little action in controlling the spasms, but it is advisable to give morphine sulfate, 0.016 to 0.032 Gm. (¼ to ½ grain), hypodermically, in an effort to diminish the severity of the spasms. Chloroform inhalations to the point of coma are given. Chloral hydrate, 1 to 2 Gm. (15 to 30 grains), avertin, 60 to 80 mg. (1 to 1⅓ grains) per kg., or bromides, 1 to 2 Gm. (15 to 30 grains), may be given by rectum as indicated to prevent the distress of severe convulsive spasms.

2. Local application of cocaine, five per cent solution, may relieve the sensitiveness of the throat so the patient may take liquid nourishment. Administration of other foods is contraindicated and no foods or fluids should be given during the last stage of the disease, although fluids may be administered by rectum during the last stage.

3. Attendants should wear rubber gloves and take other precautions since this disease is highly infectious. Dried saliva remains infectious for 14 hours, while fluid saliva is infectious for twice that long.

4. *Preventive treatment in rabies is most important because if it is not instituted a fatal outcome is almost certain.*

a. If a person has been bitten by an animal suspected of having rabies he should first be anesthetized so he may receive proper surgical care without pain.

b. Then the wound should be opened and blood forced out. The wound should be cleansed with bichloride of mercury solution diluted 1:1000 or with a warm saline solution.

c. Fuming nitric acid or pure phenol should be used to cauterize the wound, though another cautery may be used. The nitric acid should be applied by drops to the torn surface, especially to the deep punctures, but care should be taken not to get the acid on bony or bloodless parts or on sound skin. Carbolic acid may be used on these parts. Some doctors object to the fuming nitric acid treatment because it may result in severe infections and scars.

d. Finally, the wound should be washed with a saturated solution of bicarbonate of soda and then alcohol. No attempt should be made to close the wound. The dog should be saved for observation.

e. The *Pasteur* treatment for rabies is given as follows: A series of inoculations of rabies virus is administered if there is any suspicion that the wound was caused by a sick dog or one known to have rabies. The dosage is 2 cc. administered daily into the subcutaneous tissues in different areas for a period of about 21 days. Care should be taken to give sufficient amounts of serum or it will be useless; the amount of vaccine necessary is dependent on the location and severity of the bite. It may be necessary to give 35 or 40 doses. Because there may be an untoward reaction from the antirabies vaccination, inoculations should not be given unless it is quite certain that the bite was from an animal with rabies. Sections of the brain of the animal should be put in glycerin at the same time the original smears or sections are made and kept for either mouse or rabbit inoculation.

f. A recent suggestion for treatment is using immune transfusions in victims who have been severely bitten about the head. Small blood transfusions from people who have recently completed a 21-day treatment by the Pasteur method are given.

TRICHINOSIS

Trichinosis is an acute or subacute disease caused by the *Trichinella spiralis.* It occurs wherever uncooked or improperly cooked pork is eaten, and age, sex, race, occupation, location, and climate appear to have no effect on the incidence. The disease occurs most often during the summer months, according to the author's experience, probably because during this season the roadside stands selling hamburgers, barbecues, and homemade country sausage are open.

Etiology: Most patients reveal a history of having eaten raw hamburger or inadequately cooked pork. The disease is produced by the Trichinella spiralis, a slender roundworm developing from the encysted larval form in trichinous meat. When a person ingests this meat, the cyst wall is digested in the stomach and the worms pass into the small intestine where they reach maturity in about three days. The females are fertilized and on about the seventh day burrow into the mucosa of the small intestines and allow the embryos to escape into the tissues and lymph spaces. By the tenth day, the embryos are usually found in the muscles where they grow to maturity; they coil up and become completely encysted by the twelfth week and may live in this stage for 20 or 30 years.

The development of trichinosis in humans is accidental, but the lower animals are the normal hosts for the organism. It is probable that swine become infected when their food contains uncooked pork scraps. The disease is not transmitted from person to person, and humans do not appear to be immune after an attack.

Signs and Symptoms: Trichinosis does not always present a uniform clinical picture, but the forms following the classic outline are usually easily recognized. The incubation varies, but symptoms begin 6 to 14 days after the ingestion of the trichinous pork in most cases. However, occasionally gastrointestinal disturbances commence a few hours after eating, while in other instances characteristic symptoms may never appear. The severity of the symptoms depends partly on the amount of infected meat eaten and on the number of parasites in the meat. Other factors include the size, physical condition, and resistance of the individual and the amount of tissue invaded.

The disease process may be divided into three stages:

1. The stage of intestinal infestation occurs a few hours after the infected food is ingested. The symptoms are referable to the gastrointestinal tract with loss of appetite, nausea, vomiting, diarrhea, and abdominal cramps. There is a gradual rise of temperature, prostration, and some pain and stiffness in the muscles.

2. The stage of dissemination begins about a week later when the embryos enter the blood and lymph stream. Muscular pains are more pronounced, and the function of the muscles, especially those of respiration, mastication, and of the eye, is disturbed. Edema of the face and eyelids is common, as are fever and profuse sweating. Rash with tingling or itching of the skin may occur.

3. The stage of encystment begins about the seventh week when the embryos become encysted in the muscles. It is a period of convalescence in which the symptoms become less severe, and gradually the temperature returns to normal and the edema subsides. The patient is anemic and emaciated, and the muscular pains and weakness may continue for months.

Early in the disease, the percentage of hemoglobin is moderately raised and the number of red blood cells may be increased. Later, anemia may develop, with the number of red cells falling as low as 2,500,000 per cmm., and the hemoglobin to 45 per cent. Leukocytosis, usually about 25,000 white blood cells per cmm., may be present. The number of neutrophiles rises with the eosinophiles proportionately increased. This eosinophilia is one of the main characteristics of the disease, but it is not always present. Besides these clinical manifestations which constitute the clinical picture of the typical case, other less common signs and symptoms have been noted. Fatigue, generalized edema, cough, headaches, chills, furuncles, hoarseness, and marked hypotension may be present. The electrocardiogram may confirm the clinical evidences of various degrees of temporary myocardial involvement. Frequently trichinosis is complicated by the involvement of various organs, with the presence of ocular, neurologic, or mental symptoms.

Diagnosis: The lack of a regular course and the many deviations from the clinical picture which are encountered may make the diagnosis somewhat difficult. Usually the blood counts, muscle biopsy, and skin test are valuable diagnostic aids. However, a positive Widal

reaction, in the presence of persistent fever, may suggest typhoid fever. The muscle and joint pains may lead to a diagnosis of rheumatic fever or influenza, and the rash and stiffness of the neck may confuse the physician as to whether the patient has trichinosis or meningitis. Other conditions which may simulate trichinosis are acute nephritis, tularemia, sinus infection, or la grippe.

A history of having eaten hamburger, sausage, ham, or pork of any kind which may have been undercooked, an eosinophilia, gastrointestinal disturbances, generalized aches, and fever are very suggestive of trichiniasis. If there is any doubt, a muscle biopsy often reveals larvae and makes the diagnosis certain. Other diagnostic aids include the Bachman skin test in which the injection of trichinella protein causes a specific local skin reaction, and the study of the blood for precipitins, though this test is of little value before the twenty-first day of the disease.

Prognosis: The immediate prognosis is good. Few patients die, and many cases are so mild that they go unrecognized. However, the brain, meninges, kidneys, and heart may be invaded, and then the outlook is not so satisfactory. Complications are usually limited to pneumonia, pleurisy, thromboses, and thrombophlebitis.

TREATMENT

Unless patients are seen before the larvae become encysted in the muscles or organs of the body, only palliative treatment is of value. However, if the case is observed in the invasive stage, a brisk cathartic, as castor oil, 15 to 3 cc., or a saline purge, as a solution of citrate of magnesia, 200 cc. (1 bottle), followed in several hours by magnesium sulfate, 10 to 15 Gm. (150 to 225 grains), is very effective. Good results have been reported in treatment with thymol dissolved in sterile olive oil, 0.066 Gm. (1 grain) in 1 cc. of oil, giving 2 to 3 cc. subcutaneously or intramuscularly every day for seven days. Sedatives, as phenobarbital, 0.1 Gm. (1½ grains) daily, and acetylsalicylic acid, 1 to 2 Gm. (15 to 30 grains), three times a day, may be administered to relieve the pain and headache. To aid in the encystment of the larvae in the muscles after the invasive stage, calcium lactate, 1 Gm. (15 grains) three times a day, or some other calcium preparation, may be given.

The chief factor in treatment is the prevention, which is accomplished by refraining from eating pork or pork products unless they are cooked properly.

VINCENT'S ANGINA

Vincent's angina is an ulceromembranous inflammation of the mucous membrane of the cheeks, gums, and fauces. Its synonyms are ulcerative stomatitis, fusospirillosis, trench mouth, and ulceromembranous angina.

Etiology: This rather common disease is found most often in young persons, though it may occur at any age. Poor health, lesions of the mouth, decayed teeth, inflamed gums, and oral uncleanliness predispose a person to this malady. It is geographically widely distributed, though it is seen most commonly in temperate or tropic climates, where its incidence may be epidemic in character. It spreads from person to person by kissing, towels, dishes, or some such contact. The disease may gain entrance through the ear, vagina, or glans penis.

The two organisms associated with Vincent's angina are a fusiform bacillus and a spirochete, which are found together in the lesions and most plentifully in the immediate vicinity of the ulcer. They survive best in an acid medium.

Pathology: The inflammatory process is described as going through three stages: (1) Hyperemia and edema; (2) ulceration, and (3) pseudomembrane formation with necrosis. These stages are not, however, clearly separated from each other, and may follow each other in rapid succession. The lesion most commonly occurs on the gums, cheeks, pillars of the fauces, tonsils, and uvula, though it may appear on any of the other mucous membranes. The mucous membrane of the female genitalia may become infected. The organism may pass from the vulva through the vagina and involve the endometrium. Noma, gangrenous stomatitis, and gangrene of the fauces are the most serious lesions. Pulmonary involvement with bronchopneumonia and pulmonary abscess are also known to result from this disease. These severe complications are most likely to come on if there is granulocytopenia.

Symptoms and Findings: Sore mouth and gums, headaches, general malaise, chills, fever, and tachycardia are the symptoms associated with the disease. Sometimes there are no constitutional symp-

toms, only local pain on swallowing, or tender gums, hoarseness, aphonia, and paroxysmal cough. No leukocytosis is present; on the contrary, there may be polymorphonuclear leukopenia. This leukopenia probably is preëxistent to the disorder, and allows the infection to invade the mouth without much protective cellular response. The spleen is not palpable.

Ulcers are discovered in the mouth. The ulcer may be single, or the membrane may spread rapidly as in diphtheria. In children, the first sign may be painless enlargement of the cervical glands.

The disease may be acute, subacute, or chronic with the lesions persisting for weeks or months. Recurrence of such an attack is common.

Diagnosis: Diagnosis is confirmed by the presence of the typical Vincent's bacteria, fusiform bacilli, and spirilla. Vincent's angina must be differentiated from syphilis, diphtheria, and tonsillitis.

If a smear of the exudate is stained with carbolfuchsin and studied under the microscope, there will be little trouble differentiating between Vincent's angina and diphtheria. The fusospirillosis are found plentifully in Vincent's angina, while they are absent in diphtheria. Cultures will give further proof for the diagnosis. The hyperemia surrounding the membrane is intense in diphtheria, but not so marked in Vincent's angina. In tonsillitis, too, the hyperemia is much greater than in Vincent's angina, and the exudate is more punctate.

A serious case of fusospirillosis with conspicuous edema is harder to diagnose, as it is easy to confuse it with tonsillitis and diphtheria. The bacteriology, the necrotic character of the slough, and the relatively mild surrounding hyperemia of fusospirillosis are the main differential points. However, it is well to remember that in tonsillitis, there may be small numbers of the fusospirilla present, and in the cryptic exudate of chronic tonsillitis this spirochete may be found in large numbers.

The best way to differentiate syphilis is to examine a smear of the exudate. *Spirocheta pallida* is very fine and shaped like a corkscrew, while the other is coarser and has long, undulating curves. One should note that the fusospirillum often is found in syphilitics, especially in those undergoing mercury therapy.

Prognosis: Vincent's angina is rarely fatal, but may persist for weeks and recurrence is common. Troublesome complications are

rare. The Vincent bacteria are more active in the presence of diphtheria bacilli than with streptococci. The presence of pyorrhea, decayed teeth, or infected tonsils increase the severity of the attack.

TREATMENT

Oral and dental cleanliness should be carefully maintained in all cases. In order to avoid contaminating others, towels and eating utensils should be kept separate. After the attack is over, local mouth disease and teeth may be attended to, but operative work should not be performed until the Vincent bacteria are proved to be absent.

The most satisfactory active treatment may be described as follows: Hydrogen peroxide is applied to the lesion to remove the slough. After that the lesion is washed thoroughly with saline solution, and the ulcers dusted with arsphenamine. If the gum margin is invaded, arsphenamine can be best applied with a spray. If the middle ear or nasopharynx is infected, it should be cleaned according to the usual cleaning procedure and the ear canal carefully dried. Arsphenamine is then blown into the middle ear.

Glycerin, 8 cc.; wine of ipecacuanha, 12 cc., and liquor potassii arsenitis, 12 cc., in combination are a good local application. The solution may be diluted and used as a mouthwash. There should be no granulocytopenia if arsenic is to be used. If there is granulocytopenia, every effort should be made to increase the granulocytosis.

If the lesions are inaccessible, arsphenamine can be given intravenously, 0.3 to 0.6 Gm. (4½ to 9 grains) for several doses at two- or three-day intervals. Novocain, one per cent solution, will relieve the cough due to severe laryngeal ulcerations and the dysphagia.

Sulfadiazine is the most effective method of treatment at the present time. It is given in doses of one gram every four hours until the sulfa level of the blood is approximately seven milligrams per cent; then this level is maintained until the disease subsides. Subsequently, one gram once or twice a day is given for several weeks. Corresponding amounts of soda bicarbonate are administered at the same time.

LUDWIG'S ANGINA

Ludwig's angina involves the cellular tissues of the floor of the mouth, and sometimes the submaxillary space or tissues of the neck. It is a phlegmonous process resulting from infections within the floor

of the mouth or from the teeth localizing in the floor of the mouth. This disease is rare, but virulent and often fatal.

Etiology: Ludwig's angina occurs most commonly in the young, and young adults, though no age is immune. Males are more often attacked than females.

Trauma of the interior of the mouth, local mouth infections, dental caries, tonsillitis, peritonsillitis, trauma of dental extraction, Vincent's angina, facial erysipelas, otitis media and externa, and ulcers of the lip and nose are all said to cause Ludwig's angina at one time or another. Infections of the tonsils and front teeth, however, are not likely causal factors.

Streptococci, staphylococci, bacilla coli, and sometimes gas producing organisms of the anaerobic type are found as a rule.

Pathology: Ludwig's angina is probably due to cellulitis, though it has been attributed to lymphadenitis and a perilymphadenitis; lymphadenitis would not cause a sublingual or submaxillary cellulitis unless there was direct extension of the infection to the cellular structures by contiguity.

The sublingual space must be involved for a diagnosis of Ludwig's angina. Infection may be above or below the mylohyoid muscles. If above, the abscess would point inside the mouth; if below, to the submental region.

Symptoms and Findings: In Ludwig's angina, the first complaint is generally stiffness of the tongue and pain in the floor of the mouth and on clearing the throat. A boardlike swelling of the submaxillary and submental regions with marked trismus is typical. This swelling may extend to the clavicle in severe cases. There is also swelling and induration of the mouth, gums, and tongue, which is pushed backward and upward. Suppuration is not always present in such cases, but abscess formation is evident in the majority of them. The constitutional symptoms resemble those of severe toxemia.

Fever is not always present in the earlier stages, but it may rise as high as 41.1° C. (106° F.) later on. The leukocyte count may be from 10,000 to 35,000 or more. Asphyxia may occur as a result of the swelling and displacement of the tongue.

Prognosis: The prognosis in Ludwig's angina is bad; the mortality may be as high as 43 per cent. Death may result from suffocation or exhaustion. Serious complications, such as osteomyelitis of

the mandible and involvement of the submaxillary, the parotid, or the pharyngomaxillary space, may develop. Jugular thrombosis may be brought on by invasion of the carotid sheath. Mediastinitis is common. If there is suppuration, heart failure may come on rapidly.

TREATMENT

Bed rest and a liquid diet are required. The heart should be stimulated by caffein and digitalis. Oxygen must be kept on hand ready for use.

Surgical drainage of the pus should be effected. Incisions below and parallel to the body of the mandible should be made and exploration carried out with a blunt forceps. Another vertical incision should be made above the hyoid bone to the lower border of the chin. Some surgeons split the geniohyoglossus muscles apart by passing the median raphe of the mylohyoids, with the object of relieving tension. Hajek's clinic follows the procedure of making an incision along the anterior border of the sternocleidomastoid muscle and carrying out dissection with a blunt instrument, or a sharp one if necessary, as deep as the mucous membrane of the pharynx.

If simple incisions fail, the Mosher operation for parapharyngeal abscess may be performed. If the condition is severe, tracheotomy may be necessary, and should not be delayed until the case is desperate.

Hot fomentations consisting of ten per cent aqueous solution of ichthyol or of saturated solution of magnesium sulfate should be used as a supplement to surgical drainage.

Convalescence, which is always slow, requires the use of tonics, a liberal diet, and an extended vacation.

SEPTICEMIA

The commonest cause of septicemia is the streptococcus, but it is often caused by other pyogenic organisms. There is little difficulty in making the diagnosis, especially if one takes advantage of laboratory facilities for blood cultures and other bacterial studies. As a rule, a septic focus may be found which is responsible for the invasion of the blood stream.

Signs and Symptoms: An abrupt onset with chills and high fever is characteristic. The chills follow no definite pattern as in malaria, and the same may be said of the fever. There may be gen-

eralized aches and pains, and a thorough investigation of the chest, abdomen, sinuses, meninges, and pelvis must be done. As endocarditis is commonly associated with hemolytic streptococcus, the heart is examined most carefully. The neck is investigated for the stiffness of meningitis. Palpation is done to determine if the spleen is enlarged. The urine and the blood are examined, and albuminuria, red cells, and pus cells are not uncommonly found in any case of septicemia. Leukocytosis is the rule, but leukopenia may be present. There is always a decided increase in the band forms of polymorphonuclear leukocytes. Blood cultures, not one but many, should be done as the first culture may fail to show the growth of organisms.

TREATMENT

The course and prognosis of septicemia has been altered by the use of the sulfonamides and penicillin. It matters little what organism causes septicemia, the use of one of the sulfonamides is indicated, and the following method is advocated: The regular dose of one gram every four hours and the intravenous administration of 5 to 15 grams daily until the optimal sulfa level of 8 to 12 millograms per cent is obtained.

Penicillin, with or without sulfa drugs, is advocated in severe cases. While there may be differences of opinion, the commonly used method of administration is as follows: 80,000 to 100,000 units are given intravenously in 1000 cc. of normal saline solution and administered by the drip method. Simultaneously, 10,000 units are given intramuscularly every four hours. A response to this treatment is noted on the fourth or fifth day. Unless there is a favorable reaction by the fifth or sixth day of treatment, the outcome is likely to be unfavorable. In subacute cases, for example in subacute bacterial endocarditis, such doses of penicillin have been employed over a much longer period of time, but the results have not been encouraging.

NOMA

Definition: This is a form of microbic gangrene in and about the mouth and genitalia, caused by a mixed infection, generally with the *Spirocheta refrigens* and *Vincent's spirillum*. Clinically, it manifests itself as cancrum oris, Ludwig's angina, gangrenous balanitis, and noma pudendi.

(*a*) Cancrum oris is noma of the lips and gums. It begins as a indurated red pimple on the mucous membrane (very commonly following an attack of measles) and this goes on to a sloughing ulcer and then to a wet gangrene which may involve the cheek, jaws, and whole side of face. There is little pain, but constitutional symptoms are severe. Mortality is about 70 per cent.

(*b*) Ludwig's angina (see page 381).

(*c*) Gangrenous balanitis is a spontaneous gangrene of the male genitalia, occurring in middle-aged individuals, during or following an infectious fever. There may be considerable tissue destruction, but regeneration without deformity always occurs. There is no mortality.

(*d*) Noma pudenda is a moist gangrene of the vulva in children which follows infectious fevers, particularly measles. Recovery is usual.

Treatment: Intravenous arsphenamine is a specific in noma. The nonresponsive case is treated as in cellulitis by free incision and drainage.

CHAPTER XXI

Tropical Diseases

MALARIA

Malaria is a specific infectious disease which is commonest in the tropical and subtropical regions where there is a heavy rainfall, though it also occurs in more temperate climates. India, as an outstanding example, averages more than a million deaths each year from the disease. It is characterized by intermittent chills and fever, recurring at regular intervals, and by enlargement of the spleen.

Etiology: This disease is caused by the *Plasmodium malariae* (quartan parasite), the *Plasmodium vivax* (tertian parasite), and *Plasmodium falciparum* (estivoautumnal parasite). These are one-celled protozoa which are related but each has fundamental qualities which are peculiar to that one, and each causes a certain type of malarial fever.

Man is infected through the bite of the female Anopheles mosquito which has become infected by sucking the blood of a person with malaria.

Asexual Cycle: When the infected mosquito bites man, sporozoites or spores (rod-shaped parasites) are liberated into the blood stream. Each of these spores penetrates a red blood cell, becomes rounded and matures, and initiates the stage of asexual development. The red cell becomes pale and swollen, and the parasite contains dark brown granules of pigment which it produces and later releases. At maturity, some become schizonts (asexual form) and some become gametocytes (sexual form). In asexual division, the nuclear chromatin divides into fragments, the cytoplasm separating so as to surround each of these. These new bodies (merozoites) form a rosette within the periphery of the erythrocyte. The rosette of merozoites breaks up at the end of a certain period of time (48 hours in tertian malaria, 72 hours in the quartan type, and variable in estivo-autumnal form) and these are discharged into the blood stream. This occurs in all the infected red cells at about the same time and the sudden outpouring of foreign protein causes the chill, fever, and

sweat of the malarial paroxysm. In time, gametocytes begin to develop in the peripheral circulation of the patient.

Sexual Cycle: The female mosquito sucks female macrogametes and male microgametes into her stomach when she bites a malarial patient. These enter into a sexual union and form the zygote which penetrates the stomach mucosa producing an oöcyst. The oöcyst matures in 7 to 12 days, depending on the species of plasmodium, and bursts into the coelomic cavity, dispensing thousands of fusiform sporozoites. These migrate to the salivary glands, and when the mosquito again bites a human, each sporozoite injected into the blood stream enters a red blood cell, becomes amebulae, divides into merozoites, repeating the asexual schizogonic cycle.

Signs and Symptoms: Experimentally, the incubation period may vary from 3 to 20 days, though the time in humans is not known. Paroxysms of chill, fever, and sweat are the main characteristics of malaria. In the tertian type, paroxysms occur every 48 hours, every 72 hours in the quartan type, and about every 24 to 48 hours in estivoautumnal malaria. Other features include jaundice; pain in the head, back, extremities, and elsewhere; vomiting, and anorexia.

The paroxysms are explained by the fact that the foreign protein or toxin which enters the blood stream when the infected red cells rupture suddenly causes a general relaxation of the entire vascular system. Less blood flows through the capillaries, and the surface of the body assumes the temperature of the surrounding air, is cooled, and the patient has a chill. The fever continues until the toxin is neutralized, when the sweat lowers the fever and eliminates the toxins.

Pernicious malaria is usually fatal. It occurs most often in the estivoautumnal type of the disease, and is classified as follows:

1. Comatose type—the most fatal form in which the patient goes into coma. The cerebral capillaries are blocked with parasitic thrombi.
2. Delirious—the toxins stimulate the patient and he becomes delirious or acts insane.
3. Algid type—in which the temperature is subnormal.
4. Cachexia—the spleen is greatly enlarged from the added function of trying to destroy parasitized erythrocytes; after the malaria is cured, it kills off normal red cells, which results in severe anemia.

5. Blackwater fever or hemoglobinuric fever is an allergic type. The patient is sensitized to malarial toxins over a period of two years of insufficient malarial treatment. The attack occurs either as a result of new infection or from the flaring up of a latent infection due to intensive quinine therapy or other debilitating causes.

Pathology: In malaria, the spleen and liver are most frequently involved. In fatal cases, the spleen is greatly enlarged, smooth, and ranges in color from gray to black because of pigment deposits. The capsule is thin, the pulp soft, containing parasites, pigment, and other débris. Microscopically, the blood vessels are swollen and thick, and often obstructed by large collections of parasites. These parasites are found in the endothelial cells of the blood vessels and in the reticuloendothelial system too. The liver is enlarged and congested with deposits of pigment. The small vessels may be blocked and the endothelial and reticuloendothelial cells are gorged with parasites. The kidneys, brain, bone marrow, and vascular system are also congested.

Diagnosis: There is not much difficulty in making a diagnosis of acute malarial fever, though in some cases the disease may resemble some other acute infectious disease, as typhoid, relapsing fever, dengue, and bacillary dysentery. A definite diagnosis may be made after a study of the circulating blood which shows the malarial parasites, or by splenic puncture. A history of exposure, of residence in a malarial district, or enlarged spleen, should suggest the diagnosis. If doubt still remains, the quinine test may be done, though it is not a definite aid. If the fever persists after the administration of quinine, the diagnosis of malaria is ruled out, but the disappearance of fever does not make the diagnosis of malaria positive nor does it eliminate the possibility of another disease being present.

