THE DIAGNOSIS OF TYPHOID FEVER

BY

CLINICAL, HÆMATOLOGICAL, AND BACTERIOLOGICAL

METHODS

THESIS FOR THE DEGREE OF M.D.

PRESENTED BY

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SEPTEMBER, 1906.

ProQuest Number: 27626708

ProQuest 27626708

TYPHOID FEVER,

THE acute infectious disease, caused by the invasion of the body by the specific bacillus of Eberth, is so protean in its character and its clinical picture so variable with regard to severity, duration, grouping, and development of the individual symptoms, that any description, however exhaustive, is impossible. No acute disease is so varied in its manifestations, and it may be truly said that, with the exception of the typical roseolous eruption, no single clinical symptom is pathognomonic. In an epidemic we meet with all grades of the disease, between those so mild as to be able to walk about and scarcely take to bed, and those severe from the onset, and rapidly pursuing a fatal course; and even in house endemics, where circumstances that would play an important rôle in a general epidemic are not to be considered, we may see cases passing rapidly to a fatal issue, while others are so mild that, but for the immediate circumstances attending the development of their illness, the true nature of it would probably have escaped recognition.

Recognised now as a modified septicæmia—a septicæmia, because, as the result of recent methods we know that the bacilli are present in the circulating blood and in the various organs; and modified in that, in the greater number of the cases, if not in all, there is a primary local lesion in the intestine, from which the dissemination of the bacilli takes place—the terms typhoid and enteric are alike inappropriate, as the former conveys the impression that the disease resembles typhus, and implies the development of the "typhoid state" pointing to profound toxæmia; while the latter gives undue prominence to the local intestinal manifestations, which in some cases are a-wanting.

The importance of early diagnosis is only too obvious, even if one has only to consider the question of the proper treatment for the case, but it becomes more so if looked at from a public health view point. As illustrative of the latter statement, I may here mention that two local epidemics of typhoid which came under my care in hospital could both be traced to two atypical and unrecognized cases in children.

Osler says of it, "that it is a general infection caused by the bacillus Typhosus, characterized anatomically by hyperplasia and ulceration of the intestinal lymph follicles, swelling of the mesenteric glands and spleen, and parenchymatous changes in other organs. Clinically, the disease is marked by fever, a rose-coloured eruption, diarrhœa, abdominal tenderness, tympanites, and enlargement of the spleen." He adds however, "that the symptoms are extremely inconstant, and even the fever varies in its character." It is now known, however, that the local intestinal lesions may be so slight as almost to escape detection, and some eminent observers even declare that they may be entirely absent. As regards the symptom complex mentioned, it is beyond dispute that it is rarely complete, one or more of the elements therein not

being present, and as the result of later bacteriological investigations, we know that they may all be present in cases not due to the bacillus typhosus, but to one or other member of the paracolon or paratyphoid group of organisms. The result of the great variability in the symptomatology of typhoid fever is, that cases are met with in which the most skilful physicians, after a most painstaking and careful observation, cannot, on clinical grounds alone, make an absolute diagnosis, this being only arrived at after they have invoked bacteriological aid.

The question might well be raised—"What are the causes of such diversity of manifestations in the course of typhoid fever?" This, in the light of our present knowledge, it is impossible to answer with certainty. Undoubtedly we find marked variations in the course of other acute infectious diseases, as diphtheria without membrane, and scarlet fever without the typical rash (scarlatine sine eruptione), but in none of them are the symptoms so capable of such wide variations as in typhoid. The symptoms are no doubt due to two main factors : (a) the effects of the bacillus on the body and its vital activity ; and (b) the individual reaction of the patient, and the variations may be attributable to the degree of virulence of the bacillus and the special conditions of the patient. Among the more important of the factors relating to the individual may be mentioned : age, occupation, mode of life (alcoholic excess, &c.), constitution (may be affected by wasting disease, &c.) As regards those that, to a certain extent, may affect the degree of virulence and development of the bacillus, are the local conditions, state of habitation, water supply, &c. It must, however, be borne in mind that certain of the clinical pictures are altered as the result of a mixed infection, other pathogenic organisms, having previously, or it may be, simultaneously invaded the body. Some authorities maintain that the milder cases are attributable to the action of toxins alone, such as might happen if in the cooking of the food, the bacilli were destroyed while their toxins remained active, or to these together with attenuated bacilli. Not a few maintain, and in this they receive considerable support, that the bacillus Coli and its toxins are in great measure responsible for deviations from the usual train of symptoms. It is easy to conceive how this organism, which we know, multiplies greatly, and is in great numbers in the intestine in typhoid fever, and can become pathogenic, can throw a great quantity of toxins into the circulation, or can enter itself through the various breaches in the intestinal wall. A suggestion of Durham's, in his attempt to explain the causation of relapses, may throw some light also on the matter. This eminent authority is of opinion that there is an invasion of the body by different "types" of the bacillus at the same time, and that only agglutinins belonging to, or corresponding to, certain of these "types" are developed. However, this matter must in the meantime be left sub judice.

