from other causes. In these patients depression is extreme, often not associated with delusions except possibly the pardonable idea that they are going insane; there may be with the depression a nervousness so great that the patient presents a typical picture of *melancholia agitata*, walking the floor in agony. Such cases are acute. A deficiency of the hydrochloric acid of the gastric juice may cause a mild chronic depression, simple, and easily improved or cured by appropriate treatment.

In all of these cases it is not known where or how the poisons generated in the alimentary tract have their effect. As the emotions are sensations from the viscera, and as the sensory nerve endings of the affected viscera are bathed in the poisons, it is not a remote possibility that their action may be a local one and not due to their being absorbed and in this manner producing an effect on the sensory centre. The prompt action of local remedies, stomach washings, purgation and enemas, favors this view.

The prevailing emotion in consumption is moderate exaltation. This may be heightened by the stimulus of an attack of referred pain, especially that due to disease of the upper pulmonary lobe; disease of the lower lobes is likely to cause referred pain with attacks of depression.

Uterine and ovarian disease is especially prolific of emotions, either simple depression, to which in extreme cases delusions may be added, or exaltation amounting in some cases to mania. The most deceptive forms of these affections are those in which there are no accompanying symptoms, sensory or otherwise, calling the patient's attention to the affected organs. The difficulty is further increased by the fact that digestive disturbances may make their appearance and mask the other symptoms. The difficulty of distinguishing between these cases and cases of insanity with coincident visceral lesions may be considerable, as these patients possess many or all of the symptoms of insanity, and yet it is not very important to make the distinction between the two classes of cases. Organic defects should be remedied, if possible, even in the insane, and in addition it may be fairly doubted whether even in cases of hopeless insanity, organic visceral disease may not often be the determining cause of the mental breakdown.

The pelvic organs sag and pull on their attachments and as a result there are sent out to other parts of the nervous system signals of distress which take not only the form of moods, but of pains in the back and head, vasomotor disturbances, flushing, fainting, palpitation and the like. In the same way sagging abdominal organs set up all these classes of symptoms. In especial a prolapsed kidney is often responsible for attacks of dizziness, headaches, flushings, and faintness which are often attributed to anything but their real cause.

One of the most striking emotional changes from visceral disease is the fear suffered by patients afflicted with angina pectoris. A good deal of anxiety is felt by many patients who suffer from palpitation, over and above what would be warranted by the nature of their complaint. The fear in angina pectoris is inherent and does not proceed from a knowledge of the danger incident to the disease. It is a signal to the brain direct.

Little more has been attempted in the present article than an outline of the subject of sensory disorders, with the idea, especially, of tracing the complex relations which exist between the sensory system of the skin and that of the viscera. Consciousness is not, in this connection, of prime importance. It is a mysterious light that shimmers on a few of the actions and reactions of the nervous system; in considering the part played in disease by the sensory system, it is of especial importance to recognize the fact that sensory phenomena may and often do take place without its intervention.

Henry S. Upson.

SEPTICÆMIA AND PYÆMIA.—Historical Memoranda.—A constitutional disturbance accompanying putrefaction in wounds, particularly fractures and injuries of the skull, was described by Hippocrates. In the Middle Ages Ambrose Paré and Paracelsus, both noted metastases following certain injuries in which suppuration occurred. In 1720 Boerhaave first enunciated the doctrine that the condition was due to pus in the blood. His contemporaries, Morgagni and Petit, also tried to prove that metastatic abscesses were brought about by penetration of pus into the blood. In 1774 John Hunter recognized phlebitis as an intermediate factor in producing metastatic abscess, but the exact relation of the two was not clearly defined. In the early part of the nineteenth century (1808–22) Gaspard initiated the experimental method of studying septicæmia by injecting putrefying materials into the veins of animals. Later, the investigations of Virchow, Billroth, O. Weber, Koch, and others formed the basis upon which Gussenbauer built the following definitions: "By *putrid infection or septicæmia* we mean that general disease of the body which results from the introduction into the circulation of the products of decomposition, and which is characterized by definite changes in the blood, a typical succession of inflammatory processes, and a continuous fever together with peculiar nervous symptoms and critical discharges." *Pyæmia* is defined by him as "a general infective disease which arises from the entrance into the blood of the constituents of infected pus, and is distinguished from other septic infective diseases by the development of multiple pus foci in different organs, and an intermittent fever."

Since Gussenbaur formulated these definitions, extensive investigations have been made from both a bacteriological and a pathological standpoint. From the studies of Ogston, Rosenbach, Doyen, von Eiselsberg, and others the conclusion is drawn that the general systemic disease known as septicæmia depends upon the *introduction of pathogenic, especially pyogenic micro-organisms into the general circulation.* Marmorek further limits the definition of septic intoxications, infections (mycoses), and pyæmia to those general systemic diseases caused by the activity of the streptococcus pyogenes and staphylococcus aureus, for, he claims, that these are the only two micro-organisms which can cause all the various phases of septicæmia, from a carbuncle to the most severe pyæmia. He excludes as etiological factors such agents as bacterium coli, pneumococci, etc., which he claims cannot cause furunculosis, lymphangitis, and lymphadenitis. However, this cannot be accepted by the clinician, for not only are his premises and therefore his conclusions incorrect, but in addition there are so many forms of septic intoxication and infection presented to the observer, in which the etiological factor is other than the streptococcus pyogenes and staphylococcus aureus, that it is impossible to limit the disease to those agents alone.