Prognosis: In mild or moderate cases of malaria, especially those of the tertian or quartan types, recovery is almost certain. However, if treatment is delayed or insufficient in estivoautumnal malaria, the death rate may be quite high. In general, unless the disease is very severe, the mortality rate is about two per cent.

Relapses occur most frequently in the quartan type. They are due to insufficient treatment, and may be brought on by exposure, fatigue, overheating, alcohol, and emotional upsets.

TREATMENT

1. **General Management:**
   - *a.* The patient should be protected so mosquitoes cannot bite him; he should be kept in bed during the acute stage.
   - *b.* Fluids should be given only during the acute stage of the disease, and when this has passed a light diet may be substituted. Large quantities of fluids are necessary because of the fever and profuse sweating.
   - *c.* Hot-water bottles and warm blankets should be applied to the patient during periods of chills.
   - *d.* After the chill, when the temperature rises, an ice pack should be placed on the head and tepid sponges given.

2. **Specific Treatment:** Fernan-Nunez recommends the following procedure as the most effective treatment in malaria:
   - *a.* Acute malaria:
     - (1) Calomel, 0.66 Gm. (10 grains), followed in eight hours by 30 cc. (1 ounce) of salts (magnesium sulfate).
     - (2) Neoarsphenamine, 0.6 to 0.8 Gm. (9 to 12 grains), intravenously.
     - (3) Standard treatment: Quinine sulfate, 0.66 Gm. (10 grains), after meals for two weeks, followed by 0.66 Gm. (10 grains) nightly for two months.
   - *b.* Chronic malaria:
     - (1) Same as the routine mentioned above for acute malaria.
     - (2) Repeat neoarsphenamine weekly for two months.
     - (3) In cases of relapse plasmochin, 0.1 Gm. (1½ grains), is also given daily for seven days.
   - *c.* Pernicious malaria (except Blackwater fever):
     - (1) Quinine dihydrochloride or bisulfate, 0.66 Gm. (10 grains), in 10 cc. of distilled sterile water is administered intravenously immediately and slowly. An injection of adrenalin, ½ to 1 cc. of a 1: 1000 solution, should be given at the same time.
     - (2) If the red cell count is below 2,000,000 a blood transfusion is given; it may be best if the transfusion is given before the count reaches this level.
     - (3) Quinine in the same dose as mentioned above is given intramuscularly immediately and repeated every four hours until the patient improves; then the treatment is continued as in acute malaria.
     - (4) Atabrin, 0.1 Gm. (1½ grains), may be administered intravenously, or 0.3 Gm. (4½ grains) intramuscularly, if the patient is atopic to quinine.

3. **Prophylaxis:** The Anopheles mosquito should be extinguished as far as possible by covering stagnant water with oil or by drainage.

Swamps should be sprayed with insecticides. Houses should be screened and netting placed about the bed. A large dose of quinine should be taken at regular intervals. In malarial districts, 0.66 Gm. (10 grains) of quinine should be taken daily after the evening meal. Latent cases should be treated as long as necessary to prevent the spread of the disease. All mosquitoes around the premises of a person with malaria should be killed.

4. **Quinine Idiosyncrasy:** Allergy to quinine may be detected by the dermal scratch tests with quinine, and arsphenamines, atabrin and plasmochin, methylene blue, or equinine should be used in allergic cases. Manifestations of quinine allergy include tinnitus aurium, deafness, visual disorders, urticaria, vertigo, nausea, dyspnea, and tachycardia. The following routine is indicated for these allergic patients as well as for others who cannot take the drug or where the drug is contraindicated:

a. For the first five days atabrin, 0.1 Gm. (1½ grains), is given three times daily after food to destroy the asexual merozoites. This drug produces epigastric pain, headache, diarrhea, anorexia, and a yellowish tinge of the skin and conjunctivae. Its cumulative effect lasts three weeks.

b. For the second five days 0.1 Gm. (1½ grains) of plasmochin is administered three times daily after food to destroy the sexual phase gametocytes. Small doses of quinine should be given with plasmochin to prevent cyanosis, cardiac irregularities, and methemoglobinemia.

c. For the next five weeks atabrin, 0.4 Gm. (6 grains), is administered in a single weekly dose. On a different day of each week 0.033 Gm. (½ grain) plasmochin is given.

As most patients suffering from malaria have a secondary anemia, the administration of iron, in the form of iron and ammonium citrate, 0.66 Gm. (10 grains) three times a day, or Blaud's pills, six pills three times a day, is always indicated.

BLACKWATER FEVER

Blackwater fever is an acute disease, often seen in persons residing in malarious regions for 12 months or more. It is usually a complication of malignant tertian malaria.

Etiology: The etiology is unknown, though precipitating factors include fatigue, alcoholism, quinine, trauma, or chilling. The disease is found in the same areas in which malignant tertian malaria is seen, and is observed in its most severe form in equatorial Africa.

Those who have stayed in malarial districts a year or more and who have had repeated attacks of subtertian malaria are most apt to contract the disease, and persons returning from malarial districts to cool or temperate climates may also be affected.

Pathology: The pathological changes are similar to those of malaria, such as congestion of the kidneys, congestive enlargement of the spleen and liver, and hemosiderosis of the spleen, liver, and kidneys. The gallbladder may be distended with thick, blackish bile. The bone marrow extending into the long bones may be hypertrophied.

Symptoms and Signs: Blackwater fever is preceded by enlargement of the spleen and liver associated with tenderness, and by the passing of urine containing a great deal of albumin, urobilin, and detritus. The incubation period is unknown and onset is sudden. Often the passing of black or red urine is an early symptom. Chill, prostration, and sudden lysis of red cells mark the disease. The hemoglobin is changed to bilirubin which is deposited in the skin and tissues. Hemoglobinuria and hemoglobinemia may occur when the destruction of red cells is so great that the liver cannot convert the hemoglobin. The passage of hemoglobin leads to kidney irritation and acute nephritis, and death frequently is due to anuria caused by precipitation of acid hematin in the tubules.

Diagnosis: Diagnosis is based on the history and symptomatology. The disease may be confused with yellow fever and bilious, remittent malarial fever. However, in yellow fever, the spleen is not enlarged and the jaundice comes on later. The clinical manifestations of subtertian malaria are slower, and the signs and symptoms less severe.

Prognosis: This depends on the severity of the onset. The mortality rate is from 10 to 60 per cent. Anuria is an unfavorable sign. The number of attacks influences prognosis and three attacks are usually fatal. Complications include heart failure in the posthemolytic period, severe anemia, hyperpyrexia, uncontrollable vomiting, hiccough, and sudden drop in temperature with prostration and coma.

TREATMENT

1. Quinine and atabrin are contraindicated until convalescence is established.

2. Complete bed rest and warmth are indicated. The patient should not be moved.

3. Alkalinization of the urine should be accomplished by giving large quantities of fluid (about 3000 cc. daily). Sodium citrate and sodium bicarbonate are the best alkaline salts and may be given orally, 0.6 Gm. (10 grains) by mouth every one to two hours until the urine is alkaline, and then in doses large enough to maintain alkalinity. Intravenous sodium bicarbonate, 0.5 per cent in five per cent glucose or glucose saline solution is good. Hot saline enemas have been beneficial.

4. Whole blood transfusions should be started when the condition of the urine begins to improve.

5. If plasmodia are present in the blood, atabrin may be started, 0.1 Gm. (1½ grains) three times a day for five days, after the patient has passed over the acute stage and hemolysis has been absent for five days. After recovery the patient should be removed from malarious districts for a year or more.

Prophylaxis: This is based on the adequate treatment of all malaria cases, and especially those of malignant malaria. When the preblackwater fever state is recognized (dark urine, toxic appearance with slight jaundice, and enlarged, tender liver), antimalarial therapy should be supplemented with alkalis. On recovery, cases of blackwater fever should be removed to nonmalarious districts.

DENGUE

Dengue is an acute, self-limiting fever, also known as Dandy fever and breakbone fever.

Etiology: Dengue is caused by a filtrable virus transmitted by the Aedes mosquito. This disease occurs wherever the Aedes mosquito is found, that is, in almost any part of the tropical or subtropical world, especially about the China Sea, South Pacific Islands, West Indies, and the Mediterranean. Dengue fever may occur in epidemics.

Pathology: Little is known concerning the pathology, as fatalities are not the rule. Inflammation of the brain, lungs, myocardium, and kidneys has been seen. The viscera, particularly the liver, may show cloudy swelling. The liver may be fatty and there may be petechial hemorrhages in the gastrointestinal tract.

Signs and Symptoms: The symptomatology is extremely variable. Typically, this disease is ushered in by a sudden rise in temperature to 39° to 40.5° C. (102° to 105° F.). The face may appear congested

and blotchy. Headache and pains in the joints and back are prominent, and there are also malaise, prostration, and mental depression. The pulse is slow in comparison to the temperature, and leukopenia is present. The lymph nodes may be enlarged.

In a few days the fever drops to normal and remains so for several days. Usually, though not always, it rises again, and at this time, a morbilliform rash appears on the backs of the hands and feet, and spreads over the body. Desquamation and pruritus follow.

Diagnosis: Influenza and yellow fever must be considered in the differential diagnosis. The rash, "saddleback" fever, geographic location, and presence of Aedes mosquitoes are helpful in pointing out the true nature of the malady. Denguelike fevers may confuse the diagnosis. These fevers, as Sandfly fever, Panama six day fever, seven day fever, all resemble dengue, but are milder and of shorter duration. The recurring phase and rash are often absent.

Prognosis: Prognosis in uncomplicated cases is favorable.

TREATMENT

Treatment is symptomatic.

Preventive measures against the Aedes mosquito, as screening and bed nets, are in order.

DYSENTERY

Dysentery, or diarrhea as it is sometimes called, is due to an inflammation of the intestinal tract. In general, it may be divided into two distinct forms—the amebic and the bacillary.

Amebic Dysentery

Amebic dysentery is an infectious disease, either acute or chronic, involving especially the large intestine, though the small intestine and even the stomach may be included. It is characterized by discharges of blood and mucus from the bowel. Until recent years, amebic dysentery was looked upon as a disease of the tropics, but in reality it is a widespread infection seen throughout the world. Perhaps heretofore the disease was not suspected and the amebae were not looked for or were not recognized in the stools.

Etiology: Amebic dysentery is caused by a protozoan or one-celled organism known as *Entamoeba histolytica;* the disease is contracted

by the ingestion of the cyst of the ameba. The organism undergoes three stages of development: (1) The motile form is seen during the acute dysenteric period, and when the warm fresh stools are examined under a microscope, the amebae may be observed to be moving around. (2) Then as the disease progresses, a large number of amebae begin to form the cystic stage in which a genuine cyst with four nuclei develops in the intestines. (3) It is this cyst, excreted in the feces, which is ingested by an individual and carried into the intestinal tract. The cyst gives rise to eight motile amebae. The trophozoites and cysts of this organism, though excreted in the feces, do not multiply outside the host. The trophozoites degenerate rapidly and are destroyed by the digestive fluids, but the cysts are much more resistant and carry the infection from man to man.

The organism may enter the body through drinking contaminated water, the eating of uncooked vegetables, or it may be carried and transmitted by food handlers or flies. Other sources of infection include the bowel discharges of patients, convalescents, carriers, or hand-to-mouth transmission.

Pathology: The *Entamoeba histolytica* penetrate the mucosa and submucosa of the large intestine, but even in the most severe cases there may be normal areas which have not been attacked by the organisms. The injury caused by this tissue-invading species is probably due to a cytolysis of the cells in proximity to the invaders. The toxic action causes edema, fibrin formation, and lesions of varying severity ranging from superficial necrosis to deep abscess and ulceration. The amebae live and multiply in these lesions, and cysts may be formed which pass into the feces and carry the infection to another host. Amebic lesions may also affect other tissues and organs, with abscesses forming in the brain, liver, and lungs.

Signs and Symptoms: The incubation period varies from a few days to a few weeks. The onset of symptoms may be gradual or sudden. The chief manifestations are intense diarrhea with crampy, colicky pain in the lower abdomen and tenderness over the right and left lower quadrant and colon. The stools are usually small and numerous, and contain blood, mucus, and pus. However, at times diarrhea is lacking, or later in the course of the disease there may be alternate periods of diarrhea and constipation. Nausea, vomiting, and tenesmus are absent in most cases, and the appetite is not greatly

affected. Thus, we see that violent gastrointestinal disturbances do not play a large rôle. The muscles of the body, especially those of the legs, often become very weak, and the patient may be irritable, drowsy, and lack energy. A chronic anemia, which tends to become acute during the stages of diarrhea, may be present. The acute form of dysentery, if not properly treated, usually progresses into the chronic stage, though the disease may be chronic from the start. In some cases, the dysentery may remain latent or quiescent for a long period of time and the patient believes he is cured, when in reality there is a residual focus of infection in the large intestine which will suddenly flare up.

Diagnosis: Amebic dysentery is very much like the bacillary type; however, in the latter the patient is usually somewhat toxic and may show fever and leukocytosis, though these features do not rule out the amebic form. A definite diagnosis can be made from a study of the warm, fresh stools. In amebic dysentery, the stools usually contain quite a bit of fecal matter with some blood and mucus, and ameba are present; in bacillary dysentery, there is little fecal matter, considerable blood, and a moderate amount of mucus. In doubtful cases, Shiga's bacillus agglutination test should be done.

Prognosis: Prognosis as far as the disease itself is concerned is quite satisfactory, since death seldom occurs except in severe epidemics. However, while a patient does not usually die from the first attack, repeated attacks which are not diagnosed or not properly treated may cause chronic invalidism and even death.

One of the commonest and most serious complications is liver abscess, though it is not seen so frequently now since the diagnosis is being made earlier and treatment has improved. It may be found in carriers who have never actively had amebic dysentery, or in patients who have long since recovered from the disease. Frequently, hepatic abscess is noted after hepatitis and, if untreated, ruptures into the lung, pleura, stomach, and peritoneum. There may be bowel perforation leading to peritonitis or abscesses of various parts of the body. Obstruction may result from scar tissue forming in the intestine.

TREATMENT

In general, certain procedures must be carried out in the treatment of amebic dysentery. The bowel and urine discharges should be

disinfected with either five per cent cresol or chlorinated lime; the linen, bedclothes, and other clothing should be soaked in cresol before washing.

1. The patient should be put to bed and fed a light or liquid diet. Boiled milk is especially recommended; cocoa, eggs, custard, or toast may be added. It may be necessary to force fluids in small amounts or to administer them intravenously.

2. Intramuscular injections of emetine hydrochloride, 0.066 Gm. (1 grain) daily for two weeks, are usually effective during the acute stage. However, this therapy does not cure the infection but only controls the alarming symptoms. During the administration of this drug, it is important to watch for toxic reactions, as evidenced by a fall in blood pressure, asthenia, cardiac irregularity, mental depression, painful muscles, and other signs. Bismuth subnitrate in large doses, 2 Gm. (30 grains) four times a day, may be given in addition to emetine.

3. Emetine bismuth iodine, in 0.133 Gm. (2 grains) capsules, may be given about four hours after the evening meal for ten nights. If given in tablet form with stearin, there is a tendency for it to be passed unabsorbed in the feces; thus, proper absorption is an important factor in the administration of the drug. Luminal, 0.66 Gm. (1 grain), effectively combats nausea and vomiting in most cases, though allonal or 0.66 cc. (10 minims) of tincture of opium may be more satisfactory. Emetine periodide is less toxic than the above preparation, but is not as effective.

4. In the chronic or cystic stage of dysentery, diarrhea is not a prominent symptom or it may be absent, and in these cases emetine is of little value since it has practically no effect on the cysts or lumen dwellers. Sir Philip Manson-Bahr introduced a combination of quinoxyl retention enemata by day and emetine bismuth iodide by mouth at night. Usually a two per cent sodium bicarbonate enema is given first, followed by a quinoxyl retention enema, 2½ per cent in 200 cc. These may be retained for four to eight hours, and are well tolerated; even a five per cent solution is without disagreeable effects in refractory cases. This therapy combined with emetine bismuth iodide is continued for 10 to 12 days; the patient is given as much breakfast and dinner as he wishes, but no supper. Chiniofon, as this drug is sometimes called, may also be given by mouth in four,

0.266 Gm. (4 grains), doses after each meal for a week. If the stools remain positive, therapy should be discontinued for a week and then a new course started. If two courses fail, diodoquin in 1.66 Gm. (25 grains) daily doses for two or three weeks should be tried.

5. Vioform, 0.266 Gm. (4 grains) in capsules three times a day for ten days, has been recommended instead of chiniofon. It is a chlorine derivative of quinoline, and has a much higher percentage of iodine. It cannot be used rectally, since it is an irritant and not very soluble. Both this substance and chiniofon act on cysts and motile forms.

6. Carbarsone, 0.266 Gm. (4 grains) twice daily for ten days, has been suggested. However, because it is an arsenic compound there is danger of poisoning which may outweigh its effectiveness. It must not be given to patients with kidney or liver damage. Carbarsone by mouth combined with retention enemas of chiniofon has been successful in many cases.

Bacillary Dysentery

Bacillary dysentery is an acute infectious disease due to toxins generated by the Shigella dysenteriae and characterized by pain in the intestines, tenesmus, diarrhea, mucus and blood in the stools, and toxemia.

Etiology: The disease is especially prevalent in tropical countries, but it may occur in any part of the world. It is most apt to occur where living conditions are crowded, as in prisons, military camps, and other institutions. The etiological agent is the dysentery bacillus of the genus Shigella. The classification of the Shigella on page 396 is given in *Notes on Tropical and Exotic Diseases of Naval Importance,* published by the United States Naval Medical School.

Human beings become infected by the ingestion of food and drink which has been contaminated with the feces of patients with bacillary dysentery or carriers of the disease. Flies help to carry the infection.

Pathology: The intestines are particularly affected, and there is diffuse, catarrhal inflammation of the colon often extending above the ileocecal valve. As the disease progresses, the inflammation may increase to necrosis and ulceration of the mucosa, associated with a

Name of Organism	*Common Terms of Designation*	*General Properties in Relation to Dysentery*
Shigella dysenteriae	Shiga's bacillus	Only organism in group producing a true, soluble, exotoxin. Causes severe form of dysentery. Commonly found in Orient.
Shigella flexneri	Numerous types. Occasionally divided into various cultural types: Flexner, Hiss-Y, and Strong bacilli. More correct to divide into serologic types depending on composition of antigens V, W, X, Y, and Z.	World-wide distribution. Frequently causes severe dysentery; may produce mild illness. Common cause of outbreaks in jails, asylums, military camps, etc.
Shigella sonnei	Sonne bacillus	Frequent cause of dysentery. World-wide distribution. High degree of contagiousness. Frequently causes a mild disease often not recognized clinically which may account for much of its spread. May cause severe dysentery.
Shigella ambiguus	Schmitz's bacillus. Culturally similar to S. dysenteriae.	Infrequent cause of dysentery; generally produces a relatively mild illness.
Shigella newcastle	Newcastle bacillus	Recently discovered organism; has been observed with increasing frequency. Wide distribution.
Shigella alkalescens	Bact. alkalescens	Does not cause true dysentery. Reported as cause of food poisoning.
Shigella dispar	Dispar bacillus. Culturally similar to S. sonnei. May be mistaken for it.	No evidence that it causes dysentery. May be regarded as non-pathogenic.

superficial exudate. There is thickening and edema of the wall of the colon. The most severe reactions are found in the rectum. Severe cases present necrotic ulcerated mucosa covered with a greenish-purple membrane, while milder cases may show only discrete superficial ulcers separated by inflamed mucosa. Under the layer of necro-

sis are small, sharply circumscribed or diffuse hemorrhages with small, red spots scattered about them. Ulcers may persist after the acute infection and form a focus for chronic infection. This may be the reason some carry the disease for long periods of time.

In the bowel contents, the inflamed areas, and sometimes the mesenteric glands, there are many bacilli. Bacilli are not usually found in the blood stream or urine.

Symptoms and Signs: Symptoms may vary from those of mild diarrhea without fever to those of great intensity. Typically, the onset of dysentery is sudden and accompanied by fever, abdominal cramps, and the passage of loose, watery, greenish or yellow stools. Later the stools become bloody and mucopurulent. Tenesmus, vomiting, prostration, toxemia, and dehydration are prominent in severe cases. The disease may be followed by neuritis or arthritis, and sometimes also by conjunctivitis, iritis, otitis, or myocarditis.

Prognosis: Prognosis depends on the severity of an attack, and on the age and condition of the patient. Infants and older individuals are most apt to die. The presence of complications is unfavorable prognostically, and severe intestinal symptoms with collapse offer a poor outlook.

Diagnosis: This is made by the identification of species of Shigellae from stool cultures, and this is done most easily in the early part of the disease. Several cultures may be required, and stools should be examined as soon as possible after being passed. Selective culture media, as desoxycholate citrate agar S. S., are best. Agglutination reactions with the patient's sera and known antigens have been done, but are not so practical, especially in the early stages. Microscopic examination of the stools on an unstained slide will show an absence or marked reduction of fecal elements, red cells often in rouleaux, many pus cells, desquamated epithelium, numerous macrophage cells, and ghost cells.

In the absence of laboratory facilities, particularly when the case is complicated by toxemia or in the presence of epidemics, diagnosis may be made with reasonable assurance when on gross examination the stools appear mucosanguinous with a purulent exudate mixed with the feces.

TREATMENT

1. Absolute bed rest is necessary.

2. The diet should be liquid or soft with low residue until the stools are formed. In very severe cases it should be supplemented with vitamins.

3. Enough fluid to insure a urinary output of 1200 to 1500 cc. daily, usually about 3000 cc., must be provided. In severe cases, intravenous fluid is needed and physiological salt solution with five per cent glucose in amounts large enough to insure a 1200 to 1500 cc. output of urine daily should be given. Intravenous plasma, 500 to 1000 cc., should be administered to combat shock, but not until the dehydration is controlled.

4. Codeine or morphine may be used for the relief of pain. Belladonna and chloral hydrate in combination with codeine may also do good, or paregoric, 1 to 2 cc. (15 to 30 minims), may be given after each stool until 20 cc. (⅔ ounce) have been taken in 24 hours.

5. Sulfaguanidine has been used effectively in the treatment of bacillary dysentery. For the acute case, the initial dose is 6 Gm. (90 grains) followed every four hours night and day by 3.5 Gm. (52½ grains). When the number of stools is five or less a day, the dose may be reduced to 3.5 Gm. (52½ grains) every eight hours night and day until the stools are normal for 96 hours. In cases which do not respond to sulfaguanidine within 96 hours of the initial dose, or in cases in which toxicity occurs, the drug should be stopped. Chronic cases and carriers are given 3.5 Gm. (52½ grains) every eight hours day and night for a maximum of two weeks.

Succinylsulfathiazole (sulfasuxidine) has not yet become widely used, but experience so far suggests that it may prove superior to sulfaguanidine. Sulfathiazole and sulfadiazine may be used as alternatives for sulfaguanidine.

6. Monovalent antiserum for S. dysenteriae may be used, but not until after bacteriological confirmation of the diagnosis. The dosage is 40 to 80 cc. intramuscularly or intravenously every day until the toxemia and dysentery become improved. Intramuscular doses are best given into the buttocks. Intravenous doses should be diluted in 500 cc. of normal saline and given slowly. Sensitivity tests before therapy are indicated. Polyvalent antidysentery serum is of doubtful value.

7. Measures such as purgation, high enemas and colonic irrigations, and bacteriophage are not recommended.

Prophylaxis: Preventive measures include control of milk, water, and food supplies; sanitary disposal of waste and sewage, and protection from flies. Isolation and treatment of mild cases will prevent them from spreading the disease. Vaccination is not recommended.

Patients should be strictly isolated and the room screened or the bed covered with mosquito netting. Attendants should wear gowns when in contact with patients and they should scrub afterwards. Linens, wastes, furniture, and all other materials contaminated by the patient should be sterilized or disposed of safely. It is well to provide individual utensils, as thermometers and toilet articles, for the dysentery patient. Visitors should be prohibited when possible, and if any are allowed to enter, they must observe the same precautions required of attendants. Patients should not be discharged until they have had four negative stool cultures over four to eight days. Discharged patients should not become food handlers and they must be taught how not to pass the disease. The room they occupied must be thoroughly sterilized.

TYPHUS FEVER (BRILL'S DISEASE)

Typhus fever is an acute specific contagious disease conveyed by body lice and fleas. The onset is abrupt, and a high continuous fever, purpuric eruption, and nervous symptoms characterize the early stages. The disease terminates by crisis on about the tenth to fourteenth day.

Etiology: Typhus fever is caused by the *Rickettsia prowazeki*, which are tiny, rod-shaped, gram-negative organisms. It is transmitted from man to man by the louse, and the rat flea carries it from rat to rat as well as from rat to man. The disease is commonest among poor people who live in overcrowded and dirty areas, and is infectious by contact with the patient or with bedding or clothing. However, ordinarily the organisms are deposited on the skin by the flea or louse, and enter the blood stream when the skin is scratched or punctured. Typhus fever is known to be one of the great epidemic diseases of the world. Outbreaks have occurred during almost every war in Europe, but it is comparatively rare for one to occur in peacetime under modern sanitary conditions. The epidemics occur most frequently in the

winter; an explanation for this fact is that fewer baths are taken and clothing is changed less often, thus creating an agreeable situation for louse propagation.