The chief difficulties in arriving at a conclusive diagnosis are met with in the atypical cases, or it may be, during the early part of the first week in typical cases, before the development of the intrinsic symptoms, fever, roseolous eruption, splenic enlargement, and diarrhœa. In the former group clinical observation alone may fail us, and in the latter if a positive diagnosis is to be arrived at, before awaiting

development of the symptoms mentioned, bacteriological and haematological methods must be resorted to. Difficulties in diagnosis have been encountered ever since the disease was known. In the days of Spigelius, Willis, and Morgagni, only post-mortem examinations revealed the differences between typhoid fever on the one hand, and malaria, plague, and certain septic processes on the other, the clinical observations at that time not having been in complete harmony with the anatomical findings. Later, the discrimination of typhoid, from typhus and relapsing fevers was attended with difficulty. Eventually, in the early part of the 19th century, owing chiefly to the labours of Gerhardt, Jenner, Stewart, Murchison, Louis, Greisinger, and Liebermeister, typhus and typhoid came to be recognised as separate diseases, but even after that time certain cases were confused. In more recent years, chiefly as the result of bacteriological and haematological methods, we have been able to still further distinguish between typhoid and certain affections that were formerly thought to be this disease, and to relegate to the category of typhoid certain cases that were classed otherwise. With the older clinicians, cases of "continued" fever, which did not conform to the classical description of typhoid by Murchison, were thought to be due to tubercle. In later years, the prevalence of influenza caused many doubtful cases to be attributed to this cause. We can now, however, separate those cases of continued fever in the adult due to the bacillus typhosus from those attributable to other causes. A moment's reflection makes it probable to us that, in children, the cases termed by the older writers, "febris meseraïca," and "febris gastric remittens," were typhoid fever, in a modified or mild form. At the present time, as the result of careful bacteriological examinations, we are able to isolate cases which present most, if not all, of the characteristic clinical signs of typhoid (fever curve, enlarged spleen, roseolæ, diarrhœa), and which are not due to the bacillus typhosus, but to one or other of the closely allied paratyphoid or paracolon group of organisms. By such means, and with the aid of hæmatological methods (serum agglutination) we can say with a fair degree of precision and at a comparatively early stage of the disease whether a case of gastro-enteritis in a child is typhoid fever in an atypical form, or is simply one of gastro-intestinal irritation, and this, from a public health view point, is a matter of no small moment.

Before proceeding to discuss in detail the value of the different clinical signs, and to describe the different methods, bacteriological and hæmatological, by which we are enabled to form a conclusive diagnosis, it may be advisable to mention briefly the different types of the disease and the chief features of each.

Cases of moderate severity and well characterized.—This is the type which answers to Murchison's classical description of the disease. The onset is insidious, the patient complaining of slight chilliness, headache, malaise and feeling of lassitude, short cough, finally taking to bed. The temperature rises in step-like fashion, the evening record being a degree or a degree and a half higher each evening. The pulse is increased in frequency and dicrotic. Tongue is coated, but moist. Slight abdominal pain and tenderness are complained of. If the temperature is high, there may be, especially at night, some slight delirium or mental confusion.

Diarrhœa may be present, the stools being peasonpy. By the end of the first week the spleen is felt to be enlarged, and a roseolous eruption appears from the 7th to the 10th day. With the second week the picture becomes aggravated, the fever keeping high and remittent. In the third week the temperature shows morning remissions, and there is a gradual decline of the fever.

Malignant or Fulminant type.—In this form the patient presents from the beginning the symptoms of profound intoxication. The onset is usually more or less abrupt, and the temperature, instead of rising in staircase fashion, mounts to its acme by one or two leaps, reaching 103°F. or 104°F. by the third or fourth evening. The pulse is rapid. The tongue rapidly becomes dry and brown. Marked nervous symptoms develop early, and the patient succumbs by the end of the first week or early in the second, sometimes before the development of the roseolous eruption, or before enlargement of the spleen is manifest. The bowels may be constipated or loose. This form fortunately is not very common, but is met with, and may, as I have experienced, be one admitted from a house endemic, the other cases being of a mild type. One such case that was under my care died on the ninth day, while the remainder from the same house ran a mild course, one presenting very few symptoms. Some doubt may exist from the clinical picture alone as to the true nature of the case, especially where, in addition, there may be cerebro-spinal symptoms, and where a history of infection is unable to be traced. Some authorities regard such cases as examples of a mixed infection, pyogenic cocci being present in addition to the bacillus typhosus.

Mild type.—In this group the picture is that of a mild infection. One or more of the cardinal symptoms may not be present. The temperature does not touch high records, and may reach normal by the end of the second week.