Classification.—Konrad Brunner ("Erfahrungen und Studien über Wundinfektion und Wundbehandlung, III. Theil. Die Begriffe Pyämie und Septhämie im Lichte der bakteriologischen Forschungsergebnisse") classifies the disease from an etiological and symptomatological standpoint. Slightly modified by the present writer, it is as follows:

I. *Septicæmia Not due to Bacterial Activity.*—A general disease brought about through necrotic or putrefactive processes.

II. *Systemic Diseases due to Pyogenic Microbes; Pyæmia, Acute or Chronic.*—General infections in which metastases make their clinical appearance, due generally to staphylo-, strepto-, pneumo-, and gonococci, or to proteus, pyocyaneus, coli, or typhoid bacilli; the fundamental principle being that the signs and symptoms of metastases break in upon the general symptoms.

2. *Pyotoxinæmia, Toxinæmia, Toxæmia.*—A general disease without the clinical signs of metastases, but with the symptoms of a constitutional intoxication, brought about by all kinds of bacteria.

III. *Pyosepticæmia or Septicæmia.*—A general disease in which the products of pyogenic bacterial activity combine with those of decomposition to cause the symptoms. For a fuller discussion of the subject of classification the reader is referred to the above work by Brunner.

Etiology.—So far as the classification is concerned, the bacteria, in all but the first form of the disease, play the chief rôle. There is *no specific micro-organism*, but a whole series of them as etiological factors. The same micro-organism acts differently under different conditions. There are many factors which tend to change or govern the result of their activity. The point of infection, the character of the media into which they penetrate, the personal factor, the microbic association, the varying virulence of the micro-organisms themselves, the lowered vitality of the parts—all these influence the course of the infection.

The *mode of entrance of bacteria* into the system has been the subject of much investigation. In some cases they are, through the medium of a seemingly slight wound, introduced rapidly into the circulation, presumably being taken up by the capillaries. In the great majority of the cases, however, the bacteria first gain access to the lymph spaces and are carried through the lymph channels to the blood. Starting from a localized pus focus the bacterium first has to pass the barrier of *granulation tissue*, which has been thrown up by the tissue as a bulwark against the bacterial invasion. That healthy granulation tissue does act as a successful barrier has been conclusively demonstrated by Noetzel in his experiments on sheep. When these granulations, however, are not sufficiently developed, the micro-organisms pass through them and enter the lymph spaces. By the lymph they are carried to the lymph nodes, which present the next barrier against their invasion. In their course to the nodes varying degrees of *lymphangitis* may be set up. The nodes increase in size and in some way, as yet not definitely known, they retard the growth of the bacteria and in many cases limit their further growth. Dr. Mallory, of the Harvard Medical School, has lately demonstrated that in the periphery of the node there sometimes occurs a proliferation of the endothelial cells lining the trabeculæ which traverse the lymph spaces. These take upon themselves phagocytic properties and enclose not only the bacteria but also leucocytes themselves, which may already have ingested some bacteria and in addition large numbers of red blood cells. In the nodes the pyogenic bacteria often bring about suppurative processes and, destroying these organs, pass on and are emptied into the blood stream. More often the resistance of the nodes is overcome without producing suppuration. Upon reaching the blood the bacteria are again attacked. Through the production of so-called *sozins* and *alexins* (the mode of origin of which is unknown) the growth of the bacteria is again hindered; in fact, these sozins and alexins, aided by the leucocytes acting as phagocytes (Metschnikoff), may destroy the bacteria. Canon believes that the chief difference between septicæmia (pyotoxinæmia) and pyæmia depends upon the phenomena, that in septicæmia the bacteria increase and produce their toxins in the blood, whereas in pyæmia the bacteria are introduced into the blood but do not increase there. Brunner holds that there never occurs any marked growth of bacteria in human blood, and he thinks that this is one reason why bacterial blood tests sometimes fail. An acute mycosis is met with in no human infection. He further holds that the micro-organisms are especially prone to collect in the parenchymatous organs, and in the acute cases they set up metastatic processes, which, however, remain microscopically small, the duration of the disease being too short to develop macroscopic foci or to be clinically evident.

The bacteria carried by the blood may be deposited in the various tissues and organs of the body and there continue their activity and bring about local inflammatory or suppurative processes. They may, on the other hand, be destroyed in the tissues and be excreted. The relation of thrombophlebitis to the blood will be discussed later.

