

pyosepticæmia run a more subacute or chronic course. The following case reported by Brunner (*loc. cit.*, p. 101) is an excellent example of this, and his analysis of the same is of interest:

Diagnosis: Chronic myelitis; decubitus sacralis. Putrid abscess of thigh. Polyinfection by streptococci, bacillus pyocyaneus, bacterium coli, proteus vulgaris. Death. Pyosepticæmia.

History: Patient well until three years ago. First signs of disease appeared as feeling of fatigue in the feet, chilly sensations and formication. The symptoms were steadily progressive. Disturbance in the function of the bladder and rectum appeared, and finally loss of control of same. In December complete loss of use of the legs; later, decubitus sacralis. Admitted to hospital January 25th, 1898.

Status præsens (at time of admission): Both legs useless. Hardly any sensation in them. Beginning involvement of upper extremities. Involuntary micturition and defecation. Decubitus spots, about size of silver quarter of a dollar, on each heel. Over the sacrum a deep decubitus about the size of the palm of the hand; sacrum exposed, a further defect over the lumbar vertebrae and over the trochanters. High temperature. Urine cloudy, strongly ammoniacal.

Course: February 13th: The decubitus slowly enlarging. Application of vinum camphoratum. In the region of the left trochanter a collection of foul-smelling pus, undermining the skin. February 19th: Always high temperature with morning remissions (see accompanying chart, Fig. 4188). On right thigh a large fluctuating abscess has formed.

Incision and drainage. A large amount of filthy, bad-smelling material and gas evacuated. During the night *exitus lethalis*.

Autopsy: Ten hours after death. Extract from the protocol. On back, over the sacrum and over the trochanters, the above-described decubitus defects. The abscess cavity on the right thigh reaches from the patella to the middle of thigh; its periphery presents masses of bad-smelling necrotic tissue, with threads of fascia running through it. A sound can be passed from this abscess cavity up to gluteal region. Spleen very much enlarged and soft. Both kidneys contain small abscesses, the size of a pea.

Bacteriological Examination.—I. During life: 1. Examination of urine: bacterium coli. 2. Examination of blood. February 19th: Blood aspirated from vein of arm, under aseptic conditions. Cultures made on glycerin-agar and in gelatin. Result negative. 3. Examination of pus evacuated from abscess cavity at time of incision. Smear examination: streptococci in short chains, numerous small rod-shaped bacteria. In the glycerin-agar and gelatin cultures, copious growth of pure culture of proteus vulgaris. Pathogenesis: Injection of 1 c.c. of original culture into ear vein of rabbit, evening of February 24th, caused death during night of February 25th. Guinea-pig: Injection

of 1 c.c. of the same culture subcutaneously into wall of abdomen on February 24th, 4 p.m. February 27th, local infection. February 28th, fluctuation. March 1st, incision and thick yellow pus evacuated! Culture on agar showed proteus in pure culture. Injection of 1 c.c. of the same growth into abdominal cavity of guinea-pig. Animal lived.

II. At the autopsy: 1. From the deepest portion of the decubitus; proteus vulgaris greatly predominating; Bacterium coli and bacillus pyocyaneus also present. 2. Thigh abscess: proteus vulgaris. 3. Heart blood: pure culture of proteus vulgaris. 4. Liver: proteus vulgaris. 5. Spleen: negative. 6. Kidney abscess—could not be properly examined owing to use of non-sterilized knife in making the section.