Signs and Symptoms: The incubation period is from 10 to 12 days, and at the end of this time there may be slight fever, headache, and general malaise. On the other hand, this early stage may be lacking and instead the disease sets in abruptly with chills, rigors, fever rising to 40° C. (104° F.) with proportionate pulse, nausea and vomiting, and body pains. Intense headache is usually the outstanding symptom. The conjunctivae are injected; pupils contracted; face tense, hot, and flushed, and the tongue is thickly furred. Patients are usually excited and may be stuporous. Delirium is common.

About five days after onset, the typical rash appears, first on the abdomen, upper chest, and hands, and spreading to the trunk and extremities but seldom to the face. The lesions are rose-colored macules which disappear on pressure. They may be overlooked in the beginning because of erythema in some cases. Moderate leukocytosis is commonly noted, and if marked, is a serious sign. Cough and râles in the chest are common findings. The rash becomes more pronounced, depending on the severity of the disease, and the lesions increase in size and progress in color from rose-red to deep-purple. If the temperature falls while the patient is in a state of coma, prognosis is guarded. If a distinct improvement is noted in the clinical picture about the twelfth day, and the delirious patient becomes quiet, recovery is probable. Fever usually declines by lysis.

Bronchitis and pneumonia are the most frequent complications, the latter causing most fatalities. Occasionally death is due to myocardial degeneration. Gangrene of the extremities, bed sores, neuralgia, and neuritis may also complicate the picture. Thrombosis of the large arteries as well as of the small cutaneous vessels resulting in gangrene of the skin is frequently noted.

Diagnosis: Until the rash appears, the clinical picture of typhus resembles that of any acute infectious disease and offers difficulty in diagnosis unless an epidemic prevails. Blood examination for parasites will rule out malaria and relapsing fever. Typhoid fever can usually be differentiated because the mode of onset, symptoms, and severity of rash are different. The possibility of a diagnosis of pneumonia must be considered. Measles, smallpox, and scarlet fever are

distinguishable by their rash. Rocky Mountain spotted fever may offer some difficulty in diagnosis from endemic typhus. The Weil-Felix reaction is positive in typhus fever after the fifth day and may continue to be positive for weeks or months.

Prognosis: The mortality rate for the epidemic louse-borne typhus ranges from about 10 to 70 per cent, while the endemic rate is as low as five per cent. Few young people die of the disease, but the mortality is higher amongst the older individuals, since pneumonia is more likely to develop and the disease as a whole is much more severe.

TREATMENT

1. When a patient is suspected of having typhus, he should be deloused and put in a louse-free room; his former surroundings should be deloused and quarantined. All blankets and clothing should be disinfected. The patient's hair should be clipped, the skin bathed, and a light oil, such as kerosene, which is an old standby, should be applied.

2. Treatment is symptomatic rather than specific and is directed at supporting the patient. General therapeutic principles should be employed. Continuous bed rest in a quiet well-ventilated room with experienced nursing care is important. The position of the patient should be changed from time to time to prevent hypostatic congestion and bed sores.

3. A semisolid or liquid diet with plenty of fluid, orally, interstitially or intravenously, should be given. If the patient is delirious or comatose, foods should be given by tube.

4. Fever may be lowered by tepid sponge baths and ice bags applied to the head.

5. Stimulants, as coramine, 1 to 3 cc. of a 25 per cent solution, or caffeine sodium benzoate, 0.33 to 0.5 Gm. (5 to 7½ grains), subcutaneously or intramuscularly, may be given.

6. Every effort should be made to conserve the strength of the patient. Cough mixtures containing sedatives should be given for the relief of exhausting cough. Chloral hydrate, 1 to 2 Gm. (15 to 30 grains), should be given orally or rectally to overcome the insomnia, and hyoscine, 0.0005 Gm. ($\frac{1}{120}$ grain) hypodermically, with or without morphine, may be used if the patient is violently delirious.

7. Oral hygiene is important, and the mouth should be washed out at frequent intervals daily, using either normal saline, sodium perborate, or hydrogen peroxide.

8. *Prophylactic:* The best preventive for louse-borne typhus is cleanliness. Lousiness must be prevented. The attendants of patients with typhus should take every precaution for the control of the disease. They should wear one-piece gowns with openings only at the neck and wrists. Hands and wrists should be encased in rubber gloves and the neck should be sprayed daily with a louse repellent. Gowns should be inspected carefully from time to time during the day and deloused daily with heat, chloroform, or napthalene.

TRENCH FEVER

Trench fever is a specific, infectious, febrile disease, also known as Wolhynian fever, five day fever, Meuse fever, and shin fever. It appeared during the World War of 1914-18 in epidemic proportions throughout Europe and Mesopotamia. It may have occurred endemically since then in Russia and Poland.

Etiology: The etiological agent is *Rickettsia quintana,* which is commonly transmitted by the body louse. After recovery, a case may remain infective to lice for months. Dried louse excreta is virulent for four months or more and virulence is retained in the dried urine of patients.

Symptoms and Signs: The inoculation period varies from one to three weeks and the onset is sudden with fever of 39.5° to 40° C. (103° to 104° F.), severe pains in the muscles and bones, especially the shins, back, and behind the eyeballs, headache, splenomegaly, and a macular eruption occurring on the first or second day of fever. Leukocytosis of 10,000 to 12,000 is present. There are often relapses at five- to six-day intervals. Fatalities do not occur, as a rule, and prognosis is good, unless complications set in or the disease becomes chronic.

Diagnosis: The disease may need differentiation from malaria, European relapsing fever, tick fever, Weil's disease without jaundice, typhoid, and paratyphoid. While laboratory tests do not aid in the diagnosis of trench fever, they are of use in the differential diagnosis.

TREATMENT

The treatment is symptomatic. In order to prevent heart disease, prolonged bed rest is recommended. Care should be taken to disinfect the body discharges, since the virus is present in the urine and saliva of patients. Clothing and bedding should also be disinfected. Efficient delousing is important in the prophylaxis.

ROCKY MOUNTAIN SPOTTED FEVER

Rocky Mountain spotted fever is a rickettsial disease transmitted by ticks, and characterized by chills, moderate fever, severe pains in muscles and joints, rash, headache, and delirium.

Etiology: The disease is caused by *Rickettsia rickettsi* and is transmitted only by ticks. The reservoir hosts are probably small field rodents in the West, and dogs in the East. In the East the dog ticks, *Dermacentor variabilis,* are responsible for this malady and in the West the *Dermacentor andersoni.* Other types of ticks may be vectors in other places. Rocky Mountain spotted fever is commonest in spring and early summer in the northwestern states, in the East and South through the summer. This disorder occurs in all states of the Union except Maine, Vermont, New Hampshire, Connecticut, Rhode Island, Michigan, and Wisconsin; it is also found in Canada, Brazil, and Colombia.

Pathology: At postmortem, the body may be jaundiced. The blood is dark, fluid, slow to clot, and venous engorgement is prominent. Petechial spots may be apparent on the extremities and trunk. Splenomegaly and enlargement of the lymph glands have been noted. The outstanding feature in the histopathology is the distribution and character of the blood vessel lesions in the skin and subcutaneous tissues, muscles, and in the testes and their appendages. There are almost always hemorrhages into these tissues. Vascular lesions occur in the vessels of almost all parts of the body and consist of proliferative reactions of the endothelium at first. These reactions are followed by necrosis with thrombus formation. Rickettsiae are found in the endothelium and smooth muscle cells of the blood vessel walls. Focal necrosis may be present in the liver and focal brain changes have also been reported by some.

Symptoms and Signs: The incubation period is from two to five days or more in mild cases. The symptoms resemble those of endemic

typhus and their severity varies. Usually there is a frontoöccipital headache, pain in the back, and severe malaise. Muscle and bone pain, sweating, sensitive, inflamed eyes, nausea, and vomiting are characteristic. Later there may be delirium, aphasia, ankle clonus, incoördination, cyanosis, apprehension, Kernig's sign, and opisthotonos. In two to five days a rash appears, first on the wrists and ankles, and spreading to the legs, upper back, outer surface of the arms, buttocks, palms, soles, scalp, forehead, the inside of the mouth, and pharynx. The rash is rose-colored and the result of vascular inflammation. In some cases, extensive necrosis of the buttocks, external genitals, and dependent parts of the body occurs. By the end of the third week the fever drops rapidly by lysis.

During the course of the disease, there is frequently hepatomegaly and splenomegaly, and jaundice may become evident. The white cell count is commonly elevated, as are the mononuclear cells. The number of lymphocytes is decreased, and moderate anemia is present. The spinal fluid is normal.

Rocky Mountain spotted fever may be complicated by pneumonia, phlebitis, hemorrhages, hemiplegia, iritis, nephritis. Convalescence is slow.

Prognosis: In both the Eastern and Western types, prognosis is variable. Before vaccination mortality rates of five per cent for Idaho to 80 to 90 per cent in Montana were reported. Since vaccination the fatalities have been considerably decreased. The prognosis is more serious in older than younger persons, and is worse in those with increased nervous symptoms.

Diagnosis: Diagnosis is based on the history of exposure to ticks. The Weil-Felix reaction with *B. proteus* strain OX-19 is positive as a rule in titers above 1:320 or higher in the second and third week. The disease may resemble several types of typhus, making differentiation difficult. Measles, typhoid, and cerebrospinal meningitis must be excluded. Measles may be ruled out by the absence of Koplik spots and initial coryza, typhoid and meningitis by laboratory tests.

TREATMENT

Treatment is symptomatic. The same measures as those indicated for typhus are needed for Rocky Mountain spotted fever.

Vaccination is beneficial in prophylaxis. Contact with ticks should be prevented by the wearing of tickproof clothing. Repeated inspection of the entire body every six hours is necessary in the Western tick season. If ticks can be removed before they have been on the body long, the disease may be prevented, as ticks must remain attached for some time before they can transmit infection.

CHOLERA

Cholera is an acute infectious disease caused by the bacterium, *Vibrio cholerae*. Excessive diarrhea, vomiting, cramps in the muscles, anuria, and collapse mark the course of the disease. The disorder has been known since ancient times and occurs in epidemics and pandemics. It was introduced to the eastern United States in 1832 and to the western states in 1850. At present it is still common in Asia and the Far East.

Etiology: The *Vibrio cholerae* is responsible for this malady, and the infection is carried chiefly by man through carriers and patients. Humid, warm climates favor the incidence of the disease. The *V. cholerae* is transmitted by contaminated food and water, due to faulty personal hygiene and public sanitation, or the handling of food by carriers. Flies, roaches, and other insects may aid in the spread of infections. Dangerous foods include melons, lettuce, salad greens, berries, celery, milk, fish, and water. If these foods are taken in the Far East, extreme care should be taken to see that they have not become infected.

Pathology: The lower portion of the intestines are most affected by the cholera endotoxin. Rigor mortis, emaciation, a leaden skin color, and shriveled hands are characteristic of the cadaver.

Dehydration is prominent in the inner structures. The muscles appear dark-red and dry, the lungs are usually small and shrunken. The most important changes are in the abdomen. The omentum is dry and shriveled. The intestines are a pinkish-purplish color and have a ground glass appearance. The affected intestinal mucosa is congested and the lumen contains an alkaline fluid which presents the appearance of rice water. The bowel may contain foul-smelling, brownish material, if the death is late in the course of the disease. Parenchymatous nephritis is the rule. Acute cholecystitis is common.

If death is early, venous congestion is less marked and the stools are more moist.

Symptoms and Signs: The vibrios undergo lysis in the small bowel and release a powerful toxin. The incubation period is from one to five days and is followed by severe, purging diarrhea, associated with excessive vomiting, dehydration, anuria, muscle cramps, and collapse. The rectal temperature is from 39° to 40° C. (102° to 104° F.). In spite of the prostration, the patient is conscious. Peripheral circulation is diminished; the patient is in intense collapse and presents a leaden, shrunken facies. The blood is thick, dark, and tarry. The leukocyte count is from 12,000 to 50,000. Blood pressure is low.

This collapse stage may be followed by rising temperature with clinical improvement or by anuria and a uremic death. The disease may be complicated by anuria, uremia, cholecystitis, jaundice, and miscarriage in pregnant women.

Prognosis: Prognosis is serious since about 50 per cent of these patients die. Early treatment affects prognosis favorably. Cholera is especially lethal in the young and aged, and the outcome is doubtful in those with kidney disease, those who are addicted to alcoholism, or pregnant women.

Diagnosis: Bacteriological diagnosis can be made by examining stained slides of flecks of mucus from the stools. This material may be enriched in alkaline peptone solution for four to eight hours. Following this it should be cultivated on Dieudonné's media. Agglutination tests with known antisera and suspected organisms should be done. The typical cholera red reaction may be elicited by adding six to eight drops of concentrated sulphuric acid to a culture grown in Dunham's peptone medium for 24 to 48 hours. Pfeiffer's phenomena is another diagnostic aid, though a positive result does not always indicate cholera. This is a bacteriolytic reaction. A loopful of the suspicious organisms should be suspended from an agar slant in a milliliter of saline or peptone solution and mixed with a milliliter of cholera antiserum. This material is injected into the peritoneal cavity of a guinea pig. In 20, 40, and 60 minutes, a drop or so of the peritoneal fluid should be removed with a glass capillary pipette and examined microscopically. If *V. cholerae* are present, they will lose

their motility and disintegrate. A control with no antiserum or with normal serum should be used.

Clinical diagnosis is based on laboratory findings and symptoms. It should be confirmed, if the patient dies, by a postmortem examination. The differential diagnosis includes food poisoning, mushroom poisoning, malaria, and bacillary dysentery. Laboratory tests are valuable in excluding these entities.

TREATMENT

1. The patient must be kept in bed, and heat should be applied to the abdomen and arms and legs as needed.

2. The diet should be low in residue and supplemented by vitamin B complex and ascorbic acid, 100 mg. daily. Nausea and vomiting may prevent the intake of food.

3. Sulfaguanidine, sulfadiazine, and sulfathiazole may be given orally in the usual dosage.

4. Unless nausea prevents, the patient should be given as much fluid as he can take. Water, lactate-Ringer's (Hartman's) solution, 5 per cent dextrose and 0.75 per cent lactic acid in normal saline (1 tablespoon sugar and 20 drops of lactic acid per 100 cc.—3 ounces—saline), or a bouillon cube containing 2.4 Gm. salt dissolved in a cup of hot water and cooled, are all satisfactory for oral use.

Normal saline, Ringer's solution, five per cent dextrose in normal saline and lactate-Ringer's (Hartman's) solution are recommended for parenteral use. The amount needed may be judged by the patient's blood pressure, thirst, and appearance. Moderately severe cases require 2000 cc. in the first hour. In extreme cases, this should be repeated every two or three hours. Blood or plasma transfusions should follow fluid therapy, three to six hours after dehydration has been relieved.

If water intoxication occurs, the excess fluid can generally be removed by giving a salt free diet, reduced fluid intake, sweating, catharsis, and plasma. In the case of prolonged fluid therapy, 10 to 30 mg. (⅙ to ½ grain) thiamin hydrochloride should be given daily by mouth or parenterally. To prevent tetany 5 to 10 cc. of sterile ten per cent calcium gluconate may be necessary intramuscularly or intravenously. If acidosis is present, 1000 to 2000 or more cc. of lactate-Ringer's (Hartman's) solution should be administered intra-

venously or subcutaneously and repeated in six or eight hours if necessary. If lactate-Ringer's solution is unobtainable, sodium bicarbonate may be used, but it may cause alkalosis and tetany. Sodium bicarbonate solution may be made by dissolving 5.75 Gm. (86¼ grains) sodium chloride in 1000 cc. distilled water, and sterilizing by boiling. This solution is removed from the heat and 18.15 Gm. (272¼ grains) of sodium bicarbonate which has been weighed and placed in a sterile container is added immediately. This is cooled to body temperature and used at once. The three ingredients used should never be mixed together at the same time and sterilized by boiling or autoclaving, as this converts the bicarbonate to caustic carbonate. Great care should be used in the administration of this preparation in order to prevent complications.

Prophylaxis: The water supply should be chlorinated or boiled. All uncooked salads, fresh fruit, and raw shell fish should be avoided. Antifly measures should be taken. Carriers and patients should be detected and isolated, and sterilization of all articles contaminated by patients is necessary. Care in personal hygiene, and modern sanitation should be enforced when possible.

Vaccination of those living in or passing through cholera infested districts is essential. Revaccination is necessary at least once a year, and preferably more often.

CHAPTER XXII

Tropical Diseases

(Continued)

YELLOW FEVER

Yellow fever is an acute infectious disease due to a specific filterable virus which is transmitted by domestic mosquitoes. It is confined more or less to certain geographical areas, especially South America and West Africa, where it is endemic. From these points it may spread in epidemic form to other localities, but fortunately the disease does not seem to become a permanent fixture there. It prospers especially in low country with a warm damp climate where conditions for mosquito propagation are favorable. Yellow fever runs an acute febrile course with remission on the third or fourth day, and is characterized by jaundice, hemorrhages, and albuminuria. No specific treatment has been found satisfactory, but prophylaxis has brightened the outlook somewhat.

Etiology: Yellow fever is transmitted by the female mosquito which sucks blood from a patient during the first three or four days of the disease. By the fifth day, the virus disappears from the blood stream and antibodies develop. Ten or twelve days later, the mosquito becomes infective and may transmit the infection to a susceptible person through its bite. However, it takes from four to six days for the disease to develop in nonimmune people. Thus almost three weeks elapse between the appearance of the first case in a community and other cases.

Pathology: General features noted at autopsy include jaundice and evidence of hemorrhage in the stomach, intestines, gallbladder, meninges, pleura, pericardium and epicardium, uterus, lungs, and bladder. The most striking changes are in the liver, kidneys, and heart. The liver is pale yellow and fatty, the kidneys are tense and swollen, and the heart is pale and flabby. Microscopically, the lesions consist of fatty degeneration and necrosis of the parenchyma with practically no inflammatory reaction, and other degenerative changes.

Signs and Symptoms: The incubation period is usually from four to six days. The initial stage of the disease is characterized by sudden

chilliness or rigor, severe frontal headache, and general muscular pains, especially in the back and limbs. The general picture is one of intoxication rather than infection. The temperature rises to 38.3° to 40° C. (101° to 104° F.) or more within 24 hours, the face becomes flushed and bloated, and the conjunctivae injected and red. There is loss of appetite with nausea and occasionally vomiting. Albuminuria is present, and there may be slight jaundice. The tongue is red and clean along the edges and tip, with coating of the dorsal surface. The pulse, while remaining full and strong, becomes slower and slower as the temperature rises; after about 24 hours, the fever begins to drop but not as quickly nor consistently as the pulse rate. This pulse-fever symptom is one of the characteristic signs of the disease. During this period, the patient presents a picture of active congestion with severe prostration. At the end of 48 to 72 hours, these symptoms decline and a period of remission marks the end of the infectious stage. This gives the false impression that the case is a mild one, but within a few to 24 hours, more specific manifestations appear.

During this second stage, vomiting becomes severe and has the appearance of coffee grounds; the temperature rises to 39.5° C. (103° F.) or higher, followed by intense thirst, and gastrointestinal hemorrhages are severe. Large amounts of albumin are present in the urine, which is scanty in amount; there may be complete suppression which, if persistent, causes death. Venous congestion with low arterial tension takes the place of the active congestion of the infective period. The spleen is not enlarged. The conjunctivae are injected and jaundiced, and the sclerae are also jaundiced, as is most of the body. Jaundice, ranging in color from lemon yellow to a deep brown, hemorrhages and consequent black vomit, and albuminuria are the main features of this phase of the disease.

The sixth or seventh day of the disease usually marks the turning point; the patients either die then or the temperature rapidly falls by lysis. The occurrence of anuria is a bad omen because it indicates liver destruction. One of the most favorable prognostic signs in a severe case is the restoration of renal function. The period of convalescence is from two to four weeks with complete restoration of kidney and liver function.

Diagnosis: Yellow fever must be distinguished from malaria and relapsing fever by blood smears. In general, the chief manifestations of the disease in a yellow fever area make the problem of diagnosis an easy one. However, mild cases or those seen in the early stage may present some diagnostic difficulty.

Dengue in its early stage must be considered when making a diagnosis, but in this disease the spleen is enlarged and after two or three days the characteristic eruption appears. Jaundice, hemorrhage, or albuminuria are not present in dengue. Weil's disease may offer the most difficulty in differential diagnosis since the symptom-complex is almost the same as in yellow fever. However, inoculation of the guinea pig with blood or urine from the patient and consequent development of Weil's disease makes the diagnosis evident.

TREATMENT

Yellow fever is a disease of uncertain prognosis, since there is no specific therapy of definite value. Consequently, treatment is symptomatic with careful nursing.

1. Since the circulatory mechanism is involved, absolute bed rest in the recumbent position is important. The patient should not be moved, particularly not after the first day. Movement is not only hazardous but may aggravate the nephritis.

2. A saline purge, as magnesium sulfate, 10 to 15 Gm. (150 to 225 grains), should be given on the first day and enemas daily thereafter. The use of mercuric bichloride, 0.001 Gm. (1/60 grain), and sodium bicarbonate, 0.5 Gm. (7½ grains) every hour, at the earliest possible moment, has been advised.

3. Foods should be withheld during the first stage of the disease and until the temperature returns to normal. Water and citrus fruit juices should be given frequently in small amounts. If vomiting prevents the ingestion of fluids, intravenous dextrose, 2000 to 3000 cc. of a five per cent solution daily, physiologic solution of sodium chloride, 2000 cc. by hypodermoclysis daily, and tap water by rectum should be administered.

4. Vomiting may be relieved by cracked ice and cocaine hydrochloride, 0.016 Gm. (¼ grain) by mouth, and codeine sulfate, 0.033 Gm. (½ grain) hypodermically.

5. Headache and fever may be relieved by ice caps and sponge baths.

6. Stimulants are not usually necessary early in the disease, but they may be used later when collapse or asthenia develop.

7. Astringents may aid in the treatment of hemorrhage but, in general, drugs are of little help.

8. Hot baths or hot packs and cups applied to the loin may be of value if there is suppression of urine.

9. It was hoped that an immune serum could be used in the treatment of yellow fever as in other infectious diseases, but as yet this has not been fulfilled.

10. *Prophylactic:* Healthy individuals in an infected area should sleep under mosquito netting. Breeding places of mosquitoes should be destroyed. Water jars and tanks should be emptied, sealed, or protected by wire netting so mosquitoes will not be able to deposit their eggs, or oil may be poured on the surface of the water. The bed of the yellow fever patient should be screened so he will not be bitten by a mosquito during the infective phase of the disease, and the house or room should be fumigated so adult mosquitoes will be destroyed. Vaccination confers an immunity of several years' duration.

PLAGUE

Plague is an acute febrile disease attended by a very high mortality rate. Black death, Oriental plague, and pest are other names given to this malady. The disease has been known since ancient times and has occurred frequently in devastating epidemics. It begins with chills and fever, followed in a short time by great prostration; swelling of the lymphatic glands; the formation of buboes in the femoral, inguinal, and cervical regions; primary or secondary pneumonia; septicemia, and petechial and diffuse hemorrhages. Delirium, headache, vomiting, and diarrhea are associated symptoms.

Etiology: The pathogenic organism is *Pasteurella pestis.* The disease is usually transmitted to man by fleas which have fed on infected rats or wild rodents. The pneumonic type of plague may be passed by droplet infection, or by human expectoration, feces, urine, and the discharge from buboes.

The disease may be of two kinds, classical plague, a disease of domestic rats, which may be transmitted to man, and sylvatic plague,

a disease of wild rodents, transmissible to man. Classical plague is found chiefly in Asia, but also occurs in Africa and South America. Sporadic cases occur in ports in any part of the world. Sylvatic plague occurs chiefly in South America, Argentina, and the Transbaikal regions of Siberia. It has been found in western United States and Canada.

Pathology: The infection is usually acquired through cutaneous inoculation, but the site of entrance is seldom apparent. The pathological changes are characterized by marked congestion and hemorrhagic edema of the lymph glands. The primary bubo is surrounded by hemorrhagic extravasations of connective tissue and there is periglandular edema. The toxin of the plague bacillus has an extremely destructive effect on the endothelial cells of the blood vessels and lymphatics, resulting in extravasations of blood typified by petechial spots of the skin and serous membranes. The organs of the body are congested, including the brain, but meningitis is not a feature. The heart is dilated and the spleen may also be enlarged.

Symptoms and Signs: There are three clinical types of plague—bubonic, septicemic, and pneumonic. The bubonic type is commonest, especially in warm climates, and comes on suddenly with severe headache, high fever, and leukocytosis. The lymph nodes enlarge and become painful and indurated. Buboes occur most frequently in the inguinal region, then the axillary and cervical areas. Conjunctivitis is prominent. Prostration is intense and the patient may be delirious, excited, and anxious. Mucosal and subcutaneous hemorrhages are present, and petechiae and ecchymoses are evident. The average incubation period is from two to seven days. If the patient remains alive for five days, his chances of survival are good. Some mild cases may remain ambulatory, and in such instances, the first symptom may be a painful bubo.

Septicemic plague is primary or secondary. In bubonic or pneumonic plague there may be secondary septicemia. Primary septicemic plague starts in the mucous membranes of the eyes, mouth, or throat, and is usually followed by death. Symptoms resemble bubonic plague, except the localized buboes are not found. The temperature may be low due to the overwhelming infection. The incubation period for this form of plague is two days, and death may ensue in another two days.