All authors hold that *in the majority of the cases the ordinary pyogenic cocci, i.e., the pyogenic staphylococci and streptococci, alone or associated together, constitute the cause of the disease.*

The streptococci have long been looked upon as liable to bring about more virulent infections than the staphylococci. But no absolute line can be drawn. We may have an acute or a chronic streptococcus infection with or without metastases. The same is true of the staphylococci. However, many other bacteria play an important part, etiologically, in this disease. The *pneumococcus* may cause a metastatic-pyæmia, or a pneumococcus-toxæmia, in which the bacteria are found in the blood. Metastatic foci occur most frequently in the meninges and the joints. The *B. coli communis* generally invades the system from the intestinal tract. Cholecystitis, abscess of the liver, peritonitis are often sequelæ. Cystitis is set up, the bacillus being carried by the lymph vessels or the blood. Meningitis, pneumonia, strumitis, etc., have followed its escape into the blood. It has also been isolated in local phlegmon and lymphangitis. The *gonococcus* is frequently met with in pyæmic conditions. *B. typhosus, B. pyocyaneus, B. Friedländer, Proteus vulgaris, Micrococcus tetragenus*, and many others are capable of bringing about the disease.

The infection may be a mixed one, a *double infection* taking place at the same time, or a *secondary infection* taking place in a focus already the seat of microbic activity. It often happens that only one of the bacteria can be demonstrated in the blood, and when streptococci and staphylococci are associated, the streptococcus is generally the one to bring about the general infection.

Pathology.—In the mildest form of the disease, *septicæmia without bacterial activity*, or, as it is more commonly termed, "*sapræmia*," the pathological changes are limited to the site of the necrosing or putrefying focus. In the *pyosepticæmic* form of the disease we have locally the combined phenomena of pus formation and putrefying, decomposing, or necrosing tissue. It may exist in the form of a moist gangrene. Often, in the case of wounds which seem at first insignificant, but in which cases there ensues a malignant and rapidly fatal toxæmia, the pathological findings are very slight. More often we have the local changes of a pyogenic disturbance, presenting all of the characteristics of local inflammation and abscess formation. The primary focus may be a carbuncle, an infected wound, an otitis media, an osteomyelitis, a gastro-enteritis, a pneumonia, etc. From the seat of infection the inflammation spreads, the *lymphangitis* is set up, the nodes are attacked, and *lymphadenitis* follows. The bacteria reach the blood and here many changes occur. *Sozins* and *alexins* are produced, and *antitoxins* are elaborated. Ewing holds that the bacteria are present in the circulating blood only for short periods and at infrequent intervals, and that a few hours before death various bacteria, some of which may not be active in the original process, make their way into the circulation. There is a rapid development of severe anæmia. The red blood cells are diminished in number, and in the more severe cases a slight poikilocytosis and degeneration of the cells occur. Sometimes normoblasts appear. Grawitz reports a case of acute septic infection, in which after two days the red blood cells were reduced to 300,000 per cubic millimetre. The blood plaques are increased. Leucocytosis is marked, except in the very mild and very severe cases. Changes in the blood-vessels occur mostly in relation to the local pus foci, but often by means of mural inplantation the endocardium is attacked and ulcerative or malignant endocarditis ensues. When a vein in the neighborhood of an abscess is attacked the adventitia is the first to be affected. The ordinary phenomena of inflammation follow, and the other coats of the vein become involved. The intima becomes swollen and inflamed and fibrin is deposited on it, which becomes the nucleus of a coagulum. This increases until the lumen of the vein is occluded and a thrombophlebitis established. Sometimes the thrombus extends for a considerable distance along the vein. As the infective process advances from the primary focus, the microbes invade the thrombus and there bring about

purulent softening of the mass. Before this occurs small particles of the thrombus may be broken off, and, entering the general circulation as emboli, find lodgment in the various organs. In this way infarcts are produced, and these in turn may become infected by the bacteria in the circulating blood, thus giving rise to metastatic pus foci. In the original thrombus the process of purulent softening goes on, and if not checked by local forces or by treatment the whole mass breaks down and the particles laden with micro-organisms follow the course of the embolus and lodge in the portion of the vascular system where the size of the vessel retards its progress.

Post-Mortem Findings.—In *pyotoxinæmia* and *pyosepticæmia* putrefaction develops rapidly. In the subacute and chronic cases the original wound is found to be foul and unhealthy in appearance. The lungs may show congestion and œdema; small pleural and pericardial effusions are frequently seen. There is a marked degree of gastro-enteritis, the inflammation affecting especially the lower bowel; generally cloudy swelling of the spleen, liver, and kidneys is present; the nervous system is not much affected; bacteria may be demonstrated in the connective tissues; the lymph nodes are enlarged. In the rapidly fatal *peritoneal pyotoxinæmias* the gut is found greatly distended with gas; the peritoneum is grayish and lustreless, and shows a fine network of congested vessels.

In *pyæmia* the wound looks gangrenous. The adjacent veins are thrombosed. Metastatic abscesses are seen, most often in the lungs, liver, spleen, and kidney. The intestinal tract is not so often affected. The brain may show a passive hyperæmia but metastatic foci are rare. In the joints there may be either serous or purulent effusions. Heart lesions are not frequent, but they do occur.