Protracted type.—Some of these cases pursue a severe course, while many are mild throughout. The prolongation may affect all the stages, or may be limited to the period of defervescence, but it is usually the fastigium that shows the extension, lasting several weeks in some cases, and as the temperature shows marked fluctuations, assuming an intermittent character often, or becoming very irregular, the accuracy of the diagnosis of typhoid may be disputed; or in the event of no other signs of the disease being present, the question may be raised as to the awakening of latent tubercle or the development of septic mischief. Several cases illustrative of this came under my care, and are quoted elsewhere. On the other hand, the period of defervescence may be protracted, it may be for weeks, the temperature showing fluctuations wholly inexplicable. Some of these cases suffer from post-typhoid anæmia (Thayer) while others show no complications and no special organic changes. Rokitansky attributed this to atrophy of the intestinal villi, mesenteric glands, and lymph follicles, and Curchmann quotes such a case where post-mortem showed only smooth cicatrices in the ileum in place of Peyer's patches.

Abortive type.—This is the typhus abortivus or typhus levissimus of the French writers, and is a form of the disease that was frequently overlooked by the older physicians. The credit of first demonstrating the true nature of such cases is due to

Greisinger and Jurgensen, who recognised two sub-divisions, viz.—*(a)* abortivus; *(b)* levissimus. While both are characterized by the shortness of the course, the latter, in addition shows marked mildness. The former, however, though brief in duration, is often pretty severe. The impression obtained from the study of such cases is that we are dealing with an imperfect development of the disease. The whole period of the disease is shortened, though occasionally the period of convalescence may be interrupted. The onset is abrupt, the temperature reaching its acme in 24 or 36 hours, sometimes after a single chill, then the fastigium is continued for a few days, and finally, the temperature declines in a critical fashion, either by a true crisis or by a rapid lysis, reaching normal in about ten days from the onset. Splenic enlargement and roseolæ usually appear early, though both may be absent. Diarrhœa may be present, or the bowels may be constipated. Sometimes a relapse occurs in such cases, and even perforation and hæmorrhage have been known to occur. In the milder forms (levissimus) the onset is not so severe, though it may be characterized by abruptness, and after an acme lasting two or three days, the temperature declines in an intermittent or sometimes irregular fashion. The general condition of the patient is not much affected. Several cases illustrative of the abortive type of the disease came under my care in hospital, and presented, some of them at least, very few symptoms, and but for a positive Widal's reaction or differential leucocyte count, no positive diagnosis could have been arrived at. These cases would certainly have escaped detection outside, but for the fact that they came from an infected area, and in some cases from an infected house. In the absence of a history of infection, the majority of these cases are diagnosed as influenza (gastro-intestinal type) or pneumonia, their true nature being overlooked. Some authorities maintain that such cases are due to the typhoid toxins alone, but my observation on one such throws some doubt on this statement, as I was able to isolate the bacillus typhosus in pure culture from the blood on the fourth day of the disease.

Ambulatory type.—As the name implies, this form is characterized by such a degree of mildness of the subjective symptoms that the patient keeps going about, it may be to his work, totally unconscious of the gravity of his condition; and only collapse, hæmorrhage, perforation, or the development of a relapse compels him to take to his bed. Some cases belonging to this group, complaining only of an ill-defined feeling of discomfort, are considered malingerers, and only the thermometer recording some degree of pyrexia causes one to submit them to critical examination. Enlargement of the spleen and diarrhœa may be present. The temperature may be only slightly elevated or may be high, and may be remittent, intermittent, or irregular. The pulse is more apt to be rapid than in other cases, chiefly on account of the patient having gone about. This type of the disease is one the early recognition of which is all-important, as it is not only fraught with grave danger to the patient himself, but as the result of the elimination of the bacilli in hisfæces and urine, he is a great source of danger to those with whom he comes in contact; and this becomes more alarming if, as occasionally happens, he travels considerable distances before finally taking to bed. I have met with several instances of this type. One patient, W.S., presented himself at the

receiving room of the Royal Infirmary, and his only complaint to me was loss of appetite and total disinclination for food. From a hurried survey of his physiognomy, I concluded that he was suffering from malignant disease, and took him to the ward. Judge of my surprise when the nurse recorded his temperature as 104°F. This patient's illness pursued a severe and protracted course with intestinal haemorrhage. Another case which I admitted was a man who thought he had influenza, and only took to bed when intestinal haemorrhage developed ; while a third was walking about when the ambulance was sent for him.