Pneumonic plague may also be primary or secondary. The secondary form occurs in a small percentage of the cases of bubonic plague, and these secondary cases may cause primary pneumonic epidemics, especially in colder climates and where living conditions are crowded. Primary pneumonic plague is contracted by droplet infection of the respiratory mucosa or conjunctivae, or directly from infected rats. It is characterized by a sudden onset, fulminating course, fever, and mucoid, bloody sputum. Death occurs as a rule.

Diagnosis: A smear of aspirated contents of buboes or sputum stained with methylene blue shows the bacilli as short organisms with bipolar staining and swollen, vacuolated involution forms. A culture taken from a bubo, blood, or sputum on nutrient agar, or in broth, shows characteristic gram-negative organisms. Mice, rats, and guinea pigs when inoculated intraperitoneally or by skin will die in two or three days, and autopsy will show organisms and changes typical of plague. Care must be taken to see that the animals are free of fleas or other insects. Aseptic technic is important. In all laboratory tests, great care must be taken in handling infected material.

TREATMENT

1. Morphine and sponging may relieve the restlessness and fever. Fluids should be forced both orally and parenterally.

2. Sulfathiazole or sulfadiazine sometimes brings about good results. The initial dose is 4 Gm. (60 grains), followed by 1.5 Gm. (22½ grains) every four hours day and night until the temperature has been normal for seven days. In serious cases, sodium sulfathiazole may be given intravenously in five per cent solution of water, 0.06 Gm. (1/10 grain) per kilogram (2.2 pounds) of body weight. This is to be followed every six hours by 0.03 Gm. (1/20 grain) per kilogram (2.2 pounds) of body weight. Oral sulfonamide therapy should be resumed as soon as possible.

3. Antiplague serum, 100 to 250 ml. or more intravenously every 8 to 12 hours, is recommended after routine desensitization.

4. The use of hot, wet applications on the buboes may aid in localizing the infection. Incision is not recommended until localization is complete, as blood stream infection may occur.

Prophylaxis: Patients should be strictly isolated in a separate screened room, and all waste articles contaminated by patients must

be burned. If the plague is pneumonic, attendants must wear hoods with goggles or celluloid eye openings, rubber gloves, gown, and mask. All equipment contacted by the patients should be sterilized. The walls and floor of a room and furniture should be washed with five per cent creosol after the patient is discharged, and the room should be aired for two days. Strict asepsis in the handling of patients is imperative.

Buildings should be rat-proofed and rats should be exterminated. Dead or dying rats should be examined for plague, as a rat dead of plague may be the first warning of the onset of a human epidemic. In rural areas wild rodents should be avoided and care taken that they do not come near the food supply. Ships should be examined for rats periodically and if rats are found they should be killed.

Vaccination is a valuable preventive measure and gives protection for two years. Vaccine made from two billion dead *Pasteurella pestis* per 1 ml. is used. The first injection is 0.5 ml., and a second injection following in a week to ten days is 1.0 ml. Injections of 1 ml. are then given when indicated to boost immunity.

RELAPSING FEVER

Relapsing fever is an infectious disease transmitted to man by lice or ticks.

Etiology: Two types of organisms are involved, *Borrelia recurrentis,* which is passed to man by the louse, and *Borrelia duttoni,* which is carried by ticks. Louse-borne relapsing fever occurs chiefly in eastern Europe, most of Asia, north and equatorial Africa, Peru, Central America, French Indo-China, and Japan. This form of relapsing fever tends to occur in epidemics.

Tick-borne relapsing fever does not occur in epidemics, but outbreaks are localized to the place where the ticks are found. The malady occurs in Africa, Asia, Europe, Central America, and South America.

Pathology: Visceral hemorrhages, nose bleed, jaundice, and bile-stained viscera are characteristic. The spleen is soft and enlarged, and may present infarctions. On cut surface, the malphigian bodies may be infiltrated and prominent. Smears made from the liver and spleen reveal spirochetes.

Symptoms and Signs: The onset of the louse-borne variety is sudden, with chills, persistent high fever of 40° to 40.5° C. (104° to 105° F.) for four to six days, headache, vomiting, enlargement of the spleen, albuminuria, and leukocytosis. The fever drops by crisis. There may be an asymptomatic afebrile period of four to eight days followed by a relapse, but during relapses symptoms are not as severe as the first attack. Relapses may occur more than once, but immunity seems to increase with each relapse. Jaundice, delirium, vertigo, and hemorrhages may occur. The tick-borne type presents similar symptoms except that the cerebrospinal symptoms are commoner in some areas, and there are more relapses, usually at least four. The paroxysms are more intense, but of shorter duration.

Complications are serious and include pneumonia, intense jaundice, diarrhea, herpes, iritis, hemorrhages from the nose, stomach, and kidneys. In the cases with jaundice, myocarditis may occur. There may be a meningismus resembling that of cerebrospinal meningitis.

Prognosis: Mortality is 2 to 50 per cent in the louse-borne type and about five per cent in the tick-borne form. In some epidemics in Africa, however, as many as 80 per cent have been reported dead from relapsing fever.

Diagnosis: The Borrelia may be demonstrated in the blood during the febrile period by dark field examination by Giemsa-stained thin or thick films or by mouse inoculation which becomes positive within three days.

Relapsing fever must be differentiated from dengue, malaria, cerebrospinal meningitis, plague, typhoid, trench fever, and typhus. The absence of leukopenia, postorbital pain, and presence of a tender spleen will exclude dengue. Identification of parasites will differentiate malaria, but the two diseases may coexist.

TREATMENT

1. Neosalvarsan, or neoarsphenamine, 0.6 Gm. (10 grains) intravenously, is indicated as soon as the diagnosis is made. However, these drugs should not be used in the afebrile period or near a crisis. If the patient does not respond to neosalvarsan, bismuth preparations, as sodium potassium, bismuth tartrate, 0.02 Gm. (0.3 grain) in 2 ml. of distilled water, may be given intramuscularly.

2. Good nursing care and symptomatic treatment are necessary. The patient may become very hungry during or after a crisis, but overfeeding may cause diarrhea.

3. Convalescent serum may be of benefit.

4. The heart and circulation should be watched. During crises, there may be collapse with shock.

Prophylaxis: Louse-borne relapsing fever may be prevented by eliminating lice by delousing the patient, his clothes, bed, room, and all louse-infested houses. The avoidance of the tick-borne type involves the shunning of places likely to be infested with ticks, as native houses, caves inhabited by rodents, bats, or ticks. The hands must not be soiled with rodent blood in endemic areas. Houses should be built so as to prevent the lodging of rodents beneath the floors or in the walls, and care should be taken to keep ticks out of cracks in the floors and walls. Absolute cleanliness should be maintained. When a case occurs, a careful search should be made for the ticks, and sterilization of the bedding, room, and furniture used by the patient is in order. Clothing and bedding should be examined for ticks after possible exposure.

WEIL'S DISEASE

Weil's disease, or acute spirochetal jaundice as it is sometimes called, is an acute specific infection caused by the *Leptospira icterohemorrhagiae*. It may be either endemic or epidemic in character, but it is more often the latter. The disease is characterized by sudden onset with profound prostration, muscular pain, high fever, jaundice, and hemorrhagic tendency, but these are not all necessarily present.

Etiology: The *Leptospira icterohemorrhagiae* produces Weil's disease. It is a poorly formed spiral spirochete with hooklike ends, which is found in all rats. The urine excreted by the rats contains the organisms, and thus the disease is transmitted to man, probably by some insect or through the soil, abrasions in the skin, nasal passages, mucous membrane of the conjunctivae of the eye, or gastrointestinal tract. The disease occurs most often in young adult males, particularly soldiers in the trenches, miners, fish cleaners, and others exposed to dampness or rat infested areas. It is found the world over, especially during the summer months.

Pathology: Most cases reveal generalized jaundice and lesions of the kidneys, liver, capillaries, and skeletal muscles. The kidneys are enlarged, jaundiced, and swollen with rather marked necrosis of the epithelium of the convoluted tubules and interstitial infiltration of the lymphocytes and polymorphonuclear leukocytes. Renal damage is almost entirely tubular, ranging from cloudy swelling to necrosis.

The liver is usually enlarged and bile stained. Microscopically, there is proliferation of the hepatic cells, evidence of degeneration and inflammation, as necrosis and dissociation of cells, and signs of biliary stasis in the central part of the lobule. Hemorrhages, either slight or profound, appear throughout the body, especially in the peritoneum and pleura, kidneys, brain and meninges, nasal mucosa, skin, adrenals, and gastrointestinal tract. The muscles of the calf are most frequently and extensively affected, though the pectorals, back muscles, and deltoids are often involved. Many other pathological changes are found but are not constant manifestations of the disease. The spirochetes are most easily demonstrated in the kidneys and liver, though they are also found in the myocardium, adrenals, skeletal muscle, intestinal wall, and other organs.

Signs and Symptoms: In general, Weil's disease is divided into three stages: (1) The febrile or septicemic; (2) the icteric, and (3) the convalescent period.

1. *The Febrile Stage:* The onset of the disease is sudden, following an incubation period of from five to seven days. There is usually a severe frontal headache, with chilly sensations and severe prostration. Muscular aching is marked, and there is tenderness to slight pressure over the calves of the legs. Anorexia, nausea and vomiting, and diarrhea are common symptoms. Physical examination reveals an acutely ill patient with a high fever of 39° to 41.1° C. (102° to 106° F.); a full, fast pulse; hot, dry skin; red, puffy face; injected conjunctivae; dry, coated tongue; injected pharynx, and evidence of capillary damage may manifest itself as petechial and ecchymotic hemorrhages over the entire body. Stools are usually light in color and bile stained; urine is dark, scanty in amount, and of high specific gravity, frequently containing casts, albumin, bile pigment, and red blood cells. The liver is usually enlarged and tender, the upper abdomen is tender, and the spleen enlarged. Leukocytosis is present from onset, and at times there is an eosinophilia. Red blood cells,

platelets, and hemoglobin may be reduced. Signs and symptoms increase in severity during this period. The leptospirae are found in the blood and a diagnosis may be made by dark-field examination, lysis-agglutination test, or by injecting blood from the patient into a guinea pig and thereby reproducing the disease. On about the fifth day, antibodies appear in the blood and by the tenth day the leptospirae have disappeared.

2. *The Icteric or Second Phase:* This occurs from three to nine days after the onset of the disease. Jaundice begins and increases rapidly, and the hemorrhagic tendency becomes more apparent. Evidences of renal failure manifest themselves during this period; there may be marked oliguria, occasionally anuria, increased urea retention, and renal acidosis. The temperature fluctuates toward the end of the first week and is usually near normal with a relatively high pulse rate at this time. Headache and vomiting disappear.

The patient is semicomatose and extremely toxic. Although from the temperature chart one might conclude that the patient was recovering, examination shows that he is worse instead of better. The liver is enlarged and sometimes tender. There is often moderate abdominal distention; peristalsis is diminished. The spleen is not palpable. Muscle tenderness of the back and calves is evident, and tendon reflexes are diminished. A rash may appear. A high and rising icteric index and blood urea nitrogen are noted. The white count may remain constant or rise to leukemic levels, while the red count may decrease somewhat. Urine is still scanty, deeply jaundiced with increased amounts of albumin, casts, cellular débris, and bile pigment. In fatal cases, death usually occurs between the ninth and sixteenth day. It may be due to renal or cardiac failure, renal and hepatic failure, hemorrhage, severe toxemia, or complications, as pneumonia, myocarditis, or vegetative endocarditis.

At the end of the second week, the patient becomes rational, diuresis takes place, jaundice subsides, and the blood urea nitrogen begins to fall. About this time, the blood becomes sterile and the organisms appear in the urine. During this period of leptospiruria, specific antibodies appear in the blood, and by the end of the third week, very high agglutinin and lysin titers are demonstrable.

3. *The Convalescent or Final Stage:* After two or three weeks, the third and last phase sets in. The icteric index starts to fall, and

renal disease, if present, disappears. Fever and hemorrhagic tendency are usually absent by this time, and the patient is symptom-free except for marked weakness. Convalescence is usually uneventful, lasting from a week or two to ten weeks. Relapses may occur during the third to fifth weeks of the disease, but are seldom of serious consequence. Complications noted include peripheral neuritis, leptospiral vegetative endocarditis, or iridocyclitis.

Diagnosis: Weil's disease is easily overlooked in cases where jaundice is absent or hemorrhagic tendency slight. A history of contact with rats or with a sick animal is suggestive. The presence of the classical symptoms of sudden onset, high fever, severe headache, muscular pains, albuminuria, and urea retention should make one think of Weil's disease. However, the causative organism must be found before a final diagnosis can be made.

The *Leptospira icterohemorrhagiae* is circulating in the blood during the first week, and a dark-field examination or inoculation of a young guinea pig with blood intraperitoneally, thus reproducing the disease, are helpful diagnostic methods. The first test is the simplest and most useful; the latter is of no clinical significance, since the patient will recover or die before the disease occurs in the pig. The organism is from 8 to 15 micra in length, and appears as an actively motile, rapidly spinning spirochete. It is tightly coiled with a small sharp hook at each end, so it resembles the letter "S." During the second week, the organism is excreted in the urine. A dark-field study of the urine is of little value, but inoculation of a guinea pig may be of aid. The agglutination test is probably the one of choice. Usually this test is positive at the beginning of the third week and remains so for six months to a year. Occasionally specific antibodies may be found by the ninth or tenth day; a negative reaction at the end of 30 days rules out Weil's disease.

Differential Diagnosis: During the early stage, Weil's disease resembles any acute infectious process. The diseases which are most apt to cause confusion are streptococcal infection of the throat, influenza, typhoid and paratyphoid fevers, undulant fever, acute catarrhal jaundice, yellow fever, and acute yellow atrophy of the liver. Grippe or influenza may simulate mild cases of Weil's disease; however, in these two conditions the patient feels comparatively well when the temperature drops, but he feels quite badly for several days after the

temperature fall in Weil's disease. The absence of rose spots, the negative blood culture, and cells in the spinal fluid usually eliminate the diagnosis of typhoid. In acute catarrhal jaundice, there is commonly a relatively low white blood count with a lymphadenopathy and a palpable spleen, while the opposite is true in Weil's disease. Renal disease, hemorrhagic tendency, and meningeal involvement are hardly ever present in catarrhal jaundice.

Prognosis: Mortality varies from about ten per cent in endemic cases to 30 per cent in epidemics. In general, prognosis is dependent on the age of the patient, intensity of jaundice, degree of renal failure, heart function, and severity of hemorrhagic diathesis. Mortality increases with age and is highest in those over 60 years. An old axiom states that where there is no jaundice there is no mortality. An icteric index over 200 is a grave sign. Renal failure or decreased heart function have an unfavorable effect on prognosis.

TREATMENT

1. The general treatment is the same as that for any acute infectious disease.

   a. Patient should be kept in bed in a well-venilated room.

   b. A light diet with plenty of fluid should be given. If enough fluid cannot be taken orally, it should be administered subcutaneously or intravenously. A 25 or 50 per cent glucose solution should be given if diuresis is desired, while a five per cent solution is adequate to fulfill the fluid requirements.

   c. Headache and myalgia may be relieved by aspirin and codeine.

   d. Anemia may be combated with iron, liver, and vitamin B therapy. Blood transfusions increase the red cell count rapidly and have a beneficial effect on the hemorrhages. Vitamin K also has a good effect on bleeding.

   e. Barbiturates are indicated for sedation, cardiac drugs for myocardial weakness, and oxygen for pulmonary edema.

2. The specific treatment consists of administering immune serum in full doses of 30 to 60 cc. early in the course of the disease. Unfortunately there is no such commercial serum in America at the present time. The sulfonamides have not proved successful in the treatment of Weil's disease, and the value of sodium bismuth tartrate has not been determined.

HOOKWORM DISEASE

Infection with hookworms is prevalent in the southern United States and in humid tropical regions. Etiologic agents are the *Necator americanus* in the Western Hemisphere, and *Ancylostoma duodenale* and *Necator* in the Eastern Hemisphere. Dog hookworms, *Ancylostoma braziliense* and *A. caninum* in the larval stage, can infect the skin of man and cause "creeping eruption." The parasite enters by the skin, passes through the lungs, up the respiratory tract, over the epiglottis, and down to the small intestine where it becomes attached. When sexually mature, oviposition occurs. The eggs are passed in the feces and hatch rapidly in the soil. They come in contact with human skin, and thus infect man. The Negro race is not so much affected as the white race.

Pathology: The site of entrance shows a dermatitis. The lesion consists of a serpiginous tunnel into the stratum germinativum which may be followed by "creeping eruption." The larvae in the lung may cause hemorrhages. Anemia is the rule and in severe cases ankle edema occurs. Where the worms are attached in the intestines, there may be small punctate hemorrhagic spots or larger hemorrhages. Older hemorrhages are marked by punctiform pigmentation. The heart may be dilated, and the muscle may be flabby and show fatty degeneration. The liver and kidney also show fatty changes, and the spleen is often small. The presence of grains of yellow pigment, giving reactions of haematoidin in the liver and kidney, suggests that there is intravascular blood destruction in which hemolysis is a factor.

Signs and Symptoms: An early symptom is dermatitis occurring chiefly about the toes or inner side of the soles of the feet, but this is not a necessary part of the syndrome. Epigastric distress is characteristic. The stomach may be dilated and the gastric juice is acid. Later, as the anemia progresses, achlorhydria may develop. Often patients are pot-bellied. Circulatory symptoms are palpitation of the heart, functional murmurs, and pulsation of the neck. The heart may become dilated to the right. The pulse is fast and blood pressure low as a rule. There may be cough or bronchitis and shortness of wind. Patients are both mentally and physically sluggish. Severe anemia is characteristic. There is eosinophilia and sometimes leukocytosis.

Prognosis: Prognosis is most serious in young children, as their mental and physical development is interfered with. The outlook is bad in pregnant women, and better in Negroes than in whites. Treatment is usually successful unless the patient is debilitated by another disease or has a tendency to pernicious anemia. Life expectancy is shorter in those who have hookworm disease, and they are a prey to other diseases. The mortality rate for hookworm disease itself has been quoted at from one to seven per cent.

Diagnosis: Diagnosis is established by the finding of characteristic eggs in the feces. Beriberi, chronic nephritis, malarial cachexia, and Ascaris infections must not be confused.

TREATMENT

1. The worms must be expulsed by the use of tetrachlorethylene, in the absence of Ascaris infection. The adult dose is 3 cc. in a hard gelatin capsule followed in two hours by a saline purge. If Ascaris infection is present give hexylresorcinol crystoids (caprokol), 1 Gm. (15 grains). Food should be avoided for four hours after treatment. This medication results in the killing of all the Ascaris infection and about half of the hookworm infection. It should be followed in three days by treatment with tetrachlorethylene in order to eradicate all the hookworms. These drugs have no serious toxic effects. A light meal free from fat should be eaten the night before, and the drug given on an empty stomach.

2. If anemia is present, iron is needed and ferrous sulfate capsules (exsiccated), 0.35 Gm. (5 grains) t.i.d. after meals, are suitable.

3. The diet should be high in iron and vitamins.

4. One week after drug treatment the stools should be examined, and if eggs are still found, treatment should be repeated until the patient is cured.

5. The creeping eruption may be relieved by soaking cotton in ethyl acetate, applying it to an area just a little larger than the skin lesion and covering it with adhesive tape for 24 hours. Or an area up to one inch beyond the edge of the lesion should be frozen with ethyl chloride spray or dry ice.

6. Prophylaxis consists of sanitary disposal of sewage and the avoidance of touching materials which may be infected with hookworm larvae.

ASCARIASIS

Infection with the *Ascaris lumbricoides* is world wide in distribution. The disease is transmitted from man to man, and children especially are affected. The eggs enter the alimentary tract by the ingestion of infested food or drink, hatch in the small intestine, and burrow into the gut. Thence they pass into the blood stream and are carried to the heart and lungs. They break through the pulmonary capillaries into the air sacs and pass by way of the bronchi, trachea, and esophagus back to the small intestines, where they mature.

Symptoms and Signs: Intestinal colic is the chief complaint and may be associated with anorexia and insomnia. The worms may gather in clumps to produce intestinal obstruction. They may also migrate up or down the intestinal tract and into the appendix, bile ducts, gallbladder, pancreatic ducts, nose, sinuses, middle ear, and larynx, where they can cause unusual and serious disturbances. The worms may sometimes be vomited or they may escape from the nostrils. Intestinal ulcers and infections occasionally develop. Eosinophilia occurs.

Diagnosis: Diagnosis is made by the discovery of the characteristic eggs in the feces or by the spontaneous passing of adult worms.

Prognosis: Prognosis is good as a rule, though at times the abdominal symptoms may require operation. If the pulmonary system is involved, careful nursing is necessary for recovery.

TREATMENT

Hexylresorcinol crystoids (Caprokol capsules) are given to expulse the worms, as indicated in the treatment of hookworm. Other drugs, as santonin, 0.1 to 0.2 Gm. (1½ to 3 grains) for adults and 0.01 Gm. (3/20 grain) for each year of age for children followed by a saline purge, or oil of chenopodium, have been used but they are apt to be very toxic. If the larvae are migrating through the body, they cannot be killed.

In order to prevent the disease, feces should be properly disposed of and care taken to avoid contamination of food and drink. Periodic routine fecal examinations are advised.

SCHISTOSOMIASIS

Schistosomiasis is an infection caused by blood flukes and may be very serious.

Etiology: Three etiological agents are responsible for varieties of this disease: *Schistosoma haematobium,* which causes genitourinary symptoms; the *Schistosoma mansoni,* causing intestinal symptoms chiefly, and the *S. japonicum,* which brings on liver disturbances. *S. haematobium* is found most commonly in the Nile valley and other parts of Africa, in some parts of Asia, and in the Mediterranean countries of Europe. *S. mansoni* occurs in the Nile valley, other areas in Africa, but may also be found in South America and the West Indies. *S. japonicum* is found only in the Far East, particularly in China.

S. haematobium live and lay their eggs in the region around the bladder. The eggs escape usually in the urine and when deposited in fresh water, especially slightly alkaline or brackish water often containing vegetation, the larvae hatch out and infect snails. These snails are very apt to be found in sluggish streams, irrigation ditches, reservoirs, small pools, and such places. The larvae emerge from the snail into the water and infect man or animals by way of the skin. The use of polluted water for bathing, wading, or washing is liable to spread infection. The life cycle of *S. mansoni* and *S. japonicum* resembles that of *S. haematobium,* except that the snail hosts are of a different species. *S. mansoni* lay their eggs in the veins around the colon nad rectum, and *S. japonicum* lay theirs in the veins around the small intestine. The eggs of both species are passed in the feces rather than the urine and some, especially those of the *S. japonicum,* are carried to the liver.

Symptoms and Signs: The chief sign of infection with *S. haematobium* is papular dermatitis at the site of penetration of the cercariae. In one or two months fever, giant urticaria, eosinophilia, and hematuria develop. Late results are vascular ulcers and papillomata. Urinary fistulae, splenomegaly, and cirrhosis of the liver may occur. Lesions of the kidneys and ureters are not uncommon, and the rectum may also be affected. Secondary infections are frequent. Patients often become wasted and anemic.

The symptoms of *S. mansoni* and *S. japonicum* infestations resemble those of *S. haematobium,* but in *S. mansoni* the colon and

rectum are the seat of the trouble instead of the bladder, and late clinical findings are bloody stools, rectal polyps, fistulae, and prolapse. Cirrhosis of the liver and splenomegaly are more apt to be found. In *S. japonicum* rectal and anal lesions are not so common, but hepatic cirrhosis and splenomegaly are prominent.

Prognosis: Prognosis depends on the intensity of the infection. Mild cases may not result in great inconvenience, but severe ones may be followed by chronic cystitis, calculus, renal disease, and malignant growths. The use of antimony has improved prognosis.

The outlook in *S. mansoni* infections is fairly good, if the disease is mild and treated in time, but bad in the presence of cirrhosis or splenomegaly accompanied by ascites. In these instances the disease becomes chronic, but the patient may live for years. Intestinal ulceration, dysentery, and extensive papillomata of the rectum are unfavorable signs. Infection with *S. japonicum* is most serious and treatment is ineffective unless started early before visceral lesions are advanced. Exhaustion or terminal infection usually cause death.

Diagnosis: *S. haematobium* is diagnosed by the finding of characteristic terminal-spined ova in the urine. This type of Schistosoma egg is seldom found in the feces. The ova of the *S. mansoni* are lateral-spined and occur usually in the feces. *S. japonicum* ova are spineless, though a rudimentary lateral spine may sometimes be seen, and are found only in the feces.

TREATMENT

1. The worms may be expulsed by the use of fuadin (neoantimosan, 6.3 per cent, solution of a trivalent organic antimony compound) intramuscularly. On successive days 1.5 cc., 3.5 cc., and 5.0 cc. are given, and then 5.0 cc. on alternate days for ten doses. In the presence of toxicity, such as vomiting or joint pain, the dosage should be reduced. If eggs are present after treatment, repeat this medication after one week's rest for the patient.