Analysis of the case by Dr. Brunner. Avenue of the infection. On account of the myelitis the trophic changes and anesthesia of the skin took place, and owing to pressure the mortification of the tissues occurred and pressure-necrosis resulted. Owing to incontinence of urine and feces the area became easily infected with the proteus vulgaris and bacterium coli, to which later was added the bacillus pyocyaneus. The B. coli caused early a cystitis. Subcutaneously the tissue surrounding the sacral decubitus broke down under the attack of the pyogenic micro-organisms. The process worked down along the thigh and manifested itself there in the formation of a putrid, gas-containing abscess. In this abscess the proteus vulgaris was the most active agent, and was found in pure culture in the remotest portions of the cavity. Streptococci were found only in smear preparations and could not be demonstrated in the cultures. It is probable that they were active during the abscess formation up to the time when the incision was made, but were no longer able to develop or were killed by the proteus in the culture media. From this extensive area of putrefaction with destruction of much tissue, the poisons which were elaborated were doubtless absorbed into the blood. It is also very probable that from time to time various streptococci and proteus rods wandered into the blood stream; they, however, did not develop in the blood; a bacteriæmia—bacterial septicæmia, in the sense of Koch's definition—was not present. That such a condition did not exist at the height of the disease is proven by the negative result in the examination of a relatively large amount (5 c.c.) of the blood. The bacteriæmia post mortem was in itself not proof positive.

Characteristics of the Clinical Picture. If one may ever speak of a "rotten infection" and "putrid intoxication," this case certainly falls into such a class. Putrefaction and malodorous decomposition were brought about through the activity of four dangerous micro-organisms: streptococcus, bacterium coli, proteus vulgaris, and the bacillus pyocyaneus. Together with this disintegration occur the pyogenic phenomena due to these germs. A large gas abscess developed, and this, together with the decubitus, was the chief source of the poison which brought about the general intoxication. High fever, high pulse frequency, dry tongue, enlargement of the spleen, changes referable to the nervous system—these are the symptoms of the intoxication. The temperature curve again shows the zigzag remittent type without special diagnostic significance. An intense invasion of the circulation by the causative agents, or any growth of the same in the blood, did not occur. Bacteriæmia is excluded, and a toxæmia remains. Since we have in this case a combination of pus formation and putrefaction, it falls into the class of pyosepticæmia. The small abscesses in the kidneys are explained as an extension of the B. coli infection from the bladder. In the absence of a bacteriological examination a definite conclusion cannot be arrived at.

The gonococcus starting from an initial lesion in the urethra may act alone or in combination with other micro-organisms to bring about a general infection or pyæmia. Bujwid, in his article, "Gonococcus als die Ursache pyämischer Abscesse" (*Centralblatt für Bakteriologie*, 1895, Bd. xviii., S. 435), presents the following

case: Young man, thirty-two years of age, suffering from chronic gonorrhœal urethritis, after passage of a sound had a severe chill which lasted some time. This was repeated the next day and the two or three days following. Later, four abscesses appeared: one in the region of the left shoulder, one in the right popliteal space, one on the inner side of the left leg, and one over the external malleolus of the right leg. These abscesses were all confined to the muscular tissues and did not involve the connective tissue or the joints. Upon incision they contained a small amount of odorless, brownish-red pus, in which the gonococcus in pure culture was found.

Ohmann reports a case in which the complications were multiple arthritis and tendo-vaginitis, epididymitis, and nephritis, and in which case he was able to demonstrate the gonococcus in the blood. Brunner states that in these cases the course may be very acute with all kinds of complications, but that there is very little tendency to destruction of tissue. Finger, from his observations in gonococcus pyæmia, holds that in such inflammations there is always a tendency toward the early formation of granulation tissue and later an increased connective-tissue formation. There occur in the urethra strictures; in the prostate a destruction of the glandular structure; in the epididymis, thickening of its walls; in the joints, ankylosis etc. The micro-organism is less energetic and less destructive in its action than are the other pyogenic agents.

In the cases of puerperal infection, owing to the richness of the blood and lymph supply incident to pregnancy, the disease is often very rapid and fatal. It may follow the type of a pyotoxinæmia, a pyosepticæmia, or lastly a pyæmia. In the rapidly fatal cases pyotoxinæmia is most frequent, while pyæmia is often a complication. In the subacute cases pyosepticæmia is often the form of the disease which is present, the uterus and adnexa being found in a necrotic or gangrenous state associated with pus formation.