When recovery takes place, there is a gradual regeneration, the bacteria disappearing from the blood and the local conditions subsiding.

Signs and Symptoms.—The complex of objective signs and subjective symptoms of the disease in its various forms vary to such an extent that no hard-and-fast lines can be drawn. And still there are groups of symptoms which are most frequently observed in certain manifestations of the disease.

Under the division of *septicæmia without bacterial activity* are included all those conditions in which from a specific focus of necrosis or putrefaction or decomposition the toxic elements elaborated by these processes are absorbed into the general circulation and thereby bring about a general poisoning of the system. The primary focus may become infected, and so, through the addition of the bacterial element, we have a pyosepticæmia, to be described later. Septicæmia without bacterial activity—or, as it is more commonly termed, "sapræmia"—is most strikingly exemplified in the so-called ptomaïn poisoning, which originates in the gastro-intestinal tract, and in the cases of retained secundines, in which the putrefactive changes take place in the placental tissues and without bacterial activity bring about a general poisoning. The tyrotoxicon discovered by Vaughan, of the University of Michigan, is accepted as the etiological factor in the poisoning from cheese, and is supposed to be the active principle in some of the other forms of ptomaïn poisoning.

Large masses of gangrenous or sloughing tissues which are confined within the body may bring about the disease. The symptoms which develop are those of a poison which is gradually progressive, acting as a depressant on the nervous system, and bringing about a considerable febrile movement. The disease affects more especially the gastro-intestinal tract. There is no chill to mark its onset. The patient has a persistent headache, general malaise, anorexia. At first there is only a slight rise of temperature; the pulse frequency is increased; there is some nausea. If the cause is not removed the headache becomes more intense, the temperature rises, vomiting takes place, and diarrhœa is the rule. The blood shows degenerative changes, diminution in the number of the red blood cells, decrease in the hæmoglobin index, and some leucocytosis. These changes vary with the intensity of the poison. In the fatal cases the temperature is continuously high, the pulse rapid and feeble, delirium follows restlessness, coma develops, and death occurs. In the cases which originate in the intestines the most marked symptom is the violent vomiting and purging, which may even simulate cholera. Most of this class of cases of septicæmia react well to treatment, and when the cause is removed there is a rapid return to normal conditions.

In *pyotoxinæmia* attention is first called to the local conditions. It may be a suppurating wound which is draining poorly, an unopened abscess, or some deeply seated inflammation. In the *cryptogenic form* (*i.e.*, that form in which the original focus of infection cannot be found) there may be a history of some old trouble which is supposed to have subsided. A gastro-enteritis, a pneumonia, a cystitis, or a perityphlitis may be the starting-point. The patient at first does not appear to be very ill; there is some prostration; he complains of a slight headache which does not yield to treatment; the appetite is poor; no interest is taken in surroundings; the symptoms of lymphangitis and lymphadenitis may be present; the temperature shoots up, especially in the evening, with only slight morning remissions; the pulse becomes rapid; the patient feels "feverish"; there may be some pain in the wound. Often an examination of the local condition will demonstrate the cause of the symptoms, and prompt surgical treatment may cut short the further course of the disease, the condition returning rapidly to normal upon removal of the local cause. If the disease goes on, gastro-enteritis appears, with vomiting and diarrhœa. The tongue, at first thickly coated, becomes dry and hard. The heart's action becomes weaker and increasingly rapid, often out of proportion to the temperature; the arterial tension is lowered, and in the severe cases cyanosis appears. The liver and spleen are often enlarged. The urine shows albumin and casts. The skin may show a slight yellow tinge, but icterus is not so marked here as in pyæmia, and is probably due to destructive processes in the blood rather than to hepatic disease. At first dry and hot, the surface of the body later is bathed in perspiration, the skin feeling cold and cadaveric. The prostration increases, the expression is listless, the face being drawn and colorless, the eyes are sunken, and the alæ nasi dilated; no complaints are heard. If the disease reacts to treatment, a general improvement of the sensorium is first noted; the pulse becomes a little stronger although still rapid; the temperature gradually subsides, often showing at first marked morning remissions, until finally the evening rise disappears; the desire for food gradually returns; the heart is the last entirely to recover its normal condition. The disease may run a chronic course, lasting for from three to twelve weeks. The temperature in these cases is not generally high, but is often quite irregular. The spleen is frequently palpably enlarged, this being simply a phase of the general lymphatic enlargement. If, however, recovery does not occur, the condition may rapidly become worse, the temperature continuing high and the heart rapidly failing. Finally, violent purging, anuria, delirium and coma, are likely to precede the patient's death. In the malignant cases the course may be very rapid, presenting possibly only a slight lymphangitis, an increasingly high temperature, rapid cardiac failure, rapid overwhelming of the nervous system, and death. This last form is occasionally seen in cases of wounds received at the post-mortem table, cases in which, from a seemingly slight wound, the most intense and rapidly fatal toxæmia develops.