2. If fuadin is not beneficial, give potassium antimony tartrate (USP), two per cent freshly prepared solution intravenously on alternate days. The dose is initially 2.5 cc. (0.05 Gm.) and each successive dose is increased by 1.25 cc. until 7.5 cc. are being given. The course of therapy should include from 12 to 15 doses. This drug should be administered two or three hours after a light meal and the

patient should rest for one hour after treatment. Toxicity is an indication for reduced dosage. Toxic symptoms may include coughing immediately after administration, nausea, vomiting, dizziness, and collapse. The drug is contraindicated in cases with jaundice, nephritis, or severe hepatic disease. It should be slowly injected into the lumen of a vein as thrombosis may occur otherwise. It should not be introduced to the subcutaneous tissues, as it causes necrosis.

3. The use of emetine, 0.6 Gm. (9 grains) for ten injections has been followed by good results. The first two injections should be 0.03 Gm. (½ grain) and the rest 0.06 Gm. (1 grain).

4. The diet should be liberal and nourishing. If liver damage is present it should be high in carbohydrate and low in protein. Supplementary vitamins, especially vitamins A and B, are good.

5. The treatment of the local conditions is necessary, and the urinary calculi, growths in the bladder, cystitis occurring in *S. haematobium* infections may require surgical procedures. Ascites, which may develop in *S. mansoni* and *japonicum* infestation, may need to be tapped. Splenectomy has been done for the splenomegaly, but great care should be taken in selecting patients.

6. Prophylaxis against future infection is necessary. Unpurified water in endemic regions must not be used. If one accidentally touches such water, one should immediately bathe completely with soap and clean water.

AFRICAN TRYPANOSOMIASIS

African trypanosomiasis, commonly known as sleeping sickness, occurs endemically in tropical Africa. There are two types of the disease, the gambian type, which is prevalent in the west, and the rhodesian form, which is commonest in the east. The etiological agents are *Trypanosoma gambieniense* and *Trypanosoma rhodesiense*. They are transmitted by the tsetse fly, genus Glossina, which becomes infected within 18 to 34 days after feeding on diseased wild and domestic animals or man. The flies bite only in the daytime. In epidemics other flies and insects may transmit this malady.

Pathology: There is chronic inflammation of the lymphatics, due to the mechanical action of the parasites or their toxins, and the glands become enlarged. The lymphatics of the brain and spinal cord are also concerned in this process. Meningoencephalitis, meningo-

myelitis, proliferation of the neurogliar elements and lymphocytes, and the endothelial cells about the perivascular lymph spaces follows the fever in the early stage. The changes are most prominent about the vessels of the pons and medulla. This leads to malnutrition, cerebral changes, and sleepiness. Adenitis may be seen on gross examination in the neck, groin, and other lymph glands. The cerebrospinal fluid is increased, often turbid, and the dura mater may be adherent in places. The pia mater frequently is thickened in some parts. The brain is congested, as is the cord, and hemorrhages in the cord are not uncommon. There may be ascites and excess pericardial fluid. Pneumonic changes sometimes occur in the lungs, and the spleen is enlarged. Gross lesions of the brain and other organs may not be visible. Trypanosomes are present in the cerebrospinal fluid, lymph channels, and blood.

Signs and Symptoms: The bite of an infected fly results in more marked inflammation than that of an uninfected fly. There is an incubation period of ten days to three weeks followed by irregular, remittent fever; rapid pulse; deep hyperesthesia, and asthenia. Headaches and neuralgic pains are associated with these symptoms. In the rhodesian type delirium and high fever may set in early. Whites who are suffering from this sickness have a characteristic erythematous rash on the trunk or thighs, and the skin is often dry. Hepatomegaly and splenomegaly may occur, and the Wassermann reaction is sometimes positive. The enlargement of the lymph glands is an important diagnostic sign. The cerebral stage starts in with tremors of the tongue and fingers, headache, hysteria, mania, delusions, and a desire to sleep. Wasting is prominent as the disease progresses. When the disease is far advanced, recovery is rare.

Diagnosis: The clinical diagnosis is established if trypanosomes can be demonstrated in the blood, spinal fluid, or material obtained by cisternal puncture. Thick, dry blood smears or fresh wet preparations are of aid. If organisms are not present on microscopic examination, monkey, dog, guinea pig, or white rat inoculation may reveal them. Repeated blood examinations are necessary, and the absence of trypanosomes does not exclude sleeping sickness.

The positive Wassermann reaction, fever, enlarged glands, and erythematous rash may suggest syphilis, and the increase of mononuclear cells may cause confusion with malaria, syphilis, and kala azar.

TREATMENT

1. Early cases of the gambian type may be treated with tryparsamide dissolved in 10 cc. of distilled water (not salt solution). Fifteen injections are given at weekly intervals. The initial adult dose is 1.0 to 1.5 Gm. (15 to 22½ grains) and subsequent doses are from 2 to 3 Gm. (30 to 45 grains). Treatment should be rigorous so as to avoid arsenic fastness. This drug may cause optic atrophy. The dose should be reduced, and the intervals between injections increased, if photophobia, lacrimation, eye pain, or dimming vision occur.

If tryparsamide is not tolerated, give naphuride (Winthrop) (Bayer 205, antrypol) intravenously, 10 cc. in distilled water, every four days for four to six doses. The initial adult dose is 0.3 to 0.5 Gm. (4½ to 7½ grains) followed by injections of 1 Gm. (15 grains). This drug is a kidney irritant and should not be used if albuminuria is present. If albuminuria develops during treatment, the drug should be stopped.

Before and after completion of treatment, lumbar puncture must always be made. A case should be kept under observation for two years. Examination of centrifuged, citrated blood every month for three months after treatment is indicated, and blood examinations should then be done every six months for two years.

2. The rhodesian type does not respond to tryparsamide, so therapy is started with naphuride as given for the gambian sleeping sickness. Lumbar puncture and follow up studies are also required in these cases.

3. Late cases are benefited only by tryparsamide as given for the early stages. The drug should not be given intrathecally and the first dose should be half the standard dose. Twenty weekly injections are given and repeated after a one- to three-month rest period. The spinal fluid examination is a guide to therapy and should be studied before and after the second course of treatment, and also six months and one year later. More advanced cases need to be followed for three years.

4. Patients should be segregated and kept in screened rooms.

Prophylaxis: Infected persons should be examined and treated before being allowed to go to districts where the tsetse fly is prevalent. Measures should be taken to provide protection from the bites of the tsetse fly. The breeding grounds of the fly should be eliminated and

animal reservoirs destroyed. Chemoprophylaxis with naphuride, 1.0 Gm. (15 grains) in one injection every three months is desirable.

AMERICAN TRYPANOSOMIASIS

American trypanosomiasis or Chagas' disease is commonest in Brazil, and exists to some extent in Argentina, Uraguay, Venezuela, Peru, Panama, San Salvador, Guatemala, and Mexico. This disorder is caused by *Trypanosoma cruzi,* which most often infests children, though adult infection is not uncommon. Fever, enlargement of the lymph glands, anemia, and localized edema characterize Chagas' disease in children.

The trypanosome is passed from man to man and from certain animals, chiefly the armadillo, opossum, rodents, dogs, and cats, to man by means of the bug, Triatoma. The bugs defecate when they feed and thus contaminate the bite. The trypanosomes invade the tissue cells of almost any organ in the body and change there to round leishmanial forms. The cells become packed with parasites and function is disturbed. Fibrosis follows. The heart, liver, and brain are most severely affected.

Symptoms and Signs: The disease is often mild in adults and severe in children. After an incubation period of about ten days, high fever, facial edema, adenitis, and cardiac weakness set in. Death is common, especially if meningeal symptoms occur. The disease may become chronic. In such cases, the parasites are not found in the blood, but exist probably as round forms in tissue cells. There are adenitis, convulsions, nervous disturbances, and apathy. Anemia and heart trouble frequently develop.

Prognosis: Prognosis is worst in the first year of life. The mortality rate is five per cent or more.

Diagnosis: Diagnosis is confirmed on demonstration of the trypanosomes in the blood. This is not usually possible except in the acute febrile stage. Guinea pig or puppy inoculation with 10 cc. of blood from the patient is often helpful. The animal inoculated will have trypanosomes in the blood in about two weeks. Complement fixation tests are useful if a reliable antigen is present.

Treatment: Treatment is symptomatic. Measures should be taken to prevent the bites of the Triatoma and other vectors. It is often difficult to control patients, as many, in fact most, of them are poor

and illiterate. Their dwellings often favor the survival of the vectors and should be avoided. Mosquito nets over beds are good. Animal hosts should be controlled.

FILARIASIS

Filariasis is caused by the *Wuchereria bancrofti* (Filaria) which is carried by the Aedes, Anopheles, Culex, and Mansonia mosquitoes. It is indigenous in most of the tropical world and is endemic in Central America, South America, and the West Indies. There is a small district near Charleston, South Carolina, where the disease occurs endemically in the United States. The filaria larvae develop in the mosquito and are passed to man by the bite of the mosquito which enables them to penetrate the skin. Adult filaria live in the lymph vessels where they give birth to many microfilariae which migrate to the blood stream.

Other types of filarial infections are Loaiasis and Onchocerciasis, occurring in tropical West Africa and Guatemala, respectively. The Onchocerca is also found in West Africa and southern Mexico. Loaiasis is caused by the Loa loa which causes transient subcutaneous tumors called Calabar swellings. It is spread by the biting fly, *Chrysops dimidiata.* Onchocerciasis is due to the *O. caecutiens,* which is spread by black gnats, *Simulium damnosum.* Tender, subcutaneous tumors around the head and scalp develop, and blindness may occur.

Signs and Symptoms: Clinical manifestations are not prominent and are often absent. When they do occur in filariasis, they are due to blockage of the lymphatics by inflammation and fibrotic changes around the parasites. This blockage results in elephantiasis of the scrotum, vulva, legs, arms, or breasts. Chyluria, chylous ascites, and chylous diarrhea may occur. The disease is marked by acute episodes of acute lymphangitis and "elephantoid" fever, which occurs irregularly for long periods of time.

In loaiasis symptoms are not present unless the worms migrate to places close to the skin or enter the eye. In onchocerciasis tender subcutaneous nodules, which are freely movable, are formed chiefly in the occipital and temporofrontal regions. They may also occur on the shoulders and trunk. When the tumors are close to the eye, micro filariae may migrate into the eye and cause blindness. A lichenoid dermatitis with marked itching may also be present.

Diagnosis: When caused by the *W. bancrofti* blood smears taken at night may show microfilaria. Thick smears stained as for malaria are suitable for study. If it is not convenient to draw blood at night the concentration technic may be used. One cubic centimeter of blood is drawn from a vein and discharged into 10 cc. of two per cent formalin solution in a 15 cc. conical tip centrifuge tube. This is mixed thoroughly and allowed to settle for 12 to 24 hours. The fluid may be drawn off with a capillary pipette and the sediment smeared evenly on a glass slide. The material is stained with Loeffler's methylene blue and counterstained with one-third per cent aqueous solution of eosin. Giemsa stain is also good. On examination of the stained substance, the microfilariae may be seen.

The loa loa may be demonstrated in a similar fashion, or the adult filariae may be extracted from under the skin or conjunctivae. *Onchocerca volvulus* or *O. caecutiens* may be seen in the excised tumors, or the microfilariae may be identified in fluid aspirated from the tumors.

TREATMENT

Treatment is symptomatic. Sulfadiazine will help control secondary infections in elephantiasis and is given 4 Gm. (60 grains) initially and followed by 1 Gm. (15 grains) every six hours day and night until the infection is controlled. The adult filaria may be removed surgically. The tumors in onchocerciasis should be enucleated early and care taken that others do not develop. If a nodule is suspected it should be aspirated and the material examined for microfilariae.

The disease is prevented by antimosquito measures and protection from the bite of the *Chrysops dimidiata* and the black gnats, *Simulium damnosum.*

CHAPTER XXIII

Acute Poisoning

SNAKE BITE

Snake venom varies in color from deep amber to a colorless liquid, and when dried is quickly soluble in distilled water. In general, snake venoms are composed of the hematoxin and neurotoxin elements; their proportion as well as the toxicity varies in different kinds of snakes. They are separable and each may exert its influence individually. The hematoxin destroys the red blood cells and tissue, and causes severe swelling, extravasation of blood, discoloration, and other signs. Neurotoxin attacks the nerve centers, especially the sympathetic system and the phrenic nerve. It does not produce swelling, but paralyzes the thoracic muscles often to such an extent that the patient suffocates.

Signs and Symptoms: The onset of symptoms after the bite of a viper is abrupt. As stated above, swelling and discoloration take place immediately, accompanied by oozing of the blood from the mouth, conjunctiva, bladder, and perhaps even from the stomach. Reflex vomiting is commonly noted. Within 6 to 12 hours, the patient may enter a state of coma and die. In this type of snake bite, it is obvious that the hematoxin element is especially active; the blood stream is thinned with hemorrhages over large areas. Neutralizing serum or blood transfusions are necessary for the recovery of the patient. If he does survive, a deep ragged scar will be present from the destruction of the tissue.

On the other hand, when a person is bitten by the cobra, there is slow and moderate swelling and little or no discoloration, but great difficulty in breathing is apparent. If the patient recovers, there is little or no destruction of the tissue at the site of the scar.

TREATMENT

The treatment of snake bite may be divided into first aid, early local care, and the management of late and systemic changes. The general treatment is aimed at removing the venom-laden lymph by

means of incision and suction, relief of pain, and prevention of infection.

1. Morphine sulfate, 0.01 to 0.016 Gm. (⅙ to ¼ grain), hypodermically, is given and the patient made as comfortable as possible.

2. A soft rubber tourniquet is applied just above the area of swelling, or if there is no swelling just above the bite. It should be loose enough so the blood is allowed to flow quite freely, but tight enough to occlude the lymphatics so the lymph and venom do not spread.

3. Before the patient is moved, the area surrounding the bite should be washed with an oxidizing antiseptic to remove the surface venom, prophylactic incisions made, and suction carried out. Procaine anesthesia is used, and incisions are made with a sharp-pointed blade. First the area surrounding the fang marks should be excised. Then incisions about one-fourth inch in size, cross-shaped in form, are made; the knife is inserted and pulled out, and if bleeding occurs, cotton may be used to plug the incision and another is made nearby. Incisions should be staggered at one-inch intervals in all directions around the bite, and in most cases it is necessary to cover the entire area of swelling. There may be 50 to 100 incisions. Bier's suction cups or suction apparatus, as a breast pump, should be applied to the incisions and left there. They may be changed from one place to another, being left longest on those incisions where the lymph flows most freely. Suction may be stopped when lymph no longer appears, and hot magnesium sulfate fomentations applied for 45 minutes, at the end of which time suction is again applied for 15 minutes, and this form is alternated until there is no sign of lymph.

4. If the swelling advances, the tourniquet should be raised and incisions made as indicated.

5. Antitetanus antitoxin, 1500 units, intramuscularly, should be given and repeated in ten days, since the tetanus bacillus has been found in the mouths of rattlesnakes. Some physicians advise continuing the antitoxin at intervals of eight to ten days if a lacerated wound containing necrotic tissue is present.

6. Artificial respiration and respiratory stimulants, as aromatic spirits of ammonia, 2 cc. in a glass of water at intervals of 10 to 15 minutes; strychnine sulfate, 0.008 to 0.013 Gm. (⅛ to ⅛ grain), intramuscularly, at 15-minute intervals until slight spasms occur; caf-

feine sodium benzoate, 0.33 Gm. (5 grains), intramuscularly, or caffeine in the form of strong, hot, black coffee, should be given, since death from snake bite is most often due to respiratory paralysis and failure.

7. If the venom has had time to reach the blood stream, blood transfusions and specific antivenin are usually necessary. If the red blood count is below three million, blood transfusion is indicated. Ten to 15 doses of 10 cc. of antivenin may be required, but usually 30 cc. are adequate for an adult, with more needed for children. It should be injected intramuscularly or subcutaneously into the area of the bite; in severe or late cases, it should be given intravenously.

ARSENIC POISONING

Arsenic poisoning occurs because of the accidental or intentional ingestion of rat poison or Paris green, and in industry through exposure to oxides of arsenic and arsenical salts. Arseniuretted hydrogen is primarily a hemolytic agent. Arsenic is a local irritant producing inflammation with sloughing, ulceration, and fatty degeneration. Usually within one hour after poisoning, there is burning pain in the mouth, esophagus, and stomach, followed by abdominal cramps, nausea, and vomiting. The breath may have a garlic odor. A severe diarrhea with rice water and later bloody stools occurs. Abdominal distention follows. If the patient does not die within a few hours, he may die in two or three days from collapse.

TREATMENT

1. The immediate treatment is to empty the stomach with emetic drugs, such as household mustard, 4 to 8 Gm. (60 to 120 grains) in a glass of water, or copper sulfate, 0.5 Gm. (7½ grains), or zinc sulfate, 2 Gm. (30 grains) in a glass of water. If these fail, then apomorphine hydrochloride, 0.003 Gm. (1/20 grain), hypodermically, should be given. The above drugs should be administered if no stomach tube is available. This should be followed by a thorough gastric lavage with water, to which may be added 30 Gm. (1 ounce) of sodium thiosulfate. After the lavage, a solution of 30 Gm. (1 ounce) of sodium thiosulfate in 500 cc. of water is left in the stomach and a similar dose is repeated daily. Intravenous injections of sodium thiosulfate, 0.66 Gm. (10 grains), should be given daily.

2. Freshly prepared ferric hydroxide made by mixing ferric sulfate, 50 cc. in 100 cc. of water, and magnesium oxide, 0.66 Gm. (10 grains) in 750 cc. of water, has always been considered the arsenic antidote, but its value is questionable. The dose is 15 to 30 cc. (½ to 1 ounce) every one to two hours.

3. A normal saline colonic irrigation three times a day and guarding against constipation will aid in the elimination of the arsenic, since this occurs to a great extent through the feces.

4. Since fluid loss is prominent in arsenic poisoning, effort should be directed toward maintaining the composition, volume, and distribution of extracellular fluids. The intravenous administration of 2000 to 3000 cc. of five per cent glucose in physiological saline daily will aid in maintaining the body fluid equilibrium. Degeneration of the parenchymatous organs, as the liver, kidneys, and heart, is combated by intravenous glucose, 500 cc. of a ten per cent solution twice daily.

5. Heat is applied to the abdomen for abdominal cramps, and atropine sulfate, 0.001 Gm. (1/50 grain), hypodermically; tincture of belladonna, 0.66 cc. (10 minims), three times daily, and intravenous calcium gluconate, 10 cc. of a ten per cent solution, are given.

6. Collapse is treated by the administration of stimulants, as caffeine sodium benzoate, 0.5 Gm. (7½ grains); coramine, 2 to 3 cc. (30 to 45 minims), or strychnine sulfate, 0.001 Gm. (1/60 grain), all given intramuscularly, and repeated as needed. Parenteral fluids and external heat are also indicated.

Concerning the use of arsphenamines, the two reactions constituting emergencies are the nitritoid crisis and a toxemic reaction. The nitritoid crisis is characterized by flushing of the face and neck, and a sense of precordial constriction. In addition, edema of the lids and lips, air hunger, and collapse may occur. The reaction occurs during or a few minutes after the injection. Treatment consists of stopping the injection of the drug and giving ½ cc. of a 1:1000 solution of adrenalin subcutaneously or intramuscularly and, if necessary, intravenously. The duration of the reaction is from a few minutes to one-half hour. A few minims of adrenalin given subcutaneously before the injections prevent this reaction.

The toxic reaction, consisting of nausea and vomiting, headache, and nervousness, is best treated with sodium thiosulfate, 1 Gm.

(15 grains), intravenously daily, and alkalinization, using sodium bicarbonate, a total of 2 to 4 Gm. (30 to 60 grains) being given daily. This reaction lasts from two hours to several days. The Herxheimer reaction, which is an intensification of the constitutional manifestations of syphilis, is best prevented by preparation with mercury and bismuth, and an initial small dose of the arsphenamine. This is particularly important when cardiac involvement is present.

ACID POISONING

The ingestion of strong acids, such as sulfuric and nitric, produces corrosion of the mouth, throat, esophagus, and stomach. The systemic reaction from poisonous amounts is an acidosis resulting in dyspnea, twitchings and convulsions, collapse, coma, and finally death.

TREATMENT

1. The local reaction should be treated by the oral administration of large quantities of mild alkalies, such as milk of magnesia, soap, or lime water. Sodium bicarbonate and other carbonates liberate carbon dioxide gas and will cause marked distention of the stomach.

2. Following neutralization of the acid, demulcents, as olive oil, milk, egg white, or any bland oily substance should be given.

3. Stomach tubes should be avoided.

4. For the systemic reaction (acidosis), sodium bicarbonate solution (see Acidosis) or 500 cc. of a 6/M sodium lactate solution should be given intravenously every hour until the acidosis is controlled.

5. Shock and collapse are an indication for supportive treatment consisting of external heat, parenteral fluids, and stimulants, as atropine sulfate, 0.001 Gm. (1/60 grain); strychnine sulfate, 0.002 Gm. (1/30 grain), or caffeine sodium benzoate, 0.5 Gm. (7½ grains), all given intramuscularly. Morphine sulfate, 0.01 Gm. to 0.016 Gm. (⅙ to ¼ grain), hypodermically, should be administered for pain.

6. The symptoms of oxalic acid ingestion are abdominal cramps, vomiting, and diarrhea due to gastrointestinal irritation, and nervous symptoms as a result of calcium depletion, characterized by twitchings, tetany, convulsions, coma, and death.

The treatment for poisoning from oxalic acid differs from the above in that ordinary alkalies, given as an antidote, form very soluble salts and thus promote absorption. Since calcium and magnesium salts of oxalic acid are insoluble, the antidote is 5 to 20 cc. of a ten per cent solution of calcium lactate given intravenously slowly. Thereafter, 10 cc. of this solution can be given intramuscularly once or twice daily. Calcium chloride, 5 to 20 cc. of a five per cent solution, may be given intravenously if the lactate is not on hand. The action must be quick, as the poison is rapidly absorbed. Calcium gluconate, 0.5 Gm. (7½ grains), in a glass of milk, should be given at three-hour intervals. To combat the acidosis, 6/M solution of sodium lactate, as above, is given. Large amounts of fluid should be given to foster excretion of the acid through the kidneys, since nephritis due to renal irritation may develop.

ALKALI POISONING

In alkali poisoning, there is usually corrosion of the lips, mouth, throat, and esophagus with burning pain down to the stomach. The skin is cold and clammy, the pulse feeble, and usually vomiting and purging and, in some cases, exhaustion, convulsions, stupor, or coma are present.

TREATMENT

1. To combat and neutralize the corrosive action of caustic alkalies, weak acids, as vinegar, lemon, or orange juice diluted several times with water, are given.

2. Soothing demulcents, as olive oil, milk, egg albumen, crushed bananas, starch, or water are given for the burns.

3. Morphine sulfate, 0.01 to 0.016 Gm. (⅙ to ¼ grain), hypodermically, is indicated to allay the pain.

4. Systemic shock is treated by stimulants, parenteral fluids, and external heat.

5. Stomach tubes should be avoided if strong alkalies have been taken internally because of the weakened esophageal wall.

ATROPINE POISONING

Occasionally, when used as a medication, mild degrees of poisoning with atropine and other members of the belladonna group are

seen. Dilated pupils, tachycardia and palpitation, dryness of the throat, thirst, and difficulty in swallowing are evidence of overdosage or idiosyncrasy. Extremely large doses taken accidentally or with suicidal intentions produce a stage of stimulation followed by collapse. In addition to the above symptoms, there are visual disturbances and excitement which passes into delirium and mania. The skin is flushed, and the temperature rises very high—41.1° to 42.8° C. (106° to 109° F.)—and respiration is rapid and deep. A stage of collapse follows, characterized by feeble heart action, low blood pressure, and slow, shallow respiration. The skin becomes cold and clammy in contrast to the initial stage of flushing and warmth. Death occurs from respiratory failure. Urine dropped in a cat's eye at five-minute intervals will dilate the pupil.

TREATMENT

1. Treatment consists of gastric lavage with tannic acid solution, 0.06 Gm. (1 grain), in one-half glass of water, tea, or potassium permanganate, 1 Gm. (15 grains), to a quart of water.
2. An ice cap is applied to the head for delirium.
3. Sodium bromide in doses of 1 to 2 Gm. (15 to 30 grains) is given as needed for excitement.
4. Pilocarpine nitrate, 0.01 Gm. (⅙ grain), is given every few hours until the mouth becomes moist, and is considered to be the physiological antidote.
5. Because of the tendency to depress respiration, morphine, chloral, and chloroform are to be avoided.
6. When collapse occurs, intravenous fluids, stimulants, external heat, and artificial respiration should be given.

BARBITURATE POISONING

This condition occurs from the ingestion of large amounts of barbital, phenobarbital, and other barbiturate derivatives, usually with suicidal intent. The patient lapses into a deep sleep or coma from which he cannot be aroused. Respiration becomes slow and feeble, and eventually ceases, owing to depression of the respiratory center. Collapse occurs with a rapid, feeble pulse; low blood pressure; cyanosis, and cold perspiration. Pulmonary edema results and later bronchopneumonia may develop. The pupils are fixed and constricted,

and the deep tendon and abdominal reflexes are diminished or absent. Smaller doses of the drug produce unsteadiness, giddiness, and lethargy.

TREATMENT

1. Treatment should begin with gastric lavage, after which 30 cc. (1 ounce) of magnesium sulfate is left in the stomach.

2. Picrotoxin, 0.003 Gm. (1/20 grain), should be given hypodermically immediately on entrance to the hospital and repeated in 30 minutes. If no effect is noted, it should be administered every hour until improvement occurs.