Afebrile type.—Wunderlich's axiom of "No fever, no typhoid" is not in complete harmony with the observations of modern clinicians. Just as there may be scarlet fever, diphtheria, and even measles and variola, without rise of temperature, so afebrile typhoid may occur. Some of these cases might well be classed among the "levissimus" type mentioned, but others may be attended by a fatal termination. One noteworthy fact in connection with these cases is that the majority of them occur in patients advanced in years, or in persons who have undergone great privation, or who are the subjects of wasting disease. Many of this type occurred among the German soldiers besieging Paris. Henoch has observed this type accompanied by marked cerebral symptoms, in children in a state of exhaustion due to fatigue or insufficient nourishment. As one can readily perceive, occurring as most of them do without roseolæ, or it may be with only an isolated spot, often without splenic enlargement, and sometimes with constipation, the difficulty in arriving at a definite diagnosis is extreme. As a rule it is only those cases that sicken, perhaps with headache, vertigo, and malaise, during an epidemic, or where there is a house endemic, that are detected. In spite of the afebrile nature of the disease, and this is a point which may rouse suspicion that the patient has been under the influence of some infectious process, the degree of emaciation is very marked and altogether out of proportion to the apparent severity of the trouble. If diarrhœa is present, these cases are looked upon as cases of mild gastro-enteritis, or, if absent, they are regarded as mild forms of influenza, and cannot be diagnosed with certainty on clinical grounds alone, the only definite diagnostic data being obtained by bacteriological and haematological examination.

Haemorrhagic type.—Though fortunately rare, this is a serious type of the disease, as the mortality rate attending it is very high. The haemorrhages may appear as the terminal phase of the fulminant type, but in some cases they first appear during a relapse, as occurred in one of my own series, or late in a case which has pursued a protracted course (Wagner and Gerhardt). The haemorrhage may take place into the skin, causing petechiae, into the cerebral tissue and meninges, or from the nose and gums. Haematemesis and haemoptysis may occur, and intestinal haemorrhage is common in such cases. The exact causation of this form of the disease is so far unknown. When such haemorrhages occur in the course of a case presenting other symptoms of the disease, the diagnosis of typhoid of the haemorrhagic type is not attended with any difficulty ; but when, as sometimes occurs, the attack is ushered in by violent haematemesis or haemoptysis, the obstacles to the diagnosis of typhoid are considerable.

Such a case came under my care in hospital. In the ambulance van he was seized with hæmatemesis, and on admission, besides this, he had hæmorrhages from all the mucous membranes, necessitating saline transfusion, which, however, did not avert a fatal issue. It is further noteworthy that this patient was admitted in relapse, as enquiry subsequent to his death showed.

Typhoid fever in early childhood and infancy.—This type is one of unusual interest on account of the difficulties attending its diagnosis. Anatomically the affection in children is characterized by a pronounced mildness of the lesions in the majority of cases, so much so that Henoch, in 21 post-mortem examinations of children between the ages of 2½ and 10 years, who during life had presented all the clinical symptoms of typhoid, found only 11 showing ulceration of the intestine, and "this occurred in cases lasting from 14 days to 7 weeks." In the remaining 10, he was only able to find "a soft swelling or reticular condition of the glands without ulceration." For this reason, chiefly, hæmorrhage and perforation are of much less frequent occurrence. Clinically the disease shows a milder character than in adults. It is of shorter duration, though occasionally a case pursuing a protracted course does occur. Vomiting as an initial symptom is more common than in later years, and may be so marked as to raise the question of tubercular meningitis. Convulsions sometimes usher in the disease. Like the other symptoms, the fever is milder, the temperature not touching such high records as we find associated with the disease in later life. Although the remittent type is common (it was formerly called infantile remittent fever), an intermittent or irregular form is met with. Again, defervescence by a crisis is on the whole more frequent in the abortive cases in children than in the corresponding type in adults. Splenic enlargement and roseolæ are fairly common, but there are great variations in the number of roseolæ and the date of their appearance, being present occasionally as early as the third or fourth day. In some cases their appearance is delayed until the second week. Abdominal distension and diarrhœa are of more frequent occurrence in childhood than later in life. In many cases, most of the symptoms are entirely a-wanting, and this, coupled with an irregular type of temperature, causes great difficulty in the diagnosis, other gastro-intestinal disturbances being very liable to be confused with it. Such was my experience during 1903, the last year that I was resident in the Middle Ward Hospital. I had no fewer than 52 children under 10 years of age under my care, and the greater number of them presented few clinical symptoms of typhoid, splenic enlargement and fever being often the only indications. Several children were admitted presenting almost similar symptoms, but suffering only from gastro-intestinal disturbance, and often with splenic enlargement, and so caused considerable difficulty in diagnosis.

Typhoid in aged.—As in childhood, the disease in advanced years shows great differences from the affection in adolescence. The power of resistance being diminished, the prostration is greater, and the mortality higher. The course is apt to be protracted, and the fever course relatively low.