Otitis media frequently is the starting-point of a general septic infection, the sigmoid sinus becoming involved and thrombo-phlebitis resulting. Purulent meningitis and abscess of the brain with their characteristic symptoms may cause death, or a typical embolic pyæmia with metastatic foci in the lungs, heart, kidneys, etc., may develop. The course is generally long.

Prognosis.—In septicæmia without bacterial activity the prognosis depends mostly upon the etiological factors and the ability to remove the cause. When the condition is due to retained secundines, the removal of the same is followed by rapid recovery. In the various forms of ptomain poisoning, from the ingestion of putrid foods, some prove rapidly fatal, while others recover upon removing the offending material from the intestinal tract. But, in general, the adoption of prompt treatment, as soon as the cause is discovered, is followed by recovery.

In the milder forms of pyotoxinæmia and pyosepticæmia the disease often is amenable to treatment, but all forms depend upon many factors. The age of the patient, the ability of the tissues to check the inroads of the bacteria, the virulence of the micro-organism, the site of the infection have all been referred to above. Even in the severe cases, the establishment of thorough antiseptic treatment may bring about recovery. In general the prognosis is poor. In the majority of cases of pyosepticæmia the prognosis is bad.

The prognosis in pyæmia is always grave. When metastases develop rapidly and involve important organs the result is usually death. In gonorrhœal pyæmia the prognosis is better. Warren ("Surgical Pathology," p. 278) claims that there is a relatively high percentage of cures in puerperal pyæmia.

Diagnosis.—To distinguish between the different forms of the disease from a clinical standpoint is often impossible. It must be remembered too that one form may merge into an advanced form without any marked symptoms to designate the period of transition. In septicæmia without bacterial activity surgical interference with dis-

appearance of the symptoms will establish the diagnosis. In the cryptogenic or spontaneous forms of the disease a careful examination of the entire body must be made and all of the secretions be carefully tested. The presence of a suppurating focus, lymphangitis, enlarged regional lymph nodes, with a continuously high temperature, very rapid pulse, absence of chills, indifference of the patient, gastro-enteritis, presence of albumin and bacteria in the urine, and bacteriæmia would point most strongly to pyotoxinæmia. Such conditions as a gangrene of the lungs, moist gangrene of the extremities or other portions of the body, extensive decubitus and other necrotic and putrefactive processes in which pyogenic bacteria are present, and accompanied by a markedly irregular temperature, rapid and feeble pulse, pronounced nervous disorders, no marked blood changes, and negative bacterial blood tests, together with the other phenomena of septic intoxication, may be safely diagnosed as pyosepticæmia. If, in the presence of an imperfectly draining wound, cellulitis, lymphangitis, thrombo-phlebitis, ulcerative endocarditis, pyosepticæmia, pyotoxinæmia, or any of the conditions above mentioned, there occurs a sudden sharp chill, accompanied by a marked rise in temperature, and followed by sweating and pain referred to some distant point, pyæmia must be suspected. If, in the subsequent course of the disease, the chills are repeated, the mental faculties remain clear, marked emaciation, hyperæsthesia, diaphoresis, and great prostration are present, and the symptoms of metastatic abscesses make their appearance, the diagnosis of pyæmia is definitely established.

Among the diseases which resemble the various forms of toxæmia, septic intoxications, and septic infections, may be noted acute articular rheumatism, malaria, typhoid fever, acute miliary tuberculosis, severe anæmias, and uræmia. But in each case a careful inspection of the history and a thorough consideration of the signs and symptoms which each disease presents will result in a correct differential diagnosis.