3. Diuresis is maintained by intravenous fluids, as 2000 to 3000 cc. of a ten per cent glucose solution or five per cent glucose in normal saline solution.

4. Collapse is combated by external heat and atropine sulfate, 0.001 Gm. (1/60 grain); strychnine sulfate, 0.001 Gm. (1/60 grain), repeated in one-half hour, administered intramuscularly; caffeine sodium benzoate, 0.5 Gm. (7½ grains), hypodermically; black coffee by mouth; ephedrine sulfate, 0.05 Gm. (¾ grain), orally, and coramine, 1 cc. (15 minims), intramuscularly, every two hours.

5. The foot of the bed should be elevated, and tracheal mucus aspirated.

6. If necessary, artificial respiration is applied.

CARBON MONOXIDE POISONING

Poisoning with carbon monoxide gas usually occurs from accidental or intentional inhalation of illuminating gas or exhaust fumes from an automobile. Other sources are defective flues of stoves, furnaces, charcoal fires, or imperfect oxidation of any carboniferous material.

Early symptoms before coma occurs are headache, dizziness, weakness, and occasionally nausea and vomiting. The lips are often cherry red, the face flushed, and the skin is usually pale. Prolonged exposure to a high concentration produces coma. The symptoms are due to asphyxia, since hemoglobin has a greater affinity for carbon monoxide than for oxygen. Complete elimination of the gas occurs usually in several hours. The outcome, however, depends upon how long and to what extent the brain has been deprived of oxygen. In severe

cases, coma continues and death occurs even after the elimination of all the carbon monoxide is complete, owing to irreparable brain damage.

TREATMENT

1. Treatment consists of artificial respiration as needed and the administration of pure oxygen or of oxygen containing five per cent carbon dioxide.

2. The patient must be kept warm and the patient should remain absolutely quiet in order that tissue demands for oxygen be kept at a minimum.

3. Intravenous sodium bicarbonate, four per cent solution, 500 to 1000 cc., or 500 cc. of 6/M sodium lactate solution, should be given to combat the associated acidosis.

4. Blood transfusions given within one to two hours after the onset of the poisoning may be of value.

5. Methylene blue, 50 cc. of one per cent solution, intravenously and repeated every hour until 200 cc. have been given, may be tried but its value is questionable.

6. Seriously poisoned individuals should be placed under prolonged observation.

COCAINE POISONING

Cocaine and its derivatives cause two types of poisoning. The first is sudden and severe, and is characterized by irregular jerky respirations, rapid thready pulse, convulsions, and death. The second type is more prolonged, and begins with mental excitement and loquacity followed by incoördination, nausea, vomiting, abdominal pain, and rapid pulse; respirations are increased at first and later are slow, irregular, and labored. Cyanosis, delirium, and unconsciousness occupy the final stage. The pupils are dilated, and the extremities cold and clammy.

TREATMENT

1. If the cocaine was swallowed, gastric lavage with water followed by 2 Gm. (30 grains) of tannic acid in one-half cup of water or large quantities of strong tea should be given.

2. If the stomach tube is not available, emetics, as apomorphine, 0.003 Gm. ($\frac{1}{20}$ grain), hypodermically, should be given followed by considerable amounts of warm water.

3. After the administration of tannic acid, the stomach should again be emptied. A saline cathartic, as magnesium sulfate, 30 cc. (1 ounce), should be left in the stomach.

4. For the treatment of the acute intoxication, sodium phenobarbital or sodium amytal, 0.33 Gm. (5 grains), and paraldehyde, 4 cc. (1 dram), dissolved in physiological saline, are given hypodermically or even intravenously in severe cases.

5. Ephedrine sulfate, 0.05 Gm. (¾ grain), hypodermically, or epinephrine, ½ cc. in normal saline, intravenously, is given for collapse.

6. Stimulants, as atropine sulfate, 0.001 Gm. (1/60 grain); strychnine sulfate, 0.002 Gm. (1/30 grain) or camphor in oil, 1 to 2 cc., hypodermically, and 30 cc. (1 ounce) of whiskey may be given but their actual value is questionable.

7. Prophylactic therapy consists of barbital, 0.33 Gm. (5 grains), by mouth one-half hour before, and ephedrine sulfate, 0.025 Gm. (⅜ grain), hypodermically, just before the injection of cocaine derivatives for the purpose of local anesthesia.

CYANIDE POISONING

Cyanide poisoning results from ingestion of hydrocyanic acid (prussic acid), from cyanates taken in error or with suicidal intent, or from inhalation while fumigating. The lethal dose is 0.133 Gm. (2½ grains) of cyanate. From a large dose, death may be instantaneous and the symptoms come on almost with the act of swallowing. If hydrocyanic acid has been taken, the breath has an odor of bitter almonds. Respiration becomes difficult and prolonged, the pulse is feeble, the pupils are dilated, and involuntary urination and defecation occur. Subsequently, convulsions, cyanosis, paralysis, collapse, coma, and death take place. A small dose produces a sensation of weakness and giddiness.

If potassium cyanate is taken, in addition to the above there are gastrointestinal symptoms due to the drug's caustic action. Then nausea and vomiting, constriction of the throat, and a constricting pain in the chest occur also. Confusion of sight and giddiness are common, and the patient falls into convulsions.

TREATMENT

1. Treatment consists first of maintaining the patient in a horizontal position in the open air, of stimulating respiration with spirits of ammonia, and the application of hot and cold water alternately on the chest and spine.

2. Artificial respiration is used if indicated.

3. If possible, the stomach should be washed with hydrogen peroxide, 1:3 dilution, or potassium permanganate, 1.33 Gm. (20 grains) to a pint of water, to form a harmless oxamide. In addition, ferri-sulfate, 0.66 Gm. (10 grains), should be given to form ferricyanate, with hydrogen peroxide used as an oxidizer.

4. While the stomach is being washed with potassium permanganate solution, an assistant should administer amyl nitrite pearls every three minutes. As soon as possible, 10 cc. of three per cent sodium nitrite solution is given intravenously, followed by 50 cc. of a 25 per cent sodium thiosulfate solution. If necessary, the administration of amyl nitrite pearls is continued again while the sodium thiosulfate is given. If the patient survives one-half hour, the prognosis is fairly good. Relapse may occur and consequently the patient should be watched for 48 hours. If relapse sets in, the above treatment should be repeated, using one-half the dosages.

5. Methylene blue, 50 cc. of a one per cent solution, given intravenously, has been considered fairly specific, but its actual value is still questionable. This may be repeated until a total of 200 cc. has been given.

6. Stimulants, as atropine sulfate, 0.0006 to 0.001 Gm. ($\frac{1}{100}$ to $\frac{1}{60}$ grain); strychnine sulfate, 0.002 Gm. ($\frac{1}{30}$ grain) and caffeine sodium benzoate, 0.5 Gm. ($7\frac{1}{2}$ grains), should be given intramuscularly.

7. For collapse, external heat and intravenous fluids are given.

ETHYL ALCOHOL POISONING

Ethyl alcohol poisoning brought on by the consumption of alcoholic beverages is commonly known as drunkenness and in its final stages resembles complete anesthesia. The patient is at first hilarious with a thick speech and uncertain gait, associated with varying degrees of emotional instability, as pugnacity, remorsefulness, and lethargy. Further poisoning results in coma and at times collapse.

TREATMENT

1. If the stage of complete coma is not present, the patient should be allowed to sleep it off.

2. The stomach should be emptied by lavage so the alcohol will not be absorbed.

3. In addition, black coffee and fresh air should be provided.

4. The patient must be kept warm and adequately covered.

5. If he is in coma and collapse, external heat and stimulation with atropine sulfate, 0.0008 Gm. (1/75 grain); strychnine sulfate, 0.002 Gm. (1/30 grain), or caffeine sodium benzoate, 0.5 Gm. (7½ grains), all given intramuscularly, should be administered. Carbon dioxide-oxygen inhalations should be administered. Intravenous fluid in the form of 50 cc. of 50 per cent glucose may be administered.

6. The stage of excitement is controlled by the oral administration of chloral hydrate and sodium bromide, 2 Gm. (30 grains) of each, or paraldehyde, 4 to 12 Gm. (1 to 3 drams).

6. When the patient regains consciousness, the "hangover" should be treated with a saline purge, tea, milk, and toast as tolerated, and aspirin, 0.33 Gm. (5 grains), with caffeine citrate, 0.1 Gm. (1½ grains), for the headache.

METHYL ALCOHOL

Methyl or wood alcohol poisoning results usually from the ingestion of denatured alcohol and anti-freeze mixtures used in automobiles. Since the repeal of prohibition, the number of cases has decreased, but occasionally through ignorance this substance is used as a beverage during drinking bouts. Poisoning can also occur through the inhalation of the fumes, as when methyl alcohol is used in industry. The symptoms develop in a few hours to a few days, and the onset is usually characterized by marked vomiting and abdominal pain, headache, dizziness, and stupor. Later, profound collapse and delirium develop with dyspnea; cyanosis; rapid, weak pulse, and dilated, irregular pupils. Depression of the heart and voluntary muscle results. Disturbance of vision often resulting in blindness is characteristic.

TREATMENT

1. Treatment consists of frequent gastric lavage with four per cent sodium bicarbonate solution and the introduction of some of this solution into the rectum. After the lavage, an ounce of magnesium sulfate should be left in the stomach. At times it may be necessary to administer apomorphine hydrochloride, 0.006 Gm. (1/10 grain). The lavage should be followed by an injection of morphine sulfate, 0.016 Gm. (1/4 grain), hypodermically, in order to lessen the suffering. If the patient is wild, hyoscine, 0.0002 Gm. to 0.0003 (1/300 to 1/200 grain), should also be given.

2. The acidosis may be combated by the administration of several hundred cubic centimeters of a 6/M sodium lactate solution intravenously four or five times a day.

3. The patient should be kept warm and his nutrition maintained.

4. Collapse is treated with external heat and stimulants, as strychnine sulfate, 0.002 Gm. (1/30 grain); atropine sulfate, 0.001 Gm. (1/60 grain); caffeine sodium benzoate, 0.5 Gm. (7½ grains), and camphor in oil, 2 cc. (30 minims) intramuscularly.

5. Drainage of the spinal fluid may help avoid blindness.

IODINE POISONING

Iodine is usually taken in the form of tincture; it may be mistaken for some other medicine or taken with suicidal intentions. As a rule, the only result of its ingestion is stomatitis and perhaps gastritis. On occasions, if treatment is not administered soon enough or if large quantities have been ingested, severe gastroenteritis with nausea and vomiting develop. The patient becomes pale, giddy, and faint, and the pulse is rapid and feeble. A high fever and suppression of urine may occur. At times, the eyelids become swollen and albuminuria may occur. Cyanosis and great excitement, with convulsions followed by collapse, may result.

TREATMENT

1. A solution of starch should be given, and the stomach evacuated with a stomach tube as soon as possible. Lavage should be done with large quantities of water containing egg and starch.

2. This should be followed by administration of demulcents, as white of egg, milk, and bland oils.

3. In case of collapse, stimulants, as brandy or whiskey, 30 cc. (1 ounce), or aromatic spirits of ammonia, 2 to 4 cc. (30 to 60 minims), may be given.

4. Strychnine sulfate, 0.001 Gm. (1/60 grain) every two hours; atropine sulfate, 0.0006 to 0.001 Gm. (1/100 to 1/60 grain) every two hours, and caffeine citrate, 0.24 Gm. (4 grains) every hour, should be given hypodermically.

5. Collapse also requires external heat and intravenous fluids.

6. Administration of morphine sulfate, 0.016 Gm. (1/4 grain), hypodermically, is a means of relieving pain and symptoms of apprehension.

MERCURIC BICHLORIDE POISONING

Mercuric bichloride typifies severe mercury poison and because of its availability poisoning is not rare. Death occurs from taking one 0.5 Gm. (7½ grains) tablet. Ingestion of strong solutions causes corrosion of the mouth, pharynx, esophagus, and stomach. Early symptoms are abdominal cramps and vomiting, often of blood. Later, inflammation and necrosis of the colon and upper rectum, and degeneration of the convoluted tubules of the kidney occur. The patient then dies of a severe colitis with a bloody diarrhea and an anuria resulting in uremia.

TREATMENT

1. The immediate treatment is to remove as much of the mercury from the stomach as possible. A glass of milk and a glass of egg albumen are given, followed by gastric lavage to remove the albumenate formed with the mercury.

2. On admission to the hospital, a second lavage is done and a pint of milk is left in the stomach.

3. The following treatment is then continued until no mercury is found in the urine on two successive days:

a. The patient is given 240 cc. (8 ounces) of milk every two hours, and on the alternate hour 240 cc. (8 ounces) of a mixture of 4 Gm. (1 dram) potassium bitartrate, 4 Gm. (1 dram) sugar, 15 cc. (½ ounce) lactose, 30 cc. (1 ounce) lemon juice, and boiled water to make one pint.

b. Continuous rectal drip administration of a solution of potassium acetate, 4 Gm. (1 dram), to 500 cc. (1 pint) of water. It is important

to carry on this treatment continuously, especially between the fifth and tenth days; at this time, there is a decrease in the amount of urine secreted. If the patient passes this stage of the poisoning successfully, the secretion of urine usually increases, often to high levels.

c. Gastric lavage twice a day.

d. Colonic irrigation twice a day.

e. Hot pack sweat twice a day.

f. Intravenous injections of sodium thiosulfate, 1 Gm. (15 grains), in 10 cc. of aqueous solution twice daily. In severe cases a total of 6 Gm. (90 grains) daily for three to five days should be given.

g. Caffeine sodium benzoate, 0.2 to 0.33 Gm. (3 to 5 grains); strychnine sulfate, 0.002 Gm. (1/30 grain); atropine sulfate, 0.0008 Gm. (1/75 grain), all administered hypodermically, external heat, and intravenous five per cent glucose in physiological saline solution in amounts of 1000 to 3000 cc. should be given for collapse.

h. For pain morphine sulfate, 0.016 Gm. (1/4 grain), hypodermically.

i. Decapsulation of the kidney should be considered when anuria persists for two or three days.

j. Sodium formaldehyde sulfoxylate, 500 to 1000 cc. of a five per cent solution, has been suggested, but this form of therapy does not seem to produce any better results than other measures. It must be given immediately (within one hour) to be of any value. A five per cent solution is used for gastric lavage, after which 200 cc. of the solution are left in the stomach. An intravenous injection is then given, 10 Gm. (150 grains) dissolved in 100 to 200 cc. of fluid, being infused over a 20-minute period. The sulfoxylate may thus come in contact with the mercury bichloride and convert it into an insoluble mercurous compound.

MORPHINE POISONING

Morphine poisoning occurs from either the therapeutic use of too large a dose of the drug or from injection for suicidal purposes. Mild cases show lethargy from which the patient can be aroused, constriction of the pupils, slow respiration, and occasionally nausea and vomiting. Large doses produce marked stupor, Cheyne-Stokes respiration, pin-point pupils, cyanosis, and warm flushed skin. The pulse is slow and regular, and of fairly good quality. Still larger doses produce marked coma; collapse; cold, clammy, cyanotic skin, and marked slowing and irregularity of respiration with long periods of apnea.

TREATMENT

1. The treatment in mild cases consists of keeping the patient awake and in fresh air, and giving caffeine sodium benzoate, 0.5 Gm. (7½ grains), intramuscularly every four to six hours.

2. In the more severe cases, when the drug has been taken by mouth, the stomach should be washed several times with a solution of potassium permanganate, 1 Gm. (15 grains) to a quart of water.

3. Frequent colonic irrigations aid in removing the morphine as it is excreted.

4. If the patient can be aroused at all, he should be kept awake by annoyance with some form of external activity and even walked about if possible. This should be continued ceaselessly until the patient is out of danger.

5. Caffeine sodium benzoate, 0.33 Gm. (5 grains) hypodermically; black coffee orally and per rectum, and ephedrine sulfate, 0.025 to 0.05 Gm. (⅜ to ¾ grain) orally, should be administered every hour if necessary to stimulate respiration.

6. If the patient is in a state of coma and collapse from which he cannot be aroused, the treatment is external heat, oxygen and carbon dioxide inhalations, caffeine, and ephedrine, as above.

7. Artificial respiration must be employed if the natural process ceases.

PHENOL POISONING

Phenol poisoning is characterized locally by the odor and by corrosion of the mouth and tongue with the formation of a white eschar. Systemically, phenol is a depressant of the central nervous and circulatory systems. Large doses cause collapse and unconsciousness, with muscular twitchings and rarely convulsions, followed by death in a few hours from respiratory failure. More dilute solutions cause a more gradual onset of collapse from depression of the vasoconstrictor and respiratory centers. The patient becomes weak, dizzy, and is mentally depressed. The common findings are a rapid, thready pulse; lowered blood pressure; pallor or cyanosis, and a cold, clammy skin. Recovery or coma follows. Later manifestations are ulceration of the mucosa of the stomach with cicatrization, and nephritis.

TREATMENT

1. Gastric lavage with olive oil. After copious amounts have been used, a portion of the oil should be left in the stomach to act as a diluent and demulcent.
2. The patient should be kept warm.
3. Any systemic reaction is treated with respiratory and circulatory stimulants, as caffeine sodium benzoate, 0.13 to 0.33 Gm. (2 to 5 grains); atropine sulfate, 0.0008 Gm. ($\frac{1}{75}$ grain); strychnine sulfate, 0.002 Gm. ($\frac{1}{30}$ grain), and epinephrine, ½ cc. of a 1:1000 solution, all given hypodermically.
5. Hypertonic solutions, as 50 cc. of a 50 per cent glucose solution, are given intravenously for pulmonary edema.
6. Oxygen should be given in case of collapse and cyanosis.

PHOSPHORUS POISONING

Yellow phosphorus is poisonous and is present in rat poison and some old-style matches. Red phosphorus is nonpoisonous and is used on the box of safety matches and for the ends of some other types. The rat poison, in addition to containing yellow phosphorus, may also contain arsenic and strychnine. The symptoms of acute poisoning usually occur after a period of three to four hours. There is a phosphorus or garlic odor to the breath with nausea and vomiting of mucus, bile, and blood. The vomitus is luminous in the dark. Burning pain in the esophagus and abdomen due to inflammation of the gastrointestinal tract is present. There may be diarrhea and bloody stools. Jaundice associated with a large tender liver may develop. The abdomen becomes distended. The patient complains of headache and dizziness. The urine is scanty and contains albumin. Delirium, convulsions, and coma may occur. Death may result in 24 to 48 hours from respiratory paralysis or degeneration of the liver and kidney. Autopsy shows a fatty degeneration of the kidneys, liver, and heart.

TREATMENT

1. The immediate treatment is to wash the stomach with water to which 1 teaspoonful of old oil of turpentine has been added.
2. If no stomach tube is available, copper sulfate, 0.33 Gm. (5 grains) in 30 cc. (1 ounce) of water, should be given every five

to ten minutes until vomiting occurs. The copper sulfate forms an insoluble and nontoxic copper phosphide. Zinc sulfate can be used in a dose of 1.33 Gm. to 30 cc. (20 grains to 1 ounce) of water.

3. Oils and fats and substances containing fats should be avoided as they increase the solubility and absorption of the phosphorus. Liquid petrolatum, owing to its inert qualities, may be given immediately after the ingestion of the phosphorus, followed by a lavage. Petrolatum is used only in case oil of turpentine and copper sulfate are not readily available.

4. After the stomach has been washed, the patient should be given old oil of turpentine, ½ teaspoonful, in warm water or capsules every 15 to 30 minutes. This forms an insoluble mass with the phosphorus.

5. Potassium permanganate, solution 1:1000, or one per cent hydrogen peroxide solution may be used for lavage instead of the above mentioned method.

6. Magnesium sulfate, 30 Gm. (1 ounce) in water, should be given following the above treatment.

7. Hot abdominal stupes, intravenous glucose solution, 2000-3000 cc. of a five per cent glucose in physiological saline, daily with insulin, and calcium salts, as calcium lactate or calcium gluconate, in amounts of 1 Gm. (15 grains) three times a day, should be administered to protect the liver.

STRYCHNINE POISONING

Strychnine poisoning occurs from absorption of strychnine, nux vomica, and brucine. In a mild form, it may be a result of therapeutic overdosage. The patient appears restless and exhibits twitching of fingers or jerking motions of the arm or leg. Some stiffness of the face (rarely), fingers, or gait may be present. Withdrawal of the drug and the administration of bromides or barbiturates will relieve the symptoms. In severe poisoning, a generalized convulsion involving all muscles is present. The position of the patient during the convulsion is in opisthotonos. The action of all the extensor muscles of the body predominates. During the convulsion, there is a marked cramp-like pain in the muscles. The mind is clear and therefore the suffering is great.

TREATMENT

1. The first step in the treatment is the administration of a rapidly-acting barbiturate. Sodium amytal, 0.4 to 1 Gm. (6 to 15 grains), in 10 cc. of sterile water is administered intravenously slowly, and may be repeated if necessary. The dosage cannot be stated dogmatically, but the drug should be given in amounts large enough to control or antagonize convulsions and keep the patient asleep, yet not so great as to depress respiration and blood pressure. Chloroform inhalations may be given to control convulsions until a barbiturate can be given. Prolonged ether or avertin anesthesia may be administered for a period of five or six hours.

2. If there is a possibility that some of the drug is in the stomach after the convulsions are controlled, gastric lavage, using a 1:1000 concentration of potassium permanganate solution, is indicated, or one may administer 1 teaspoonful of tannic acid in one-half glass of hot water, or 15 drops of tincture of iodine in one-half glass of water.

3. The patient should be kept in a dark, quiet room.

4. Bromides in the form of sodium bromide, 15 Gm. (225 grains) by mouth or rectum are beneficial, since they are antagonistic to strychnine in their action on the cord. The bromides may be administered as an adjunct to the barbiturates. However, the patient must be closely observed so that sedatives are not given to the point of respiratory depression.

5. Intravenous physiological saline, 3000 to 4000 cc. daily, should be given to establish free diuresis and to aid in the elimination of the drug. The patient should be catheterized frequently to prevent reabsorption of the excreted strychnine.

6. Inhalations of oxygen are indicated to aid oxidation of the strychnine.

7. Artificial respiration is used as needed.

8. Stimulants, as atropine sulfate, 0.001 Gm. (1/50 grain), and caffeine sodium benzoate, 0.2 Gm. (3 grains), should be administered when necessary.

FOOD POISONING

Contaminated food may cause poisoning characterized chiefly by gastrointestinal symptoms, which may be mild or severe. The severe kind may be fatal, especially in babies, youngsters, and in older, de-

bilitated individuals. Canned food of any kind, salmon, sausage, tomatoes, fruits, and milk may carry the disturbing toxins or organisms. Custards and pastries, such as chocolate eclairs, are excellent culture media for the germ, and are often causes of food poisoning. The term "ptomaine poisoning" is not usually appropriate for this kind of disease, because it is usually the group of organisms of salmonella which is the responsible agent. The ptomaines themselves are not the cause of the food poisoning; the real cause is bacteria. Foods in hot climates, and in warm periods of the year in any climate, must always be watched closely for slightest evidence of putrefaction inasmuch as most of these epidemics occur in the summer.

A period of from 2 to 48 hours elapses after the ingestion of the food before symptoms of intoxication develop; usually the period of incubation is about six hours. There is an explosive onset of signs and symptoms with violent nausea and vomiting, severe diarrhea, abdominal cramps, and evidence of prostration. Fever exceeds 37.8° C. (100° F.), the patient rapidly becomes dehydrated, and signs of dehydration are added to those of intoxication. Circulatory collapse may ensue. The diagnosis is usually easy, especially when it is determined by the history that more than one person eating at the same table became ill. Other conditions, as mesenteric thrombosis, embolism, acute appendicitis, acute pancreatitis, and ulcerative colitis, may simulate the gastroenterocolitis of food poisoning.

TREATMENT

1. On reaching the patient's bedside all foods that have been partially eaten should be collected for examination. The vomited material too should be taken to a laboratory for bacteriological examination and identification of the organism.

2. The stomach should be washed out with saline solution and kept up until all the contents of the stomach have been removed. The bowels should be thoroughly evacuated as soon as possible. If there has not been a free bowel movement after the stomach has been cleaned out, magnesium sulfate, 15 Gm. (½ ounce), should be given; cleansing the lower bowel with a plain water enema is often of benefit.

3. An intravenous administration of 1500 to 2000 cc. of ten per cent glucose solution should be started immediately, and repeated every eight hours to combat dehydration.

4. A hypodermic injection of dilaudid, 0.002 Gm. (1/24 grain), is often sufficient to overcome the severe cramps. Hot stupes are of benefit.

5. If the patient is able to take drugs by mouth, one teaspoonful of paregoric in warm water, repeated every four hours, is beneficial, or a teaspoonful of a preparation containing 16 Gm. (4 drams) of tincture of belladonna and 120 Gm. (4 ounces) of elixir of phenobarbital may be given every three hours to obtain sedation of the patient in general, and of the bowels in particular.

6. If the patient has gone into an episode of serious vascular collapse, external heat must be applied and caffeine sodium benzoate, 0.24 Gm. (4 grains), may be given intramuscularly. Occasionally, oxygen is indicated. Within a period of 12 hours patients usually recover.