Typhoid in which symptoms referable to certain organs predominate.—When such occur, the true nature of the patient's condition is obscured until the development of splenic enlargement, roseolæ, or diarrhœa, and if these fail to appear, or if the patient succumbs before they have had time to develop, a false diagnosis is made. Though infrequent, cases of this kind do occur from time to time, and unless the patients have been removed from a district where typhoid is rife, they are usually treated for some other affection having symptoms similar to those presented by the case, until the appearance of roseolæ or diarrhœa shows its true nature. In this group we have the following varieties :—

(*a*) Predominance of symptoms referable to the cerebro-spinal system. The onset may be ushered in with intense headache, photophobia, rigidity of the neck, and convulsions, giving a clinical picture closely resembling cerebro-spinal meningitis. An isolated case of this type may be attributable to an exacerbation of an old otitis media purulenta, but in the majority no such cause can be found, and post-mortem examination shows only pure cultures of the bacillus typhosus (Osler). To this class the name of meningo-typhoid has been given.

(*b*) There may be symptoms of a psychosis.

(*c*) The symptoms may be those of an acute ascending myelitis, and only post-mortem examination reveal the true nature of the case.

(2.) Respiratory symptoms may be so pronounced as to completely obscure the patient's true condition. The initial bronchitis seen frequently in typhoid may be extreme. Another group, to which the designation pneumo-typhoid has been given, is characterized by all the features of an acute lobar pneumonia, and only the persistence of the fever beyond the time when a crisis is looked for, and the development of other symptoms, causes a correct interpretation to be placed on the case. Another group, with symptoms of pleurisy, is designated pleuro-typhoid.

(3) Nephro-typhoid is the term applied to those cases which are ushered in with all the symptoms of an acute hæmorrhagic nephritis. Napier has recently described one of this class in the " British Medical Journal," and my predecessor at the Middle Ward Hospital left a patient under my care whose illness had conformed to this type.

Typhoid modified by the co-existence of other diseases.—Such an occurrence must certainly produce a symptom complex calculated to lead one astray, however careful one may be in interpreting clinical signs.

(*a*) Cases in which measles, scarlet fever, or diphtheria has been associated with typhoid, have been recorded by Murchison, Berthez and Rilliet, Eichhorst and Taupin, though personally I have had no experience of them.

(*b*) A more common condition is influenza preceding typhoid in its development, the temperature being continued by the latter.

(*c*) Much more common, however, than the above, is a mixed infection with pyogenic organisms. This may occur early in the disease, or later during the period of convalescence. In the former condition the fever is high, nervous symptoms are pronounced and appear early, and the whole course of the disease is much more virulent. The mortality in this group is considerable. To this class the French have given the name " forme septîcémique généralisée.

(*d*) In malarial districts patients may contract typhoid in addition to malaria, and a clinical picture is produced of mixed symptoms, causing the greatest difficulty in diagnosis. In fact, from clinical investigation alone, a diagnosis cannot be formed.

(*e*) When typhoid attacks an individual who is already the subject of some chronic disease, the recognition of the existence of the former is attended with considerable difficulty. The prostration is extreme, pulse rapid, but the temperature keeps as a rule rather low.

(*f*) Association with Tubercle.—It was thought by the older writers that an individual the subject of tubercle in one of its forms could enjoy immunity from typhoid. The fallacy of this statement has long since been proved. A patient who is suffering from tuberculosis may readily contract typhoid, and conversely, a patient recovering from typhoid may have latent tubercle kindled up. Two instances of this kind have come under my personal observation, and in both considerable difficulty would have been experienced but for bacteriological examination.

After reviewing the list of atypical forms of the disease, and considering the relative frequency of some of them, we cannot fail to be impressed by the difficulties in diagnosis that are likely to accrue, especially when dealing with isolated cases. There is no clinical sign which is of itself diagnostic of typhoid except the specific roseolous eruption, and this in many cases is not present throughout the whole course of the disease, or in the abortive and mild cases may have passed off before the patient comes under our observation. Notwithstanding this, however, there are several symptoms which, if attention be given to their characters, the time and manner of their appearance, and their sequence, may admit of considerable diagnostic certainty. The diagnosis is by no means difficult provided a case pursuing a typical course can be observed from the beginning, and especially, if in addition, one has definite information with regard to the immediate circumstances attending its development. The difficulty, however, becomes more evident if, in the absence of the knowledge of the antecedent conditions, one has to arrive at a definite decision at once, or only after a limited period of observation, and if the case is not seen until a late stage, or is one pursuing a wholly atypical course. Not only does the varied symptomatology place obstacles in the path of an accurate diagnosis, but several of the symptoms which were at one time considered distinctive of typhoid, such as splenic enlargement, and diarrhœa, are manifested by other diseases considerably removed from typhoid. For these reasons, clinical symptoms, while