Treatment.—Prophylactic.—The state of our knowledge at the present day enables us to operate almost without fear of infection, and a thorough understanding of the aseptic treatment of wounds is presupposed by the writer. It is, however, to be especially emphasized in the preparations for any operation on the knee-joint. Chronic tuberculous processes, wherever they may be, especially those of the joints and bones, are most frequently confined to the points of their primary activity and do not generally give rise to a systemic intoxication; but if, during the course of an operation upon such a process, it becomes secondarily infected the condition becomes much more serious, and any of the forms of intoxication or infection may develop. This must also be borne in mind in the treatment of any infected wound, for a polyinfection is generally more difficult to handle than a monoinfection. In the various nervous diseases in which trophic disturbances are present, much care must be exercised to prevent bedsores. If a decubitus should appear despite the frequent change of position, rubbing with alcohol, etc., they should be treated antiseptically, to prevent if possible any infection. The prophylactic measures in the treatment of compound fractures, extensive lacerated and contused wounds, and burns, should always be carried out most carefully.

Local Treatment.—In the cases of septicæmia without bacterial activity the results of removing the cause are very marked and satisfactory. If the offending substance be contained within the intestines, a course of calomel in divided doses, followed later by a saline purge, may be all that is needed to bring about recovery. In the puerperal cases the removal of the secundines, the fingers being used as a curette and the scraping being followed by a hot saline irrigation, is indicated. The same principle is to be followed in all of its forms, *i.e.*, the cause must be removed under all possible aseptic precautions.

In the other forms of the disease the care of a pus focus must first be considered. If the case presents itself

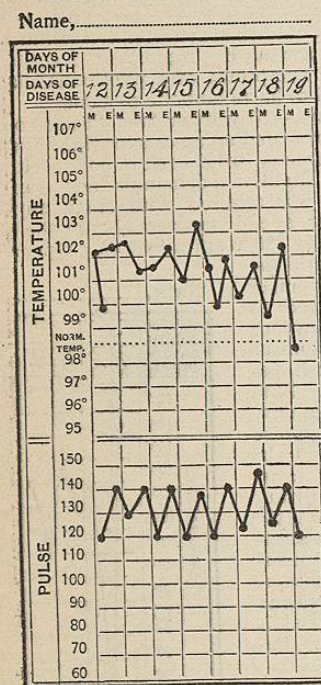


FIG. 4188.

with an abscess already formed, the indication is to evacuate the pus. *Ubi pus, ibi evacua.* If a putrefying area is associated with a purulent focus, as much as possible of the putrid material should be cut away, the surgeon being careful not to expose healthy surfaces. In such a condition it may be proper to swab out the cavity with pure carbolic acid and then immediately after to cleanse it with alcohol. All such abscess cavities should be irrigated with some antiseptic solution and thoroughly drained, at first with iodoform gauze and later by means of rubber-tube drains. In cases in which, following an operation, there develop the symptoms of toxæmia, an early inspection of the wound should be made, and if infection has taken place the sutures should be removed, the wound irrigated with some antiseptic solution, drainage established, and dressings wet with some non-irritating solution, as Thiersch's solution of boracic and salicylic acids, be applied. The wound should be dressed daily or, in the virulent cases, more often. In some cases constant irrigation is indicated. In pyæmia, where possible, the secondary foci should be opened and treated as above.

**General Treatment.**—The routine treatment always includes as a preliminary procedure the stimulation of all of the excretory organs. The bowels should be freely moved, the kidneys stimulated, and diaphoresis increased. The proper nourishment of the patient should be carefully looked after, easily digested food being given in small amounts, and, when the stomach is unable to retain food, rectal enemata of peptonized milk, peptonized egg, and whiskey should be given every four hours, in amounts not exceeding from four to six ounces. The hygiene of the sick-room is also of importance; every opportunity for fresh air, sunlight, and cheerful surroundings is to be favored. In no condition is careful nursing more necessary. The use of drugs is not very satisfactory. Antipyretics are contraindicated, for they often act as powerful cardiac depressants and mask the symptoms. Alcohol in the form of egg-nogs, whiskey, and brandy, is considered by many to have very beneficial effects. In fact, these patients bear large amounts of alcohol very well, and it should be given freely. The heart's action can be stimulated best by using relatively large doses of the tincture of digitalis. If the diarrhoea is troublesome, it may be controlled by opium, or by bismuth and salicylic acid in their various forms. Paresis of the gastro-intestinal tract may be treated by an hypodermic injection of atropine sulphate gr.  $\frac{1}{16}$ , and bisulphate of quinine gr. v., to be repeated in five hours if necessary.