MUSHROOM POISONING

TREATMENT

Treatment consists in gastric lavage with warm water as soon as possible and the administration of atropine sulfate, 0.001 Gm. (1/60 grain), intramuscularly. At times, the patient is greatly depressed, and coramine, 0.24 Gm. (4 grains), intramuscularly or intravenously may be given. It is wise also to administer 1000 cc. of ten per cent glucose in normal saline intravenously. Transfusion may be necessary. Administration of freshly chopped brains and stomachs of several rabbits by mouth is said to produce a combination with the toxin and act as a specific.

There are two main types of mushroom poisoning. In one, the symptoms are largely those of gastroenteritis. In the second, and more fatal type, the symptoms and findings are largely those of injury to the nervous system, with headache, somnolence, trismus, mydriasis, sometimes opisthotonos with other forms of muscle cramps, at times blindness, loud cries, and ultimately coma. The symptoms commonly appear four to five hours after the meal. Atropine sulfate is a specific in treatment of the latter type and should be given until the physiological effect is produced.

LEAD POISONING

Lead poisoning is one of the most important industrial diseases. It most frequently occurs among workers exposed to lead. However,

it must be emphasized that many people who are exposed to lead do not absorb it; lead poisoning only occurs when lead is absorbed over a considerable period of time. True acute lead poisoning is quite rare, since it usually develops after the sudden intake of large doses of lead, as those taken with suicidal intent. It is this type, as well as the acute exacerbation of the chronic type, that a physician is called on to treat.

Etiology: Lead may enter the body through the gastrointestinal tract, the respiratory tract, or even through the skin. Some cases have resulted from the use of hair dyes, cosmetics, or ingestion of painted surfaces by children, but the majority develop from occupational contact with lead in some form.

When painters, metal finishers, sprayers, or other lead workers do not cleanse their hands carefully before eating, they may swallow lead with their food. However, the alimentary tract is the least dangerous avenue for the entrance of lead, since most of the lead absorbed goes to the liver, where there is a barrier which it must go through to reach the other internal organs. Consequently, most of the lead taken by mouth is filtered by the liver and there are no ill effects.

The lung is the most dangerous path of entry. Since there is no protective barrier, the lead is absorbed directly into the circulation of the lung, carried to the heart, and distributed to the essential internal organs, the brain, kidneys, liver, muscles, and nervous system.

When lead is absorbed into the body by any of these routes, it is deposited in the bones. It forms a chemical combination with calcium; the calcium is deposited in the bones and the lead becomes inert. As times goes on, the deposited lead may be released from the bones and enter the blood stream, thereby producing acute lead poisoning after the initial exposure. Lead in the bones is always a potential source of an acute attack of lead poisoning.

Signs and Symptoms: Lead absorption is characterized by the presence of lead in the stools and a "lead line" on the gums. This "lead line" is not found in the absence of teeth or in a completely healthy mouth; otherwise, it is usually present on the buccal rather than the labia aspect of the gums and most often around the molars. The four principal signs of lead poisoning are colic, anemia, palsy, and "lead line."

In acute lead poisoning, that occurring after short but severe exposure, the onset consists of sudden illness with marked weakness, severe colic, nausea and vomiting, with or without constipation. The picture resembles acute intestinal obstruction or some acute abdominal condition, which is ruled out by the normal pulse, temperature, and leukocyte count and the history of lead exposure or lead in the urine. In the more chronic type, the patient becomes ill gradually. There is a history of loss of appetite and weight, weakness, lassitude, mental depression, constipation, and attacks of mild abdominal distress. Perhaps the first cause for complaint is wrist drop or some loss of functions of the hands or arms. Lead poisoning may bring about injury to almost any organ of the body. There may be lead encephalitis, lead nephritis, or lead arteriosclerosis.

The blood picture usually reveals early evidence of lead poisoning. The characteristic feature of the anemia is that the count seldom drops below three million. There is marked destruction of erythrocytes with an increase in red cells. "Stippled" cells appear, blood study showing 100 stipplings to 1,000,000 red cells, though the stipplings have ceased to be looked on as an outstanding diagnostic feature because so many patients with idiopathic anemias of other types show it.

Another important diagnostic feature is the appearance of lead in the urine, which points to lead intoxication; this is not true of lead in the feces.

TREATMENT

1. The main object of the treatment of acute lead poisoning is to immobilize the lead in the blood stream. This is accomplished by giving large doses of calcium by mouth or vein, since it combines with the lead and both are deposited in the bone.

2. A nutritious diet should be given. A milk diet, or 6 to 8 Gm. of calcium added to one or two quarts of milk, aids in the immobilization of lead.

3. The colic may be relieved by intravenous calcium gluconate, atropine, nitroglycerin, or the application of heat.

4. A saline cathartic or enema may be given if the diagnosis is certain; it will increase the elimination of lead.

5. Large doses of iron should be given.

6. Sodium citrate, 4 Gm. (60 grains) in one ounce of water, three times daily, or for severe cases, 50 cc. of a sterile 2.5 per cent aqueous sodium citrate solution intravenously relieves symptoms.

7. After the acute episode is passed, the process of "deleading" should be started. The hydrogen ion concentration of the blood is slightly increased by the administration of large doses of ammonium chloride, 3.3 Gm. (50 grains), three or four times a day. Sometimes potassium iodide will assist in the liberation of lead from the system. By slightly increasing the hydrogen ion concentration, the lead is delivered up to the blood stream and excreted in the urine and feces. Thus, small amounts of lead are given off from the deposits and acute episodes of lead poisoning will not occur.

CHAPTER XXIV

Drugs

DRUGS USED IN THE TREATMENT OF HEART DISEASE

When we speak of the drug treatment of heart disease and heart failure, we may classify the drugs into three classes:

1. Drugs that affect the heart directly:
   a. Digitalis.
   b. Quinidine.
   c. Squills.
   d. Strophanthin.
2. Drugs that are adjuncts to therapy. These drugs, called diuretics, do not help the heart directly.
   a. Xanthines, as theobromine, which increase the flow of urine.
   b. Mercurials, as salyrgan, which work on the tubules of the kidneys.
   c. Acid-forming salts, as ammonium chloride, which work out in the cells of the body, affecting the electrolyte responses.
3. Soporifics or sedatives, which are important aids in treatment:
   a. Barbiturates.
   b. Bromides.
   c. Opium alkaloids.
   d. Chloral hydrate and miscellaneous agents.

Digitalis: Of all the drugs used in the treatment of heart disease, digitalis is the most reliable and trustworthy. No other drug requires more experience, skill, and care in administration. Gastrointestinal disturbances, bradycardia, cerebral symptoms, and skin manifestations may develop in the course of digitalis therapy, but careful administration will usually avert these complications. The disappointments attending the use of digitalis arise not so much from toxic manifestations as from its use in cases where it is contraindicated and from underdosage.

For an understanding of the clinical use of digitalis, its pharmacological action must be considered. This may be summarized as follows: (1) It slows the heart rate by virtue of its depressing action on the sinoauricular and auriculoventricular nodes. (2) It acts upon the muscle of the auricles and ventricles, and retards the conduction

through the auriculoventricular bundle of His. (3) It increases the tonicity and the contractile power of the heart muscle, resulting in a more complete contraction of the ventricles and more effective emptying of the chambers. This leads to a greater cardiac output and improvement of the circulation.

Indications: There are three, possibly four, main indications for the use of digitalis: (a) Congestive heart failure associated with auricular fibrillation. The results of digitalis therapy are most outstanding in this condition. (b) Congestive heart failure with normal rhythm. Here the effects of digitalis are desirable, but they are not as dramatic as when fibrillation exists. (c) Auricular flutter. In these cases, digitalis converts the flutter into fibrillation which it controls satisfactorily. (d) Hypertensive heart disease. Some authorities believe that small doses of digitalis given before heart failure begins prevent further dilatation and hypertrophy, and forestall heart failure.

Methods of Administration and Dosage: Digitalis is most commonly prescribed in tablet, pill, powdered leaf in capsule, or in the tincture forms. These preparations are standardized so that one tablet, one pill, one capsule, and 1 cc. of the tincture each represent one cat unit, which is the American unit of the potency of the drug. A cat unit is the number of milligrams of digitalis needed to kill one kilogram of cat when the drug is slowly and continuously injected into the vein. It does not make much difference which preparation is used, for in most cases the digitalis effect is obtained from any one of them. Occasionally it is found that a patient responds better to one form than another, and the tolerance to the drug varies in different individuals.

As a general rule, the drug should be given in sufficient doses to obtain the desired effect as soon as possible. This is accomplished best by giving one cat unit four to six times a day. Although other methods have been advocated, none is superior to the oral administration of ordinary doses at frequent intervals throughout the day. Digitalis should be given until the therapeutic effect has been obtained, and then the dose should be moderated so one cat unit three times a day will be sufficient to maintain the optimum digitalis action.

Digitalis may be given intramuscularly, but this is to be discouraged as much as possible because of the pain caused by the injection and because effective action is difficult to obtain this way. For rapid

digitalization, which is rarely required, 0.2 Gm. (3 grains) (two tablets, pills, capsules, or 2 cc. of the tincture) may be given orally four times a day for two or three days. In case of emergency, 0.5 Gm. (7½ grains) in solution, such as 10 cc. of digifoline or some other preparation, may be given intravenously and repeated two or three times a day for several doses.

Contraindications: It is as important to know when digitalis should not be given as when it is indicated. In brief, the conditions in which digitalis is sometimes used and in which it is not only ineffective but may actually be harmful are as follows: (1) The tachycardia following operations and postoperative infections; (2) the rapid heart of acute infectious disorders, such as pneumonia; (3) coronary thrombosis; (4) extrasystoles; (5) tachycardia of hyperthyroidism; (6) paroxysmal tachycardia, and (7) heart block. Although the drug may be administered to patients who are arteriosclerotic, digitalis must be given to older people with considerable caution. Also, digitalis does not combine well with certain other drugs. For example, it must not be given to a patient who is taking calcium, epinephrine, ephedrine, or atropine.

It is important that a patient taking digitalis be examined frequently in order to avoid overdosage. The results of overdosage may be summarized as follows: (a) There may be nausea, vomiting, or diarrhea. (b) The heart may be slow and coupling of the beats may occur. (c) There may be cerebral symptoms, such as headache, delirium, depression, confusion, or visual disturbances. Omission of digitalis for two days usually clears up these unfavorable reactions, and the drug may then be given again in smaller doses for a period of a few days.

Recently extracts of digitalis lanata (yellow digitalis) have been used in cases where digitalis purpurea caused nausea, vomiting, or intoxication. A bright future for the preparations of digitalis lanata is forecast. They are administered in doses of 0.1 Gm. (1½ grains) as is digitalis purpurea.

Quinidine is not as widely used as digitalis because sometimes it results in embolism and death. It is a protoplasmic poison. It may be used advantageously in:

1. Young individuals with auricular fibrillation; it is not a drug for the treatment of heart failure, but only for fibrillation in young people.
2. Patients without mitral stenosis or any valve disturbance.
3. Patients without much dilatation or failure of the heart.
4. Post-thyroidectomy cases with auricular fibrillation.
5. Patients who are not helped by digitalis.

Quinidine is a destroyer of the heart muscle so it should not be used over a long period of time. It slows the impulses of the heart coming down from the auricle through the A-V node to the ventricle. It acts as a depressant.

Quinidine sulfate is usually used. It is a bitter, white crystalline powder, fairly insoluble in water, and is usually prescribed in capsules of 0.2 to 0.5 Gm. (3 to 7½ grains). Both quinidine and digitalis slow auricular impulse conduction and lengthen the refractory period, but since quinidine depresses restorative metabolism, it is used for the arrhythmia to restore the disorder to normal. Quinidine has almost the same toxic effects as quinine. It may produce cinchonism, nausea and vomiting, respiratory distress, giddiness, cyanosis, and cold perspiration. Other unfavorable results are ventricular fibrillation and standstill, embolism, or increased ventricular rate.

Before starting quinidine administration, the patient should have complete bed rest and sedation for two or three days. Digitalis should be given and treatment completed in all patients with ventricular rates over 90 beats per minute to forestall dangerous tachycardia. It is usually best to give a test dose of 0.2 to 0.3 Gm. (3 to 4½ grains) of quinidine to see how it reacts, and if there are no unsatisfactory results, a course of treatment of 0.4 Gm. (6 grains) every four hours or five times daily should be given for a period of about one week. If there are toxic effects, tachycardia over 125 beats per minute, obstinate flutter, or if normal rhythm is not restored by the tenth day, administration should be discontinued. Then two weeks later, treatment may be started again. If normal rhythm is restored, a dose of 0.2 to 0.3 Gm. (3 to 4½ grains) of quinidine should be given three times daily for a short time and then gradually omitted.

Quinidine should not be used on patients with acute infections or vegetative endocarditis, advanced organic change in the myocardium without heart failure, long-standing auricular fibrillation or

chronic valvular disease, complete heart block, embolic phenomena, when the heart is seriously damaged, or in elderly patients.

Squills as such are obsolete. A squill is a sea onion belonging to the lily family. Its glycosidal fractions are in the form of urginin, scillaren, and scillaren-B.

Strophanthin: Ouabain is a crystalline glycoside from strophanthus which contains digitalislike drugs. It is not usually used by physicians, since digitalis is preferred. Strophanthus tincture causes diarrhea and since it varies in potency and is often poorly absorbed by the intestinal tract, poisoning is apt to result. Ouabain and amorphous k-strophanthin-B (strophanthin) are sometimes used parenterally. Strophanthin is usually given in 0.0006 Gm. ($\frac{1}{100}$ grain) doses for quick action on patients with fibrillation and failure. Most physicians recommend 0.0006 Gm. ($\frac{1}{100}$ grain) once a day, but the author prefers to give it twice a day. There is a difference of opinion as to its effectiveness, but the author finds it does good. It sometimes results in nausea, vomiting, and irrationality. It must be emphasized that digitalis must not have been used for at least five days before beginning the use of strophanthin; otherwise the heart will stop still in systole.

Drugs that are adjuncts to therapy:

Xanthines: This group is composed of caffeine, theobromine and theophylline, and their salts. They act on the kidneys, stimulate the central nervous system and myocardium, and dilate the coronary vessels. Caffeine is not used very much because it acts as a stimulant on the brain. Theobromine is given in doses of 0.6 Gm. (10 grains) orally three or four times a day for four or five days. Theophylline is administered in doses of 0.3 Gm. (5 grains) on the same routine. The salts of these drugs, which include theobromine sodium salicylate, theobromine sodium acetate, theocalcin, theophylline sodium acetate, theophylline calcium salicylate, and theophylline ethylenediamine, are given in oral doses of 0.5 Gm. (7½ grains) three or four times daily. The salts usually cause nausea and vomiting.

These drugs tend to raise the blood pressure by central vasomotor stimulation, but they cause the blood pressure to fall by the peripheral action on blood vessels. When the patient has cardiovascular disease, caffeine cannot be used because of its stimulation of the nervous system. The other two xanthines are usually used in angina pectoris

and are best given at mealtime to lessen gastric irritation. Best results are obtained when they are used in conjunction with sedatives or nitrites. Theophylline is often used to bring relief in cases of paroxysmal cardiac dyspnea and cardiac asthma.

The most commonly used *mercurials* are novasurol, salyrgan, mercupurin, and mercurin. They are the most potent diuretics; diuresis starts in two or three hours and is over in about ten hours. Nearly all of the injected mercury is excreted by the kidneys. The diuretic action of the mercurials seems to be renal. Salyrgan is the most commonly used mercurial since it is less toxic yet more effective than the others. It is often combined with theophylline. Mercupurin is usually combined with a xanthine also.

Novasurol, though it produces profound diuresis, seems to cause toxic reactions in some people, and for this reason less toxic organic salts are usually used. Merbaphen (novasurol) is used with hesitancy in cases of noncardiac edema because it produces certain irritation, as stomatitis, vomiting, proctitis, bloody diarrhea, as well as a decrease in urinary output and showers of casts and red blood cells.

Salyrgan, a nonirritating mercurial, is a ten per cent solution of mercury-salicylallylamide-o-acetate of sodium. The initial dose of 0.5 cc. (7½ minims) intravenously is raised to 1.5 or 2 cc. (22½ or 30 minims) once or twice a week. This may be increased to 3 cc. (45 minims) one to three times a week, depending on the results. Diuresis usually occurs in one to four hours and is complete in eight to 12 hours, so it is best to give this drug in the morning. It is usually given intravenously though it may be administered intramuscularly or rectally in suppository form, but the latter is not recommended since it usually causes irritation. In patients with congestive heart failure and edema, salyrgan decreases tubular reabsorption and outpouring of edema fluids.

Mercupurin is a sodium salt of trimethylcyclopentane-dicarboxylicacid-methoxy-mercury-allylamide-theophylline, containing theophylline, 3.5 per cent combined and 1.5 per cent free or 21.5 per cent mercury. It differs from salyrgan in that camphoric acid is substituted for salicylic acid and is more effective and less toxic. Mercupurin and salyrgan-theophylline are given intravenously and intramuscularly, but mercurin is given rectally. Mercupurin is usually given intramuscularly if the patient has a diseased heart.

The mercurials come in ampules containing 2 cc. (30 minims) of a ten per cent solution of the drug, and this is the intravenous or intramuscular dosage. It is wise to give a smaller test dose of 0.5 cc. (7½ minims) to see if there are any toxic effects. Doses should be given every three or five days for several doses and then once a week if necessary. A medication of acid-forming salts should be administered if the mercurial alone does not produce the desired results. Mercurials are especially indicated for cardiac edema and in patients with nephrotic edema, but they should not be used in cases of nephritis. Kidney damage and poisoning result from their use in cases of impaired renal function.

The *acid-forming salts* are composed of calcium chloride, ammonium chloride, and nitrate. They exert an osmotic force in the tubular urine, preventing water reabsorption, and diuresis results. These salts are given orally in either enteric-coated tablets or capsules in divided doses of 8 to 12 Gm. (120 to 180 grains) daily. This dosage will start or continue diuresis and relative acidosis. Other diuretics, such as organic mercurials, may be used with these drugs. Ammonium nitrate is most commonly prescribed because it is less liable to irritate the stomach and cause nausea.

Sedatives:

Barbiturates: For clinical purposes this group of drugs is usually divided into the short-acting and the long-acting groups. The short-acting drugs are not usually indicated in the treatment of heart disease, except in unusual cases. A confusingly large number of the long-acting groups is available, such as phenobarbital, barbital, neonal, amytal, ortal, etc. Perhaps the most satisfactory drug in the long-acting group is phenobarbital, which may be given in the form of tablets, capsules, suppositories, or solution. Usually, it is prescribed in tablet form, 0.1 Gm. (1½ grains) being given at the hour of sleep. In the elixir preparations, the ordinary dosage is one teaspoonful three times a day. Another long-acting drug used frequently is amytal, which may be given in tablet form, 0.2 Gm. (3 grains) being the usual dosage. These preparations given in the above doses have little effect on the cardiovascular system, although the blood pressure and pulse rate may fall as a result of the quieting action or sleep produced by their administration. Untoward reactions may occur, how-

ever, when patients with congestive heart failure receive barbiturates. Patients of the younger age group tolerate barbiturates better than those of the older group.

Bromides: For sedation of a mild degree, bromides are employed frequently and tend to lessen anxiety and worry, and to quiet patients with cardiac disorders or hypertensive vascular disease. They are always given by mouth in the form of salts, such as sodium, potassium, ammonium, or calcium, in capsules, or in solution with syrupy vehicles. They are usually given after meals and with plenty of water to disguise the unpleasant taste, lessen gastric irritation, and counteract the diuretic salt action of the various preparations. Sodium bromide is perhaps the preferable drug, but triple bromide, which is a preparation containing equal parts of sodium, potassium, and ammonium salts of bromide prepared in effervescent salts, is the most pleasant form in which to prescribe the drug. Dosage of bromides cannot be stated dogmatically. Moderate sedation is usually achieved in adults who are in good physical condition by administration of 1 to 3 Gm. (15 to 45 grains) daily, providing the patient is eating well. This amount may prove toxic to some patients, and the physician must be alert for the symptoms of bromide intoxication. The drug should not be given for a period of over two or three weeks when patients cannot be kept under surveillance.

Opiates: The opiates should not be given when other drugs may be given to secure sedation, tranquillity, or sleep. In many cases, however, the opiates must be resorted to in order to provide the necessary relief from insomnia, restlessness, or excitement and thus conserve the patients' strength. Morphine, codeine, papaverine, and pantopon are the drugs most commonly used clinically.

Chloral Hydrate: This drug causes sedation usually without preliminary excitement. Ordinarily it produces sleep in from 10 to 15 minutes after administration and is given in amounts of from 0.66 to 2 Gm. (10 to 30 grains). It is ordinarily administered in water or milk, or a syrupy vehicle. Formerly, it was believed that chloral hydrate had a depressing effect upon the heart muscle, but this is largely erroneous; the blood pressure may fall slightly from muscular inactivity. Untoward cardiac effects occur only with toxic doses in patients with heart disease.

The miscellaneous agents include paraldehyde, sulfonal, trianol, etc., and are not usually used in the treatment of heart disease

THE SULFONAMIDE DRUGS

There has been such an outpouring of literature on the sulfonamides during the past few years that one may assume a general knowledge of these drugs is possessed by all. The chemical aspects, the pharmacological action, the therapeutic indications, and the toxicological reactions of the sulfonamide drugs have been studied extensively, but in none of these fields has our knowledge become very complete. To date, the following five members of the sulfonamide group have been established experimentally and clinically: Sulfanilamide, sulfapyridine, sulfathiazole, sulfadiazine, and sulfaguanidine. Most likely many other derivatives of the sulfanilamide nucleus will appear as time goes on, for research workers and clinicians alike are striving for the model drug—one that hits the invading bacteria hardest and is least harmful to the body.

When one administers the sulfonamides, it is important to know the following: When to use them, which drug to employ, the dosage, how long to continue therapy, and what toxic reactions to watch for so proper treatment may be administered. These drugs have not simplified, but have complicated, therapeutics. Employment of them requires knowledge of the drug itself, its absorption, excretion, distribution in the body, and optimum blood level. How it performs its beneficial action must be studied, and most important of all for clinicians are the effects it has on the various systems of the body.

The historical aspects of the development of sulfanilamide and its derivatives are entertaining as well as instructive. Without doubt, Ehrlich must be given some credit for the development of the sulfanilamide preparations, for it was he who studied the effect of dyes upon animals and parasites and bacterial organisms. He dealt especially with the permeability of certain organisms to various kinds of dyes. In 1908 a research chemist synthesized the chemical known as prontosil (diamino-azo-benzene-sulfonamide). While this chemical was used in the composition of dyes, its effect on disease was not considered important at that time. In 1920, this formula for prontosil was patented in Germany. It was not until 1933 that Foerster spoke of the use of prontosil in the treatment of staphylococci infections.

In 1935, Domagk's stirring paper appeared. He pointed out that prontosil was effective in controlling streptococcal infections in experimental animals in 100 per cent of cases. Clinical reports attested the value of prontosil in medicine. From 1936 until the present time, there has been continuous activity in developing the various fields of sulfanilamide and its derivatives. Sulfanilamide is the name applied in the United States for the chemical formula identical with the original prontosil of Germany. The various sulfonamides are derivatives of the sulfanilamide nucleus.

Mode of Action: These drugs of the sulfonamide series have certain general features in common, but the individual preparations possess specific therapeutic indications and are capable of selective toxic reactions.

The aphorism of Ehrlich indicates his ideal in chemotherapy—a chemical agent which is "maximally parasitotropic and minimally organotropic." Some members of the sulfonamide group appear to come closer to this sought-for ideal than others. Yet it takes years of painstaking study to determine which drugs are most effective in controlling bacteria and at the same time are least toxic for the patient. Not only the immediate toxic effects must be studied but also the remote consequences.

The exact mode of action of the sulfonamides is not entirely known. It is assumed that they have a bacteriostatic action, and for practical purposes at this time it is a satisfactory explanation, though a more precise action of the drug may be shown to exist later on. Certain animals are more susceptible to the toxic effects of the sulfonamides than others; dogs are especially resistant to them, while guinea pigs, rabbits, and human beings are considerably less so. The immediate toxic effects are well established, but the consequences that may appear later are hardly known at all. While all members of the sulfonamide drugs are used to treat almost any infection in the human being, certain of them appear to be more effective in some infections and less active in others.

Therapeutic Indications (Chart I): When confronted with a patient who has an infection, one usually turns to the sulfonamide drugs for treatment. It must be emphasized that the rules of therapeutics have not changed appreciably with the introduction of the sulfonamide drugs; that is, the best possible diagnosis should be made be-

fore applying the treatment. The tendency to resort immediately to these powerful drugs is often followed with the best intentions of saving time and establishing treatment before it is too late. It is doubtful if in most cases such haste is indicated or desirable. But if a patient has an obscure infection of severe grade and the exact bacteriological diagnosis is not forthcoming within a reasonable length of time, *e. g.,* 24 hours, there should be no reluctance in giving one of these drugs without waiting for further reports. As a rule, a correct diagnosis from the bacteriological standpoint is desirable and important because the action of certain sulfonamides is more positive in some infections than in others.