In typical cases of *pyæmia*, in which multiple abscesses are produced as a result of infected emboli, the clinical picture is somewhat different. The conditions at the primary focus may be the same as in pyotoxæmia. Severe local injuries, wounds of the joints, compound fractures, injuries of the veins, fracture of the skull, associated with pyogenic processes, are the most frequent among the primary lesions in pyæmia. The local condition may not appear to be especially active, but is

markedly persistent. The wound looks bad and exudes a semi-serous, foul-smelling pus; and the surrounding tissues become œdematous and deeply inflamed. The temperature is not very high, with moderate morning remissions, and the pulse is rapid. This may continue for about a week, during which time the induration does not lessen, but extends more deeply into the tissues. Suddenly, on the tenth or twelfth day, the patient has a severe chill, following which there are a burning fever and then a profuse perspiration. Again, the wound may have been doing very nicely, and the evidence of infection may have been slight, when suddenly a chill appears and pyæmia is ushered in. Such chills are generally a reliable index of the lodgment of an embolus in some portion of the vascular system. The chill may, however, be very slight, and in those forms of pyæmia in which the secondary foci are caused through direct infection by the bacteria circulating in the blood, and not by infected emboli, often no chill at all appears. In *pyotoxinæmia* and *pyosepticæmia* a chill rarely is noted. Chilly sensations sometimes occur, but a sudden, violent chill is the exception. Following the sweating there is marked exhaustion. The temperature immediately preceding or during the chill is likely to shoot up to the highest point of the curve only to drop in a few hours, but not to normal. The chill may be repeated the same day or on the next day. The temperature runs apace, and describes a very irregular tracing, varying from hour to hour. The sensorium is perfectly clear, and the patient exhibits none of those somnolescent features which are seen in an acute toxæmia or pyosepticæmia, but he is keenly sensible to his suffering. The local symptoms of the new foci soon make their appearance. Pain is felt in the chest or under the border of the ribs, and upon examination an abscess of the liver, a pleurisy, or a pneumonia is found. The joints may be swollen and tender. Icterus is generally seen, slight at first but often marked in the later stages of the disease when the emaciation is far advanced. There is not so much gastro-enteritis as in toxæmia, and, in fact, in the earlier stages the constitutional symptoms are very little in evidence. The temperature continues as before, possibly not so high, exhibiting, however, the same marked irregularity. The tongue, at first thickly coated, becomes later dry and hard and looks dirty. The patients are often hyperæsthetic and suffer much from local pain. They often complain of pain first in one place and then in another, and sometimes there is a general sensitiveness all over the body. The cause may possibly be referred to localization of bacteria in the tissues, where they set up inflammatory processes and, in many cases, purulent collections. Later, the patients lose all sensation of discomfort. Erythematous and sometimes pustular eruptions appear on the skin. The pulse, which at first was fairly strong but rapid, later becomes weak and rapid. At any time the local symptom of some new metastatic focus may be ushered in. Prostration is very marked, the emaciation is severe. Gradually the patient becomes unconscious and dies in a comatose condition.

In *puerperal pyæmia* the course is very similar. In the chronic form of pyæmia chills are much less frequent and recovery may occur.

Von Leube ("Specielle Diagnose der inneren Krankheiten") states that from a scientific standpoint it is not always possible at the bedside to differentiate between the two conditions septicæmia (meaning toxæmia, pyosepticæmia, etc.) and pyæmia, or, better, strictly to draw the lines between these forms. The one leads into the other, and many cases of pyotoxinæmia would develop into pyæmia were it not for the short duration of the disease Therefore he holds that in most cases it is proper to speak of a *septicopyæmia*. This is the form, he maintains, which is most likely to occur in the cryptogenic type of the disease. The patient, sometimes in fine health, sometimes suffering from a slight illness, begins to have pain in the legs, loss of appetite, eventually headache, vomiting, then a severe fever, and is very ill. The fever, often like a fluctuating typhoid, may be, however, continuously high, with slight remissions. The tendency is markedly to an up-and-down course, with irregularly intercurrent chills. The pulse in the severe cases is very rapid, varying from 120 to 150, soft, dicrotic, and sometimes irregular, especially so in cases in which, on post-mortem examination, the heart walls are found to be the seat of metastatic abscesses. The heart is dilated, and endocarditis very frequently occurs. At times the endocarditis is the only objective sign of the disease at first (a loud systolic or systolic-diastolic murmur, increased second pulmonic sound, etc.). This cardiac condition governs very markedly the course of the disease. Embolic processes in the spleen and kidney follow, and abscesses form. This is the condition commonly termed "malignant endocarditis," but von Leube believes that the so-called malignant endocarditis is really a cryptogenic septicopyæmia, in which the septic poisons become localized in their action on the endocardium and remain circumscribed for a long time here. In the majority of cases, however, the endocarditis is only a link in the great chain of multiple inflammatory foci.