The use of intravenous and subcutaneous infusions of normal salt solution acts very beneficially in these cases. It helps to maintain the circulation, protects the nervous centres, dilutes the poisons, and assists very materially in the elimination of both the micro-organisms and their toxins. The infusions may be given daily in relatively large amounts, 1,000–1,800 c.c. being given intravenously. An objection has been raised to this, the statement being made that such a regular dilution of the blood would cease, after the first day or two, to have any beneficial effect; but this is not true, for in the course of twenty-four hours the excess of the solution may be entirely excreted from the body and a new infusion be called for. With this as a basis, many experiments have been made by adding antiseptics to the solution with the hope of bringing about a direct antiseptic influence upon the micro-organisms in the circulation and tissues.

**Intravascular Antisepsis.**—Experiments were carried out by Maguire, of London, to ascertain the effects of introducing a solution of formaldehyde gas directly into the circulation. His experiments were carried out upon animals and upon himself, and he concluded that 50 c.c. of a 1 to 2,000 solution of formalin, could be safely introduced into the circulation without bringing about any serious blood changes. After injecting 100 c.c. of a 1 to 2,000 solution of formaldehyde into his own circulation, the only change that was noted was the appearance of albumin in the urine. Later, he injected 263 c.c. of a 1

to 2,000 formaldehyde solution. There followed considerable cramp-like pain in the arm, where the solution was injected, and peculiar cardiac distress. Many red blood corpuscles and blood-coloring matter were noted in the urine. This disappeared the next day. A solution of 1 to 1,000 formaldehyde, of which 63 c.c. was injected, caused severe pain in the arm and faintness. Maguire's conclusions were that 50 c.c. of a 1 to 2,000 solution of formaldehyde (1 to 800 solution of formalin) was the maximum dose to be safely injected in man. That is to say, if the total quantity of blood in an adult be estimated at 5,000 c.c., the solution of formaldehyde in the blood would be 1 to 200,000, which is a very efficient germicide. Barrows, of New York, applied this principle in the successful treatment of an advanced case of puerperal sepsis, as reported in the *New York Medical Journal*, January 31st, 1903. In his case he gave an intravenous infusion of 500 c.c. of a 1 to 5,000 aqueous solution of formalin, and on the third day following a second infusion of 750 c.c. of the same solution was given. There followed a rapid, marked, and permanent improvement which resulted in recovery. As a result of his experiments and those of others he concludes that the procedure depends on its being correctly and scientifically applied. He warns the profession against its indiscriminate use where proper blood cultures have not been made. It is also suggested that normal salt solution be used in making the formalin solution, as it has been found that no change takes place in the formaldehyde in this solution. Although no harm has been done to the blood cells by the infusion of formalin in distilled water, theoretically the normal salt solution is to be preferred.

Portesque-Brickdale, as a result of his experiments upon rabbits, published in the *Lancet*, January 10th, 1903, does not favor the use of intravascular antiseptics. He states: "That rabbits injected daily with non-toxic doses of oxycyanide of mercury, formic aldehyde, chinolol, protargol, or taurochololate of sodium are not thereby protected from the usual effects of a previous inoculation of virulent anthrax; and that chinolol and formic aldehyde in large doses (toxic) so depress rabbits infected with the pneumococcus that they die sooner than an untreated animal."