they are a guide to us in many cases, have a limit to their value, and in others may lead us into error. It was thus that the older physicians, who had to rely solely on observations of clinical signs, failed to recognise the atypical forms of the disease, and were prone to place such in the category of influenza, or regard them as some manifestation of tuberculosis. Recently introduced, the study of the morphological elements of the blood has enabled us to recognise some of these cases, but not all, as the blood of some of the affections closely resembling typhoid presents somewhat similar characters, and the occurrence of complications prevents accurate conclusions being sometimes drawn. With the advance of bacteriology, methods have been introduced which enable us to isolate the specific bacillus, during the height of the disease, from the circulating blood, from the excreta, and from some of the viscera, thereby placing the diagnosis beyond dispute. Again, the practical application of Pfeiffer's phenomenon, modified considerably, places a method at our disposal whereby we can state with precision, if a positive result be obtained, whether a patient is the subject of typhoid infection or not. We cannot, however, in spite of all this, afford to discard altogether clinical observation, for some of the methods, such as those for the demonstration of the bacillus in the blood and fæces, are attended with difficulty, and under certain circumstances, wholly impracticable. In the following pages I have placed on record the results of my observations on the clinical symptoms, and of my investigations by hæmatological and bacteriological methods on cases that came under my care, and I have attempted to draw therefrom my conclusions as to the relative value to be attached to each method in forming a positive diagnosis. All those cases, amounting to 200, came under my own care while physician in charge of the infectious diseases hospital for the Middle Ward of Lanarkshire, with the exception of eight, and I carried out every step of the proceedings detailed hereafter. Of the eight mentioned, one was under my care in Ward V. of the Royal Infirmary; while another, which I saw in private in consultation, was thereafter admitted to the same ward. The remainder came under my personal observation in private. I did not select cases for carrying out my observations, but thought to place a better value on the methods of procedure in diagnosis by applying all of them to every case that was admitted to the hospital notified typhoid fever. I have therefore included results from several negative cases, which, I rather think, enhances the value of the methods applied by me, than otherwise. I have given several temperature and blood charts, illustrative of special points mentioned in this paper, and have appended several cases to illustrate points which I have dilated upon, and have deemed worthy of special comment.

Before proceeding directly to the study of the individual clinical symptoms, I should like to call attention to a point which is frequently of utility in enabling a diagnosis to be arrived at early in the disease, viz. :—

Surrounding circumstances. *i.e.*, the circumstances surrounding and leading up to the patient's illness. Attention to this point may be of assistance, as during an epidemic of typhoid, or with a history of several persons in the vicinity being affected

with some severe gastro-intestinal disturbance, accompanied by fever. It is thus, no doubt, that in the absence of laboratory tests most of the atypical cases are recognised during the earlier days of the illness. On the other hand, such information may be misleading, as persons living in an infected area may be prostrated with some other febrile affection with suspicious symptoms, and wrongly removed to hospital with the diagnosis of typhoid. Several such instances of this character came under my notice, the patients in these cases suffering from gastro-enteritis or influenza. One such example is prominently before my mind, where two brothers were admitted, notified as suffering from typhoid. Neither of them presented any symptoms suggestive of such, and the Widal's reaction, repeatedly examined for, was always negative. That they were suffering from influenza was beyond doubt. Both were unfortunately detained in hospital, and owing probably to carelessness in the matter of disinfection in the wards on the part of some of the nursing staff, one of them developed typhoid of a somewhat mild type, but with splenic enlargement, roseolæ, and with a positive Widal's reaction. I could quote, however, on the other hand, several instances of early admissions correctly suspected, the suspicion of typhoid being based on proximity and probability of infection from undoubted cases. In sporadic cases, the history usually is of little or no practical value.

Mode of onset: initial symptoms.—The onset in typhoid is rarely abrupt—in the majority of cases at least, the symptoms developing insidiously, so that the patient is rarely able to definitely fix the first day of illness. Among the earlier symptoms usually complained of are, a feeling of languor, indisposition, and disinclination for work, although the patient may continue to attend to his work for several days in a vain effort to battle against the disease. Headache is complained of by many, and vertigo, loss of appetite, repeated chills, and epistaxis are common symptoms. Abdominal pain and tenderness, backache, and sacral pain may be present, and even a feeling of dragging in the left hypochondrium, due probably to beginning splenic congestion. Vomiting and diarrhœa may be present. The following table gives the percentage of these symptoms as illustrated by my own series of cases :—

Headache was complained of by 75 per cent.
Backache   ,,   18   ,,
Vertigo   ,,   6   ,,
Shiverings   ,,   40   ,,
Abdominal pain   ,,   56   ,,
Diarrhœa   ,,   48   ,,
Vomiting   ,,   37   ,,
Pain in hypochondrium   2   ,,
Epistaxis   ,,   8   ,,