Next in diagnostic importance comes the inflammation of the joints, which may occur as an involvement of a single joint, or many joints may be affected at the same time. In such cases the disease will very closely resemble acute articular rheumatism. The process concentrates itself most often in one joint, which becomes greatly swollen. In connection with this we often have bone involvement, which, however, may take place independently of the joint inflammation. The long bones are especially susceptible. The foci may be circumscribed or be extensive in their involvement of the bone tissues, and they may present the ordinary symptoms of osteomyelitis. Changes in the skin are almost constant. Roseola, erythema-like urticaria, purpuric spots, hemorrhagic pemphigus, blisters, pustules, herpes, etc., are among the most frequent of its manifestations. As the disease advances these cutaneous inflammations may extend into the underlying tissues and large areas of inflammation and œdema, or hæmato-purulent infiltrations, may be found.

These affections, especially the hemorrhagic forms, are met with in three-fourths of the cases of "cryptogenic septicopyæmia," and are therefore important signs from the standpoint of differential diagnosis. Symptoms referable to the nervous system are quite constant; headache, vertigo, sleeplessness, delirium, convulsions, and temporary paralysis are chief among these. When metastases develop, purulent meningitis, abscesses of the brain with their various symptoms, are among the possibilities. Retinal hemorrhages are occasionally seen. Through localization of the septic processes on the pericardium, pleura, and peritoneum there ensue at times small areas of inflammation, or serous or purulent exudations, with their symptoms. In the lungs miliary abscesses are found, or in other cases large infarcts, abscesses, lobular pneumonia; especially frequent is a diffuse bronchitis. Cyanosis and increased respiratory movements are brought about by the heart weakness and pulmonary complications.

The spleen is no more enlarged in this form than in the others. But metastatic abscesses in the spleen and liver may increase the size of these organs very markedly. The symptoms referable to the digestive tract are neither constant nor characteristic. Icterus is only occasionally seen. The kidney functions are almost always affected. Albumin in the urine is the rule, and is caused by the septic irritation of the renal parenchyma. Acute nephritis, with its characteristic symptoms, often follows. Large abscesses may be formed, but as a rule there exist multiple miliary, sanguino-purulent collections in the kidney tissue.

Résumé.—Here we have, then, a form of the disease, put down by von Leube under the name of "cryptogenic septicopyæmia, characterized by the following symptoms: A very pronounced, irregular fever with a disproportionately high pulse frequence, great emaciation, more or less marked nervous disorders, enlargement of spleen,

and special symptoms referable to the various organs in which the septic poisons become localized. In brief, then, the disease is one in which a peculiar form of exanthema develops, and in which the inflammation of the joints, the muscle and bone tenderness, the endocarditis, the embolic processes in the spleen, liver, lungs, and brain, the nephritis, the inflammation of the serous membranes, the petechial hemorrhages, all play a part in making up the complex of symptoms.

Grawitz ("Klinische Pathologie des Blutes," 1902), in discussing this form of septic poisoning, states that in most cases of "cryptogenic septicopyæmia" pyogenic bacteria are present in the blood, and that in many uncertain cases a positive diagnosis may be established by a blood examination. A negative result, however, does not exclude the disease. He further maintains that in cases of ulcerative or malignant endocarditis repeated failure to isolate the micro-organisms from the blood speaks most strongly against the disease being present, and *vice versa*.

In the cases of *pyosepticæmia* the symptoms vary somewhat, and are very largely governed by the pathological conditions which give rise to the disease. In gangrene of the lung, in tuberculous coxitis which has become secondarily infected, in chronic myelitis and myelitis transversa, in which decubitus, necroses, etc., are associated with poly-infections, we have striking examples of a pyosepticæmia. These processes, when examined bacteriologically, are found most often to harbor many different varieties of micro-organisms acting together. The streptococci, bacillus coli communis, proteus vulgaris, and bacillus pyocyaneus are frequently found associated in such a process. The symptoms then are those of the local condition and the general poisoning of the system. The fever is marked and the pulse rate is high and, as in the other forms of septic poisoning, the spleen is enlarged. The temperature is very irregular and of the remittent type. The nervous system is markedly involved, more so than in the pyotoxinæmic forms. The blood itself does not show such marked changes, and frequently micro-organisms cannot be demonstrated in the general circulation. We have then in these cases to deal with a condition of poisoning, due chiefly to the absorption of the toxic products from a localized process, rather than with disease resulting from a bacterial invasion of the whole system.

The symptoms in cases of septic intoxications and infections, as given above, are only composite pictures of the various forms of the disease. In many of the actual cases the disease manifests itself differently, and the course of these cases can be best demonstrated by giving examples of actual cases. The following cases, unless otherwise designated, have been taken from the records of the Methodist Episcopal Hospital of Brooklyn, New York.