Credé has applied the theory of intravascular antiseptics in the use of colloidal silver or collargol. This he claims to be a non-irritating, strongly bactericidal agent which may be employed as an injection or as an intravenous infusion without any detrimental effects, and which is followed by marked improvement and often by recovery from the most severe forms of septic infection. He recommends it especially in cases of general sepsis, puerperal fever, pyæmia, and septic osteomyelitis. In the less severe cases, especially where the infection is localized, he uses a fifteen-per-cent. ointment of colloidal silver, rubbing two or three grams into the skin, after mildly irritating the same and causing local hyperæmia. In the more severe cases he recommends an intravenous injection of from 5 to 20 c.c. of a one-half to one-per-cent. solution, repeated daily or every week as required. Of his more recently perfected collargol solution he uses from 2 to 10 c.c. of a two-per-cent. solution. His technique is as follows: The syringe should be cleansed, the silver solution, and no other chemical, being used for this purpose. The syringe is then partially filled with collargol solution, and the detached needle is inserted, either through the skin or, if necessary, but only after a carefully made preliminary dissection, into the vein. The syringe having been attached to the needle, some blood is withdrawn into the syringe in order to remove from it any bubbles that may be present. Finally, the fluid is slowly injected. Subcutaneous injections are not effective. Viêt used the intravenous method in a series of twenty cases of sepsis, and recommends it strongly.

The experiments of Grindes and Balardzsheff, however, do not bear out the conclusions of Credé, for they reported that a one-per-cent. solution of collargol had no effect on anthrax, staphylococcus, and streptococcus infections. They report that unless the injection is given at the

point of the inoculation of the micro-organisms, no effect followed. They claim that the simple injection of collargol intravenously causes death sometimes. Baginski, Naltenius, and Kunzl-Krause report no beneficial results. However, other experimenters have met with decided success in its use, and the failures of others may be due to faulty technique.

Unguentum Credé, an ointment of metallic silver, has been used by some in the treatment of these cases. Forty-five grains are rubbed into the skin very gradually.

**Antistreptococcus serum** of Marmorek is limited in its usefulness to certain kinds of cases, but in these it has met with marked success. The favorable cases are those which are caused by streptococci alone, and when the infection is a mixed one, the serum acts upon the streptococcus infection alone. In many of the cases reported the disease was already far advanced, and consequently they can scarcely be considered satisfactory test cases of the usefulness of the procedure. Packard and Wilson (*American Journal of the Medical Sciences*, December, 1902, p. 1033) have collected 117 cases treated during the past two years with antistreptococcus serum, and in 114 of these cases there followed either temporary improvement or prompt recovery. After citing many other cases they make the following statement: "All of these reports tend to convince us of the fact that antistreptococcus serum will at least do no harm, and that in cases in which the streptococcus is alone involved it will eliminate that micro-organism and control the symptoms caused by its toxin unless used too late for any remedy to be of avail. When the streptococcus infection is found in combination with those of other micro-organisms we have learned that the serum has no influence except in so far as it controls the streptococcus symptomatology. Undoubtedly the attempt to obtain a polyvalent serum is one in the right direction, and, as in typhoid fever, it presents a key to new accomplishments in the line of special serum therapy."

Special forms of treatment are indicated in infections of different regions of the body. In extensive processes involving the extremities amputation may save life, but even after such a drastic measure it may be found that the infected thrombus has extended too far to be checked, or the systemic disease may be developed to such an extent that amputation is contraindicated. Klebs first suggested the idea of ligating and removing the veins in which thrombi had formed before the infected emboli should become broken off and pyæmia set up. This procedure is especially considered in involvement of the lateral and sigmoid sinuses following suppuration in the middle ear. Here thrombo-phlebitis is very likely to occur, and the internal jugular vein is also frequently involved. The first step of the operation should be in most cases the ligation of the internal jugular below the point of involvement. Then the sinus may be exposed and the purulent material scooped out or gently washed out. Sometimes an excision of a portion of the vein is indicated.

In cases in which the pyogenic focus is in the pelvis, or in which a general suppurative peritonitis exists, the entire abdominal cavity may be flushed out with hot salt solution. The head of the patient's bed may be raised, which, as Fowler suggested, will favor gravitation of the purulent material into the pelvis, from which it may be aspirated every few hours.