Such a group of early symptoms occurring in an insidious fashion are often suggestive of typhoid, especially if the patient is able to give a concise history. Such is frequently difficult to obtain, as I experienced with Poles who could not speak a word of English ; and the same may be said with regard to children, from whom no reliable information is obtainable. On the other hand, many cases do occur that

present no such group of symptoms. In a few, for example, as in the abortive cases, the onset may be abrupt, with a single chill. Curchmann, on the other hand, says that "repeated chills are so much the rule, that when a febrile disease begins with a single chill almost any other disease than typhoid is to be thought of." This rule undoubtedly applies to the majority, but does not hold for a few exceptional cases. In several of the milder cases with which I had to deal, only a single chill occurred. In a few cases in children, though perhaps rare, the onset may be with one or more convulsions, and until the later development of other signs more distinctive, no accurate diagnosis may be entertained. Again, in those atypical forms where the disease is marked by symptoms referable to some special organ, other affections than typhoid, are more likely to be thought of. Such are the pneumo-typhoid, meningo-typhoid, and nephro-typhoid previously mentioned. In those cases also where vomiting and abdominal pain are prominent, appendicitis may first be suspected, or if diarrhœa be pronounced, gastro-enteritis may be the first diagnosis made. In a few cases, night sweats appear among the prodromal symptoms, and may suggest, in the absence of definite signs of typhoid, the onset of incipient tuberculosis. It must also be borne in mind that among the symptoms mentioned as occurring insidiously in typhoid cases, all or several of them may appear in the same manner in other affections. Thus, headache, backache, vomiting, malaise, and diarrhœa may all be present in influenza or even in pseudo-influenza; and in some cases of incipient tubercular disease, it is not uncommon for patients to complain of headache, languor, and indisposition, and if dietary indiscretion has been committed, abdominal pain and even diarrhœa may be added to the list. I have observed such an onset several times, in incipient phthisis and in tubercular peritonitis. A series of chills is often suggestive of some septicæmic condition.

Temperature.—Passing now from the prodromal symptoms to those which are usually developed by the time the patient has come under our notice, no one is of such interest, or deserving of such careful consideration, as the course of the temperature. It formed the basis of a long series of careful investigations by Wunderlich, and since he called attention to the typical temperature curve, observations on its course, have formed one of our best diagnostic aids. The temperature curve is by many looked upon as the expression of bacterial intoxication, and the general changes going on in the body, and Wunderlich declared that the various anatomical stages of the typhoid process are reproduced in typical cases in the form of the curve. In typical cases the rise is a gradual one, the ascent towards the acme taking four or five days, and often a week. It rises somewhat regularly in a step-like or ladder-like fashion, attaining from ·6°F. to 1° or 1½°Fah. higher each evening than on the preceding, and showing each morning a reduction of ·5 to 1°F., never becoming as low as on the previous morning. By the end of the first week of illness, 103°F., or 104°F., or in severe cases 105°F. may be reached. After reaching its acme, the temperature persists with slight remissions of from ·5° to 1°F. as a type of continued remittent fever (the fastiguim), and lasts in this fashion until the end of the second week or middle or end of the third week, depending upon the gravity of the case. At the end of that time the temperature

begins to decline by marked remissions, amounting sometimes to intermittency, variations of 2° to 3°F. being comparatively common. This stage, often referred to as the stage of steep curves, or stadium decrementi (Henoch), lasts usually from 3 to 5 or 6 days. By Traube, it was designated " hectic " on account of its resemblance to some forms of pulmonary tubercle. Following upon the subsidence to normal, a period of subnormal temperature often supervenes, which may last from one to three weeks, and during this period, however uniform the temperature may appear to be during rest and quietude, as the result of very slight external or internal influences, it may exhibit a marked degree of instability. Such is the characteristic temperature curve of a moderately severe and typical case of typhoid. It is, however, subject to many and great digressions, and of these the undernoted are the chief examples.

The period of ascent may be shortened, the rise being more abrupt and the acme reached in from eighteen to forty-eight hours, either at one bound with a single severe chill, as may occur in the malignant type, or with one or two slight remissions, as in the more common abortive cases. Such cases, illustrative of this point, are of more frequent occurrence in children, especially in those cases which are ushered in with a convulsion.

The fastigium may present the type of a true continued fever, there being no remissions, and the curve almost pursuing a straight line, or the remissions may only amount to ·3 or ·5°Fah. This occurs sometimes in the very severe cases. Occasionally the fastigium is interrupted by a sudden fall, as occurs in collapse, or from severe haemorrhage or perforation, attended by a corresponding increase in the pulse rate. In some cases the remissions may be very pronounced, and in a few, especially severe ones, days of high continued fever may alternate with others of the remittent continued type. The fastigium, or later, the period of defervescence, may be interrupted by rigors, due to the advent of some complication, to constipation, or it may be, without any demonstrable cause. Such a case as the last-named has been reported by Bolton (Practitioner No. 427, Jan., 1904) where a patient had 21 rigors in all, 19 of which occurred during the fastigium. I have seen several such, with a few rigors, but could always trace them to a definite source.