Case I. Pyotoxinæmia Following Infection of Knee-Joint.—On June 20th, 1888, an operation was done on the knee-joint to remove a foreign body. The next day there were considerable pain in the joint and tenderness. Temperature rose to 100.6° F., pulse 110, respirations 25. Second day after operation pain continued, the temperature jumped to 104° F., pulse 148, and patient felt listless. Third day: Patient began to vomit, at first at intervals of two or three hours and later in the day almost continuously, temperature remaining high and pulse becoming irregular and rapid. Some diarrhœa. Fourth day: Vomiting not so marked; bowels moving involuntarily; patient very restless. Temperature continuously above 102° F., pulse averaged 138, respirations 28. Fifth day: Joint re-opened and small amount of sero-sanguineous fluid was evacuated. Irrigated with antiseptic solutions and thoroughly drained; no change in general condition. Sixth day: Patient delirious, the bowels still moving frequently, temperature and pulse continuously high. Eighth day: Still delirious; much diarrhœa. Patient lies in a sort of stupor, twitching of muscles of the left shoulder and fingers of right hand; marked flushing of left side of face. Slight paralysis of the left facial muscles. Picking at bedclothes. Temperature had fallen to 100° F., pulse 120. Perspired freely. Under treatment, by thorough drainage and irrigation with antiseptic solutions, these symptoms gradually abated with the exception that the temperature remained continuously above 100° F., and the pulse about 100. On the thirtieth day the joint was again opened and some dead bone removed, after which the wound healed, the temperature becoming normal and the pulse dropping to 90. The patient had entirely recovered after an illness lasting over two and one-half months. In the accompanying chart are shown the temperature and pulse curves for the first sixteen days of the disease.

CLINICAL CHART.

Name,..... Disease,..... Date,.....

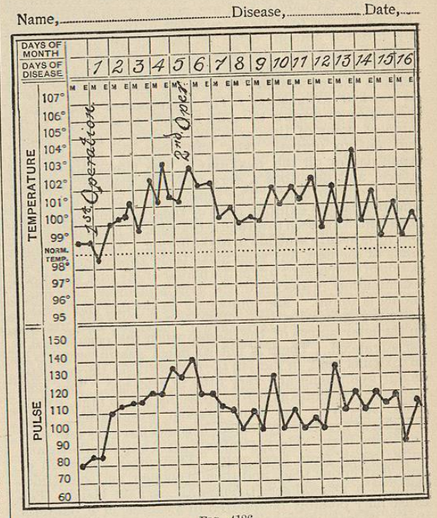

FIG. 4186.

This is an example of a case of pyotoxinæmia arising from an infection in the knee-joint. Infection of this joint is an event always to be dreaded by the surgeon, for in almost all such cases a rapid and often fatal toxæmia, and frequently a pyæmia, occurs. The synovial membranes of the joints offer very little resistance to the inroads of bacteria, and when once affected are easily destroyed and the process attacks the underlying tissues. It has been shown that streptococci may be introduced under the skin of an animal and there set up only a localized abscess, but the same organism when injected into the synovia of the knee-joint will bring about a virulent and rapidly fatal intoxication. In the present case, no bacterial examination was made. The infection evidently took place during the operation, and although the condition was soon discovered and thorough drainage established, still the process persisted for over two months. During the course of the disease the temperature and pulse were continuously high, with intercurrent remissions. The point of special interest in this case is the peculiar involvement of the nervous system, which showed itself in the unilateral paralysis of the facial muscles, the twitching of certain sets of muscles, and the flushing of one side of the face.

Case II. Cryptogenic Pyotoxinæmia.—Patient had been in poor health for about a year. Two weeks previous to admission had a severe chill, followed by fever and

sweating. Chills occurred on successive days thereafter. In a few days patient began to complain of great pain in gluteal region, and then in knee and ankle. At end of eight days there were marked swelling, pain, and tenderness of the left knee and ankle. This continued, and on admission to hospital the temperature was 103° F., pulse 120. Under local treatment inflamed condition of ankle subsided, but knee remained swollen and tender. May 19th: Knee-joint was opened and considerable pus evacuated. Drained. During the ten days following the operation the temperature abated somewhat, but the pulse remained continuously high. Patient in a semi-stupor. June 1st: Patient passed into a "typhoid state," temperature becoming irregular again. June 3d: A necrotic spot appeared on left buttock. Wound looks more healthy. June 6th: Severe chill, following which temperature reached 103° F. and pulse 140. Necrotic spot on buttock broken down and surface granulating slowly. During next six days temperature at no time high, but irregular. Pulse vacillating between 120 and 170, very weak and irregular. Frequent diarrhœal movements. June 12th: Death.

Autopsy showed only inflammatory condition in and around knee-joint; cloudy swelling of kidneys; fatty degeneration of liver. Spleen was soft and normal in size.

The question arises in this case as to how the bacteria gained entrance to the joints. The autopsy does not help us in deciding this. There were no other foci of inflammation and no history of any wound as a starting-point. It therefore comes under the head of cryptogenic pyotoxinæmia, the main point of suppuration being, as in the previous case, in the knee-joint. There evidently was also an inflammatory process in the gluteal region and in the ankle, but these were controlled. There had been no pneumonitis, otitis media, enteritis, or urethritis to attract our attention. The initial symptoms, repeated chills, and high temperature, followed later by pain in the gluteal region, knee, and ankle, would suggest embolic pyæmia. But this we cannot have without some initial lesion. The origin then remains a mystery, cryptogenic. In this case there was no enlargement of the spleen.