The question of the treatment of puerperal sepsis occupied the attention of the Fourth International Congress of Obstetrics and Gynecology in Rome, September, 1902, and formed one of its chief topics for discussion. The following extracts are taken from the report by Dr. H. N. Vineberg ("American Gynecology," January, 1903). The conclusions of H. Treub (Amsterdam) were as follows: The usual methods of treatment (curettage, intra-uterine irrigations, ice bags, cold baths, turpentine injections, antistreptococcus serum, alcohol) for puerperal sepsis localized in the uterus are in most cases followed by cure. In a few exceptional cases hysterectomy will be indicated. Tuffier (Paris) said that in a given case of

*septicæmia*, post partum, or post abortum, when there is no cause for the fever to be found either in the external genitals or in other organs, when the usual methods of treatment are of no avail and when the peritoneum and adnexa are intact, and the uterus is large, flabby, and is discharging fetid lochia, and if the patient's general condition warrants it, total extirpation of the uterus should be done, whether there be placental retention, a sloughing myoma, or the so-called "metritis desiccans." A. Pinard (Paris) recognized only the following indications for hysterectomy: retained putrid placental remains, sloughing myoma, and perforation of the uterus.

The *convalescent stage* calls more for careful nursing and attention to general hygienic principles than for drugs. Nourishing food, fresh air, and cheerful surroundings are the essentials. *Paul Monroe Pitcher.*

#### SERUM DIAGNOSIS AND SERUM THERAPY.—I.

**SERUM DIAGNOSIS.**—Serum diagnosis and serum treatment rest upon the same fundamental principles. When a group of foreign cells enters an animal body, whether in the form of disease or of experimental infection, there results a group of changes both in the foreign cells and in one or more cell groups of the body which they invade. These changes are peculiar and specific in relation both to the invader and to the territory invaded. The blood, as the representative of all organs, undergoes specific changes which are at the basis both of serum diagnosis and of serum therapy. A few examples will make this clearer. When a human body is invaded by a group of cells of that peculiar species known as typhoid bacilli, the blood acquires a number of new and specific properties, specific in the sense of manifesting their action only in relation to the typhoid bacillus. Upon one of these new properties serum diagnosis is based. The ability to agglutinate any specimen of the race typhoid bacilli is possessed to a feeble degree by the blood of many healthy human beings. But when a person is or lately has been suffering from typhoid fever, the agglutinating power of the blood over typhoid bacilli becomes greatly increased, and the resulting reaction, first brought into clinical use by Widal in 1896, is that ordinarily known as the "Widal reaction." This reaction, like all the agglutinative reactions, is specific in a double sense. The bacilli are thus agglutinated only by the serum of patients recently or formerly infected with typhoid. On the other hand, no bacillus, except the typhoid bacillus, is clumped in high dilutions by typhoid serum. The reaction has therefore a double use. Given a group of bacilli clearly identified as typhoid, we can use them for testing the serum for diagnosis in doubtful febrile cases. Or, given some serum or blood from a case known to be typhoid, we can use this liquid either fresh or dried on blotting-paper as a means of identifying doubtful cultures of bacteria.

The agglutinative reaction has now been shown to be of use, in both the ways just exemplified, as a means of identifying a considerable variety of diseases on the one hand, and of bacterial species on the other. The diseases in which it has been found of value thus far are, first and foremost, typhoid in which its use has been firmly established since 1898. Probably the number of tests performed in this disease exceeds those performed in all of the diseases put together. Next to typhoid, Malta fever and epidemic dysentery of the type due to Shiga's bacillus are the diseases in which the agglutinative reaction between the patient's blood and the specific bacillus of the disease is most frequently performed. The reaction has also been found to be of value in the diagnosis of the bubonic plague, and it is apparently our only reliable means of diagnosis in cases of infection by the so-called paratyphoid bacillus, an organism closely allied to, but not identical with, the bacillus of Eberth.

A certain amount of agglutination has also been demonstrated in infections due to the tubercle bacillus, the pneumococcus, the pathogenic streptococci, and various others, but the reaction is not distinct enough to be clinically available. An agglutinative reaction may also be obtained with the serum of cases of glanders, whether in