Sometimes there is confusion concerning which drug is to be chosen in a given case. While an exact answer cannot be given to the question every time, it is true that each of the five drugs has a special field in which it appears to outdo the others in benefit to the patient. For example, sulfanilamide is the chief drug when a streptococcal infection is present, whether it is an infection of the glands of the neck, sore throat, peritonitis, pneumonia, or infection at any site. Sulfapyridine has a special sphere of usefulness in pneumonia and in pneumococcal infections of the meninges, the middle ear, or elsewhere. It is specifically indicated in gonococcal infections. Sulfathiazole seems to be almost as good as sulfapyridine in the treatment of pneumonia and has a slight advantage in that it is less toxic. Its special field of usefulness appears to be in its action against staphylococcal infections and pneumonia. Sulfaguanidine is one of the newer preparations and its main action occurs in the large bowel. The treatment of dysenteries, particularly of the bacillary kind, seems to be the special field for this drug.

Sulfadiazine is the sulfonamide of choice in most infections with the exception of the streptococcal types, where sulfanilamide remains the main drug. Experiences with sulfadiazine in the treatment of pneumonia, meningitis, staphylococcal infections, and to some extent streptococcal infections have been satisfactory. It seems that sulfadiazine's superiority is accounted for by the fact that it passes with ease through membranes, such as the meninges, pleura, and peritoneum. The concentration of sulfadiazine in the spinal fluid can be raised to almost the same heights as that of the blood. The chief reason for the popularity of sulfadiazine is its relative freedom from toxic reac-

tions. Vomiting and agranulocytosis occur infrequently. Anemia is a rare complication. Anuria, hematuria, and albuminuria are less common than with sulfapyridine, but they must be watched for when sulfadiazine is used.

Dosages: When indications appear which require the use of sulfonamide therapy, the drug should be started promptly and repeated every three or four hours without interruption. The initial dose of any one of the sulfonamides is about the same, that is, 2 Gm. (30 grains) at once and 1 Gm. (15 grains) every four hours until the disease is controlled. Some have advocated a larger initial dose, but this does not seem to be a good policy, as the large initial dose may cause nausea and vomiting. Naturally one wishes to build up the concentration of the drug in the blood stream to the optimal point as soon as possible and keep it there. In certain individuals this is easy to do; in others, it is more difficult. It is of considerable aid to determine the concentration of the drug in the blood stream every 24 or 36 hours. The absorption and excretion determine the concentration, so it is necessary to know how much of the drug is in the blood stream for immediate action. The quantity of fluid taken in a day has a direct influence on the concentration. If 4000 or 5000 cc. of fluid are administered daily, the drug may be so diluted or washed out so rapidly that proper concentration in the blood is difficult to obtain. The generally accepted procedure is to give the patient about 2500 cc. of fluid a day which should yield about 1000 cc. of urine.

The optimal concentration runs about the same in all: sulfanilamide, 8 to 12 mg. per cent; sulfapyridine, 4 to 6 mg. per cent; sulfathiazole, 5 to 8 mg. per cent; sulfadiazine, 8 to 12 mg. per cent, and sulfaguanidine, 8 to 12 mg. per cent.

When the sulfonamides are used, doses should be adequate. Sometimes in a state of indecision, one is apt to try a middle course and give small doses less often. Experience shows that if the drug is injurious, a small dose will do about as much harm as a large one. Therefore, therapeutic doses should be given. Occasionally there is hesitancy in giving the drug when the patient is very weak, anemic, jaundiced, or when albuminuria is present. These are not contraindications, for the drug probably will not make these conditions worse. When such features develop after one has been employing the drug for some time, they may be signals that an essential organ is

being damaged by the drug, and, of course, then the drug must be stopped. An error that creeps in occasionally in the management of patients is that the drug is stopped as soon as the patient shows a little improvement or when the fever drops to normal or near normal. Continue to give the drug until the patient is well and afebrile for three or four days. Otherwise the bacteria which have been rendered static and impotent for the time being may be replaced by more active forms and shortly one will see a recurrence of the same old symptoms of the disease.

It has been a practice to use citrocarbonate or soda bicarbonate along with some of these preparations, and there is a practical value in doing so. Alkalinization seems to minimize the formation of sulfonamide crystals in the urinary tract.

Formerly, it was believed that one had to be very careful about using other kinds of therapy along with the sulfonamide drugs because toxic products might be formed. This idea, to a large degree, has been dispelled by more recent observations. It probably is best not to use magnesium sulfate as a cathartic, but usually even this procedure does not cause any trouble. In using intravenous preparations, glucose is not employed. Plain distilled water is used because glucose with the drug forms a product which is not well absorbed by renal tubules and this renders it difficult to maintain average concentrations.

Sometimes sulfapyridine or any one of the group causes nausea and vomiting, and the drug must be discontinued by mouth. When this occurs, tincture of belladonna with elixir of phenobarbital may be given shortly before the administration of the drug, and then it is borne better. In case any of the sulfonamide drugs cannot be given by mouth for one reason or another, it should be administered intravenously. Sulfanilamide, and sodium salts of sulfathiazole or sulfapyridine may be given in this way. It is best to try to supplement the intravenous injections with as much of the drug as possible by mouth. For intravenous use, 5 Gm. (75 grains) of the drug are dissolved in 100 cc. of sterile distilled water and given two, three, or four times a day.

In considering the therapeutic uses of any of the sulfonamide preparations, it is important to remember that localized abscesses or collections of pus are not penetrated to any great extent by these

drugs and therefore the usual methods of treatment, surgical incision and drainage, are indicated as in any other cases. However, vigorous treatment with the drugs may prevent the formation of such inaccessible collections of pus.

Considerable attention has been devoted to the local application of these preparations. Striking results have been obtained by some observers. Some advocate irrigation two or three times daily with sulfanilamide in cases of streptococcal infection. The use of sulfonamide powdered preparations directly on infected wounds of the peritoneal cavity has been recommended widely and seems to be a very effective method of treatment. The amount of the drug to be given depends on the concentration in the blood stream when the drug is administered by mouth.

Toxic Manifestation (Chart II): When one has decided to use a sulfonamide drug in treatment, he must be willing to take on the responsibility of seeing that the patient is more benefited than harmed by the treatment. This requires that he see the patient daily, for by simple clinical observations one can usually detect if the drug is not being tolerated well. A blood count and urinalysis must be made at frequent intervals, at least every second day, so one can discover the early evidences of an unfavorable effect upon the hemopoietic system and the kidneys. These are the safeguards that a patient may expect from the medical advisor. The practice of giving the drug and neglecting the patient is to be condemned. A patient may continue to take one of these preparations for a long time and no unfavorable complications may develop; yet in another case, a serious result may occur when safeguards are overlooked.

There are certain toxic manifestations which are characteristic of the sulfonamide drugs as a group, but some of the preparations have a special tendency toward causing definite reactions. In general, the group as a whole may affect the gastrointestinal organs, the nervous system, the hemopoietic organs, and the renal system. Nausea, vomiting, and diarrhea are features of gastrointestinal intoxication. The nervous system may become involved in more than one manner. There may be actual peripheral neuritis, but headache and mental depression are commoner. Anemia, agranulocytosis, and purpura may occur with any of the drugs, but particularly with sulfapyridine and sulfathiazole. Hematuria and calcareous deposits in the kidneys

CHART I — INDICATIONS FOR SULFONAMIDE DRUGS

Disease	*Sulfanilamide*	*Sulfapyridine*	*Sulfathiazole*	*Sulfadiazine*
STAPHYLOCOCCAL INFECTIONS:				
Sepsis	X	XX	XXXX	XX
Pneumonia	X	XXXX	XXXX	XXX
Meningtis	X	XX	XXXX	XXXX
Endocarditis	X		XXXX	XXXX
Carbuncle	X	XX	XXXX	XXXX
Osteomyelitis		XX	XX	XXX
HEMOLYTIC STREPTOCOCCAL INFECTIONS:				
Tonsillitis	XXXX	XX	X	
Peritonsillar abscess	XXXX	XX	X	
Ludwig's angina	XXXX	XX	X	
Otitis media	XXXX	XX	X	
Mastoiditis	XXXX	XX	X	
Meningitis	XXXX	XX	X	
Erysipelas	XXXX	XX	X	
Cellulitis	XXXX	XX	X	
Pneumonia	XXXX	XX	X	
Peritonitis	XXXX	XX	X	
Puerperal sepsis	XXXX	XX	X	
Septicemia	XXXX	XX	X	
VIRIDANS STREPTOCOCCAL INFECTIONS:				
Osteomyelitis	XX	XX		XX
Meningitis	XXXX	XXXX		XXX
Endocarditis	X	X		XXX
Septicemia	XXXX			
PNEUMOCOCCAL INFECTIONS:				
Pneumonia	X	XXXX	XX	XXXX
Meningitis	X	XXXX		XXX
Otitis media	XX	XXXX	XX	XXX
Mastoiditis	XX	XXXX		XXX
Sinusitis	XX	XXXX		XX
Peritonitis	X	XXXX		XX
MENINGOCOCCAL INFECTIONS	XX	XX	XX	XXXX
GONOCOCCAL INFECTIONS:				
Male gonorrhea	XX		XXXX	
Female gonorrhea	XX		XXXX	
Arthritis	XX		XXXX	
Endocarditis	XX		XXXX	
Ophthalmia	XX		XXXX	
RHEUMATIC FEVER	O	O	O	O

KEY TO TABLE:

XXXX—Preferred drug. XX—Active. X—Slight activity. O—Should not be used.

CHART II — TOXIC EFFECTS OF SULFONAMIDE DRUGS

Toxic Manifestations	*Sulfanilamide*	*Sulfapyridine*	*Sulfathiazole*	*Sulfadiazine*
Nausea and vomiting	Uncommon; occurs early	Very frequent	Rare	Rare
Cyanosis	Common, early and late	Faint; common; occurs early	Uncommon; occurs early	Rare
Fever	Common, 5th to 9th day; may occur 1st to 21st day	Uncommon; 5th to 9th day; may occur 1st to 30th day	Common, 5th to 9th day	Seldom
Rash	Common, any form; 5th to 9th day; may occur 1st to 21st day	Not common; 5th to 9th day; may occur 1st to 30th day	Common, 5th to 9th day	Mild and rare
Kidney injury	Questionable	Common, 1st to 10th day	Common, 1st to 10th day	Common
Anuria with azotemia	Rare	Not uncommon; 2nd to 14th day. Blood pressure and fundi normal	Reported 7th day	Rare
Acute leukopenia with granulocytopenia	Not uncommon; 1st to 10th day	Common, especially in children; 1st to 10th day	May occur 3rd to 10th day	Less than 2 per cent
Acute hemolytic anemia	Common, especially in Negroes; 1st to 5th day	Uncommon; 1st to 5th day	Not reported	Rare
Stomatitis	Rare	Not reported	Not reported	None
Gastrointestinal tract	Bleeding rare, diarrhea common	Bleeding reported	Not reported	Very little

do not occur with sulfanilamide, but they are often present when sulfapyridine, sulfathiazole, or sulfadiazine are given.

Sulfanilamide has a tendency to destroy the red blood cells, and anemia is one of its characteristic toxic reactions. Very little evidence has been shown to the effect that sulfanilamide injures the kidneys. It rarely causes agranulocytosis and hardly ever produces a fever or a rash. Nausea and vomiting, of course, are features of all members of the sulfonamide group; even sulfanilamide may occasionally cause these effects. Headache and mental depression are also features of sulfonamide intoxication.

Sulfapyridine tends to cause agranulocytosis, but not anemia. Renal irritation is another of the toxic effects of this drug. Sulfathiazole has about the same characteristics as sulfapyridine, but the rash and fever of sulfathiazole are almost specific features of its intoxication. Sulfadiazine is peculiarly free from toxic manifestations. Any of the reactions seen with the other drugs may occur with sulfadiazine, but they hardly ever do. Renal complications have been observed.

When general toxic reactions to the sulfonamides appear, the following treatment is instituted:

1. The drug is discontinued until the toxic reaction clears up.
2. When vomiting is the chief reaction, the drug may be given intravenously in five per cent solution.
3. If hemolytic anemia occurs, transfusions and injections of liver extract intramuscularly are necessary.

Injury to the kidney is the most frequent and serious toxic manifestation in sulfonamide therapy. The two types of reaction are: (1) Mechanical complications, produced by masses of sulfonamide crystals in the kidneys, pelves, and ureters; and (2) toxic intrarenal lesions occurring within the kidney but without mechanical obstruction. The chief evidences of kidney damage include oliguria, anuria, and albuminuria. Microscopic hematuria, pus cells, and granular casts are common. Treatment of toxic reactions is now adequate, and prevention of such reactions is steadily increasing. Treatment includes the following:

1. The drug is discontinued when evidence of damage is present.
2. Fluids are given orally and/or intravenously to augment excretion of the drug.

3. Alkalinization by soda bicarbonate orally or intravenously maintains the *p*H of urine at seven or above.

4. Catheterization and lavage cleanse ureters and pelves.

Alkalinization and maintenance of proper fluid intake and output during sulfonamide therapy keep toxic reactions and kidney impairment at a minimum.

ABUSES OF THYROID THERAPY

Thyroid substitution therapy is one of the most reliable types of endocrine treatment, but certain therapeutic hazards must be taken into consideration, as well as opportunities of doing good.

Excessive amounts of thyroid given to a patient for therapeutic purposes may bring on hyperthyroidism. This kind of hyperthyroidism can sometimes be controlled by discontinuing thyroid therapy; but at other times, stopping the treatment does not regulate the condition, and thyroidectomy may be necessary.

In myxedema care must be taken lest certain organs be overtaxed. This is particularly important when treating older patients. There is danger of causing acute pulmonary edema, coronary thrombosis, or dilatation of the heart with left-sided failure. Too much thyroid may also produce shock of the addisonian type. Diuresis may occur.

The dosage varies with different people; though young patients can tolerate as much as 0.26 Gm. (4 grains) a day, such doses are not recommended for all. Thirty-three milligrams (½ grain) a day will in a month bring metabolism up to −35; 0.066 Gm. (1 grain) to −25; 0.13 Gm. (2 grains) to −15, and 0.2 Gm. (3 grains) to −10. One usually starts with 0.033 Gm. (½ grain) for ten days and elevates the dosage each week as required. Some patients may not be able to reach a normal level, as their hearts will not stand the thyroid without developing cardiac failure or angina pectoris. In cretins great care must be taken with the dosage, as the margin between an inadequate dose and one large enough to produce untoward mental symptoms is small. In women thyroid may cause menstrual scantiness or irregularities, but it can correct menorrhagia.

In addition to the symptoms cited, thyroid can produce maniacal attacks, echolalia, diarrhea, palpitation, restlessness, cardiac arrhythmias, and fibrillations.

In conclusion, it is well to remember that all the endocrines are

in balance. A change in the thyroid balance alters that of the other glands. Though some of the symptoms of overdosage are merely troublesome, as are diarrhea or excessive sweating, others, as heart failure or shock, may cause death.

THERAPEUTIC HAZARDS OF BENZEDRINE

Benzedrine is a sympathomimetic amide resembling ephedrine, except that it possesses greater ability to stimulate the higher centers, particularly the cortex.

The indiscriminate use of benzedrine may cause toxic effects, varying with the individual. Cerebral symptoms are the outstanding toxic effect. The drug may cause restlessness, tremors, insomnia, talkativeness, irritability, confusion, assaultiveness, hallucinations, delirium, panic states, or homicidal or suicidal intentions. Such central stimulation may be followed by fatigue and depression. Gastrointestinal disturbances, such as dry mouth, metallic taste, anorexia, nausea, vomiting, and diarrhea have been known to occur. The cardiovascular reactions are chilliness, sweating, palpitation, marked hypertension or hypotension, extrasystoles, anginal pain, circulatory collapse, and syncope.

Prolonged inhalations according to Waud may result in hypertension lasting four days, anorexia, loss of weight, mental stimulation followed by fatigue and depression. Permanent organic changes do not often occur. The inference is that benzedrine is a safe drug for normal persons. However, severe reactions, including coma, clonic convulsions, and panic, have been recorded. Smith told of a case of death possibly due to benzedrine.

Benzedrine should not be used to overcome sleepiness or to increase the energy. It is contraindicated for persons with hypertension, advanced arteriosclerosis, coronary artery disease, states of mental excitement, agitated depression, hyperthyroidism. It should be used cautiously in those with anorexia, insomnia, vasomotor instability, asthenia, psychopathic personalities, or suicidal tendencies. Habituation similar to that of nicotine and caffeine may develop, but addiction is unknown. Some patients report increased tolerance after continued use of the drug, but change in susceptibility does not occur, as a rule, in most people.

CHAPTER XXV

Penicillin

In 1929, Professor Alexander Fleming gave the name penicillin to a bacterio-inhibitory agent produced by a strain of mold of the penicillium notatum. Fleming saw the advantages of penicillin over the chemical antiseptics then in use, and he suggested that penicillin might be "an efficient antiseptic for application to or injection into, areas infected with penicillin-sensitive microbes."

Today, although strictly speaking it is not an antiseptic, these properties of an ideal antiseptic are recognized in penicillin: (1) It possesses enormous bacteriostatic power; and the number of bacteria present does not affect its action to a noticeable extent; (2) it acts effectively in almost any medium. Blood, serum, and pus do not inhibit its power; (3) it is almost completely nontoxic to the body as a whole and to the organs of the body; (4) it is soluble in a number of substances, normal saline solution, distilled water, and five per cent dextrose, and it is also effective in powder and cream form; (5) it may be administered in several ways, intravenously, intramuscularly, topically, intrathecally, and locally, depending upon the type and severity of the infection.

Since penicillin is an unstable substance, it is combined therapeutically with sodium, barium, and calcium, although sodium salt of penicillin is most commonly used.

Indications: Penicillin is bacteriostatic, and it has been suggested that the action of the drug may be on bacterial fission since it is most effective when multiplication of bacteria takes place. With the exception of the gonococcus and meningococcus, susceptible bacteria are almost all Gram-positive.

The diseases which are known to respond to penicillin, recommended in a report by Dr. C. S. Keefer, Chairman of the Committee on hemotherapy of the National Research Council, and his Associates, are the following:

Penicillin is the best therapeutic agent in the treatment of:

1. All staphylococcic infections with and without bacteremia: This includes acute osteomyelitis, carbuncles—soft tissue abscesses, meningitis,

pneumonia—empyema, cavernous or lateral sinus thrombosis, carbuncle of kidney, and wound infections.

2. All cases of clostridia infections.
3. All hemolytic streptococcic infections with bacteremia and all serious local infections: This includes cellulitis, mastoiditis and its complications, pneumonia and empyema, puerperal sepsis, peritonitis.
4. All anaerobic streptococcic infections.
5. All pneumococcic infections of meninges, pleura, and endocardium, and all cases of sulfonamide-resistant pneumococcic pneumonia.
6. All gonococcic infections complicated by arthritis, ophthalmia, endocarditis, peritonitis, epididymitis, and all cases of sulfonamide-resistant gonorrhea.

Penicillin has also been found to be an effective agent in syphilis, actinomycosis, and bacterial endocarditis, but its position has not been definitely defined.

Penicillin is of questionable value in mixed infections of the peritoneum and liver in which the predominating organism is of the gram negative flora. This includes ruptured appendix, liver abscesses, and urinary tract infections.

All gram negative bacillary infections constitute a contraindication for penicillin. It is also ineffective in the treatment of tuberculosis, rheumatic fever, Hodgkin's disease, leukemia, poliomyelitis, virus infections, and cancer.

These indications and contraindications cannot, in any sense, be considered the final statement on penicillin therapy. Much research work is being done at the present time and will be done in the future on this drug, its indications, dosages, methods of administration, and its usefulness in combination with other substances. There is no doubt but that even more successful results will follow a more inclusive field of therapy.

Dosage: The dosage varies with the type and severity of the infection. The age, weight, and general condition of the patient are also taken into account. Exact dosage for many infections and diseases is not known, but enough penicillin must be given to prevent the growth of the infecting organisms. The antibacterial action parallels the concentration of penicillin in the blood. While an overdose has not been proved harmful, an underdose may result in therapeutic failure and possible death. To determine whether an adequate amount of penicillin is being given, the blood is titrated and the concentration of the drug determined. The entire clinical

response of the patient is determined by the temperature, pulse, disappearance of pain, negative results of blood or urine cultures, and general improvement.

Recently, simplified dose schedules have come into use. All routine cases of acute and chronic infection receive 100,000 to 120,000 units per day. Dosage is continued for from three to seven days after the infection subsides and the temperature returns to normal. During this time, there is also a marked improvement in the general mental and physical condition of the patient. If, however, there is no response to therapy after 48 hours, the dosage is increased.

Methods of Administration: Here again, the type of administraiton depends upon the type of infection present. C. S. Keefer and his Associates recommended the following methods of administration: Serious infections due to the hemolytic streptococcus, staphylococcus, or pneumococcus are best treated by constant or frequent intravenous injections; chronically infected compound injuries, by parenteral injection plus local treatment; sulfonamide-resistant gonorrhea, by intravenous or intramuscular injection; empyema, by injection into the empyema cavity after aspiration of pus or fluid; meningitis, by injection into the subarachnoid space, or intracisternally, in conjunction with systemic administration.

Intravenous administration of the drug may be continuous or intermittent. Continuous infusion of penicillin maintains a constant therapeutic level in the blood. The standard solution consists of 100,000 units of penicillin dissolved in 1000 cc. of physiological saline. When therapy is initiated, 100 or 200 cc. are given rapidly, and then the rate is regulated to 30 or 40 drops per minute. Disadvantages lie in the difficulty of continuous infusion, the possible discomfort of the patient, and the frequent occurrence of superficial venous thrombosis. However, this is the preferred method if the infection is serious and if the time element is important. Intermittent intravenous administration is done every three hours to maintain a therapeutic level. The interval between doses cannot safely be prolonged because of the rapid fall in blood concentration and the rapid urinary excretion.

Intramuscular administrations are best given in the gluteus maximus or deltoid muscle. A higher concentration of penicillin

is maintained for a longer period of time in intramuscular than in intermittent intravenous administration, and injections are given at three- or four-hour intervals. These injections are given more easily and may be better tolerated, especially by patients who cannot take the amount of fluid necessary for continuous intravenous infusion. In addition, after the danger of severe infection is past, equal intramuscular injections may replace intravenous therapy. A change in the vehicle in which the penicillin is administered will usually relieve any discomfort on injection, but it is important to keep the volume of fluid as low as possible, 5000 units per cc. of fluid, and to change the site of injection to prevent or minimize discomfort.

Following subcutaneous injection, the absorption of penicillin is decidedly delayed, and the concentration of the drug in the blood does not reach the levels obtained in the methods of administration discussed above.

Intrathecal injection has been successfully used, in conjunction with intravenous or intramuscular injections, in the treatment of meningitis. 10,000 units in 10 cc. of isotonic sodium chloride solution injected once or twice daily is the recommended dose.

Local application of penicillin calls for comparatively small amounts. It has proved successful in pleural and joint infections, wounds, burns, and scalds. The drug may be used locally in powder form, diluted with a powder of one of the sulfonamide compounds, in cream form, or in a solution of isotonic sodium chloride. In wounds and infections which require constant therapy, wet dressings are applied. In infections of the extremities, frequent immersions in penicillin solution are helpful. In deep wounds, continuous installations or frequent injections are valuable. Care must be taken to assure adequate access of the drug to all parts of the infection or wound.

Injection of penicillin has been made into the pleura, pericardium, joints, bone marrow, and subarachnoid space, either alone or in combination with other penicillin therapy, and excellent results have been obtained because the drug is absorbed slowly.

Oral administration is unsatisfactory, because penicillin is destroyed by acid. Administration of alkali prior to penicillin does

not overcome this fault, and, as a result, very little of the drug is absorbed. Absorption following rectal administration is poor, and the drug is destroyed by bacteria in the intestines.

The quantity of penicillin excreted in the urine depends upon the route of administration, the amount given, and the urinary output. However, excretion averages between 50 and 60 per cent of the amount of the drug given. It has been proved that renal suppression decreases the amount of the drug excreted in the urine. If the urinary output could be controlled, the need for large and frequent doses of the drug might be done away with. Excretion of penicillin by other routes has not been completely studied, but thus far, none has been recovered from saliva, tears, or spinal fluid, and the fate of approximately 40 per cent of the drug remains undetermined.

Toxic Reactions: Normally, penicillin is nontoxic in doses far exceeding those given in treatment, and the majority of toxic reactions are thought to be caused by impurities or adulterants. As it is now used clinically, penicillin contains from 10 to 51 per cent pure penicillin, the toxicity is low, and systemic reaction is infrequent. Reactions reported by G. F. Schmitt attributable to the drug itself are: (1) Urticaria; (2) fever in afebrile patients; (3) transient azotemia; and (4) thrombophlebitis at the site of injection.

Reactions which may be caused by impurities in the penicillin are : (1) Chills with or without fever; following intravenous injection; (2) eosinophilia; (3) burning pain at the site of intramuscular injection; (4) headache; (5) faintness and flushing; (6) unpleasant taste following parenteral injection; (7) tingling in testes; (8) muscle cramps; (9) femoral phlebothrombosis.

Frequent comparisons of penicillin and the sulfonamide compounds have been made and the following advantages are possessed by penicillin: (1) It is more powerful in its bacteriostatic action against streptococci and staphylococci; (2) its action is minimally affected by the number of bacteria present; (3) it is not affected by the medium in which it acts; (4) it is essentially nontoxic, even in large doses. However, combined penicillin and sulfonamide therapy is believed to be more effective than either drug alone in streptococcic and staphylococcic infections.

A whole new field opens when the possibility of penicillin combined with other drug therapy is considered. Alexander Fleming believes the most important step for the future is the analysis and synthesis of penicillin, which may lead to a series of new preparations having wider application than penicillin itself.

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