Case III. Staphylococcus Pyotoxinæmia with Transition to Pyæmia.—February 19th, 1888: Patient fell downstairs, sustaining an injury to left ankle. No external wound. February 28th entered hospital complaining of pain in and around ankle-joint, which was somewhat swollen, tender, and red over a circumscribed area. No fracture could be demonstrated under chloroform. Pain increased in spite of local applications, and on March 2d patient had a temperature of 103° F. There were slight remissions of the continuously high temperature. Patient's general condition poor, pulse 110 to 120 per minute. March 5th: Very restless and during night slightly delirious. Area of redness extended slowly. March 6th: Fluctuation appeared at ankle. Incision was made and considerable pus was evacuated. Bone not involved. Following the operation there was a slight fall in the temperature, which, however, rose again the next day to above 103° F. March 7th: Temperature still high, respirations very rapid and superficial, but examination of the lungs was negative. Over the cardiac region, most distinctly over the aortic area, were heard a distinct friction sound and a blowing murmur, where previously there had been none. In the evening this friction sound disappeared. During the night the patient became very restless, and toward morning began to vomit at long intervals. Temperature reached 104.5° F., pulse increasingly rapid, 130 to 160. There was marked emaciation. Vomiting became more frequent, bowels moving involuntarily. Gradually the patient became comatose, pulse imperceptible. Death.

Autopsy: Pericardium injected and the sac distended with pale, greenish-yellow fluid and flocculi of fibrin. No fluid in either pleural cavity. Lungs in places adherent. Heart is covered with a layer of fibrin, thicker in some places than in others; fibrin also seen on the pericardium. Left lung: Scattered through the lung are areas of congestion surrounding infiltrated patches with whitish centres; none of these areas is larger than a pea. Right lung: On surface, especially on anterior border, are a number of small circumscribed white spots, cone-shaped upon section. On posterior surface are a number of small punctate spots of hemorrhage. The lung is somewhat œdematous and congested; bronchi are normal. Heart muscle is very pale. Spleen enlarged and soft. Right kidney: Just beneath the capsule is a single small abscess.

Microscopical examination: The nodules described in the lungs and kidney proved to be small infarcts, the blood-vessels leading to them being occluded by firm thrombi. They consist of masses of inflammatory tissue with small pus collections.

Bacteriological Examination: Original wound, infarctions of kidney and lungs, showed pure culture of staphylococcus pyogenes aureus.

Diagnosis: Acute pericarditis, multiple infarctions of both lungs, abscess of kidney. Staphylococcus pyotoxinæmia passing into pyæmia.

Remarks: We have here the history of an injury to the ankle-joint without any external wound being present. The staphylococci may have gained entrance through the skin which was evidently bruised, although no actual open wound occurred. Again, the micro-organisms may have been conveyed to the joint by the blood from some other undiscovered focus. The only clinical evidence of pyæmia was noticed on March 7th, when a pericardial friction sound was heard. There were no chills, but there were marked gastro-intestinal symptoms, a continuous remittent fever, and a weak but rapid heart's action —in fact, all the clinical symptoms of a pyotoxinæmia, which at autopsy proved to be an embolic pyæmia.

Case IV. Pyosepticæmia.—November 8th: Patient on admission to hospital presented an area, over right eye, about three inches in diameter, bright red in color, with a well-defined margin, slightly œdematous and gangrenous in places. It was covered with small suppurating points. Upper eyelid enormously swollen. Temperature 106° F., pulse 120, respirations 35. Operation: Curetting of necrotic tissue, free incisions. November 9th: Temperature dropped to 95.6° F., pulse 75, respirations 25. Patient delirious, tinnitus aurium. Extensive reddish, papular eruption on chest. Skin cold and clammy. Later in day, temperature rose to 104° F., pulse 110; vomiting. November 10th: Diseased area shows the characteristics of a sloughing phagedæna. November 11th: Restlessness and delirium alternating with stupor. Great prostration. Temperature continuously high. The phagedæna spread rapidly and involved a large portion of the head. Patient died in coma.

A glance at the accompanying chart (Fig. 4187) will show the remarkable deviation in the temperature and pulse curves. The disease, originating in an inflammatory condition of the face, developed into a virulent phagedæna, combining a suppurative and a putrefactive process, which resulted in a rapidly fatal intoxication and infection of the entire system. It therefore falls into the class of *pyosepticæmia*. However, most cases which may be classified as

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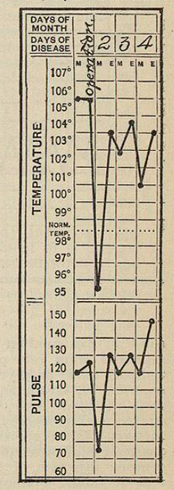

FIG. 4187.