In children, we frequently see the fastigium especially in protracted cases, characterized by marked remissions and intermissions, and we may even observe the fastigium begin with all the characteristics of a continued fever, this giving way to a period of marked fluctuations. In the milder cases in children, the remittent and inter-mittent type is usual, but on the other hand, the temperature curve may be totally irregular. Marked fluctuations alternating with periods of comparatively low temperature may occur, or the inverted type of temperature may be observed—high in the morning, and depressed in the evening ; and if such cases run a protracted course considerable anxiety as to the diagnosis is felt. **In old age,** even in severe cases, or in younger people as the result of chronic alcoholism, chronic wasting disease, or privation, the temperature remains remarkably low, and the course may be very irregular with marked remissions and collapse-like depressions, or a totally afebrile course may be exhibited.

In some mild cases in adolescents, the temperature from the onset shows great daily fluctuations, with a complete absence of true continued fever, or this may only be evident for a day or two. Sometimes the intermittency is so regular as to suggest true intermittent fever.

Defervescence may take place not by a remitting lysis but by a gradual, steady descent, like a true lysis without remissions, reaching normal in two or three days. In some cases which I have seen, after wide fluctuations for several days, sometimes amounting to 2° or 4° F., a rapid descent took place in 12 to 18 hours. Sometimes such a decline, preceded by fluctuations, follows upon a continued fever course. Again, the descent may occur by a crisis, with or without a precritical elevation, or may occur by a pseudo-crisis. This abrupt decline is more common in children than adults, but in the latter it may be witnessed in the abortive cases. I have observed several such cases.

As regards the total temperature curve, it may be shortened in mild abortive cases and in children, the fastigium as such being scarcely appreciable. (See J. R.) Again, in well-marked cases pursuing a moderate or mild course, although the whole period may be shortened, the individual stages preserve their usual relative proportions. In severe protracted cases both the fastigium and the period of defervescence are prolonged, the former perhaps for three weeks or more, and may be remittent, or show such marked fluctuations and irregularity as to lead to the suspicion that a revision of the diagnosis is necessary; and this may be the more so if during the period of defervescence the steep curves are totally obscured by the irregularity of the declining temperature. In milder cases, the fever from the beginning may not be high, and may be so irregular as to cause some difficulty in coming to a definite opinion on the nature of the case. It must be remembered, too, that fluctuations, sometimes very wide, are apt to occur as the result of mental effects, dietetic errors, constipation, profuse diarrhœa, or repeated hæmorrhages ; and the onset of secondary infections, inflammatory or suppurative conditions, malaria, or tubercle is always followed by irregularity in the temperature curve.

Value of temperature in diagnosis.—Although the temperature in a typical case is one of the most important diagnostic aids we have, yet in atypical cases it presents nothing characteristic, and so observations on the course of the fever must not for diagnostic purposes be regarded too exclusively, or apart from other features of the case. If we should be fortunate enough to see a case sufficiently early, the step-like ascent towards the fastigium would suggest to us the probable existence of typhoid, for in typhus, pneumonia, and most of the acute fevers, the advance towards the acme is more abrupt; on the other hand, in acute articular rheumatism, affecting several joints, in catarrhal pneumonia, in acute tuberculosis, and in some cases of phthisis, the ascent of the temperature is usually spread over several days. The onset, however, may be just as abrupt as in typhus, a condition which occurs in the abortive type, or in children with or without convulsions, or in the meningo-typhoid or pneumo-typhoid types. Although Wunderlich taught that typhoid would be excluded by a temperature of 104° F. on the first or second day, or if the temperature did not reach 103° F.

by the sixth day, there is little doubt but that he paid too little attention to the atypical forms of the disease, and in the light of present-day knowledge our observations are not in accord with these statements. A sudden ascent of the temperature at the onset would suggest typhus, influenza, or gastro-enteritis, or if with localizing signs, pneumonia, meningitis, or appendicitis, but as we have pointed out, would not exclude typhoid. If the fastigium were characterized by continued fever with slight remissions, followed by a period of steep curves, and later by a subnormal temperature, subject to fluctuations from very slight causes, the diagnosis of typhoid might be made with comparative safety. On the other hand, the protracted cases with marked intermittency might suggest malaria, or remissions and intermissions might lead to the suspicion of tuberculosis; while, if there were wide fluctuations with considerable irregularity, the question of crypto-genetic septicæmia would be considered. Should such fluctuations occur with distinct rigors, one would be justified in regarding the condition as one of pyæmia. The inverted type of temperature, while it may occur in typhoid with comparative rarity, is much more common in acute miliary tuberculosis. A fall by crisis, or pseudo-crisis, in the absence of localizing symptoms, would suggest influenza, typhus, or one of the atypical forms of pneumonia.

The following list of cases, selected from those which were under my care, may serve to illustrate some of the points commented upon in the course of the temperature in typhoid fever.

CASE I.--M.B., æt. 21.--Fastigium closely approximating continued type—at one part remissions almost imperceptible—temperature gradually declining without distinct remissions—finally defervescence by marked remissions lasting over three days. Roseolæ present—Widal positive—spleen only enlarged to percussion—bacillus isolated from blood.
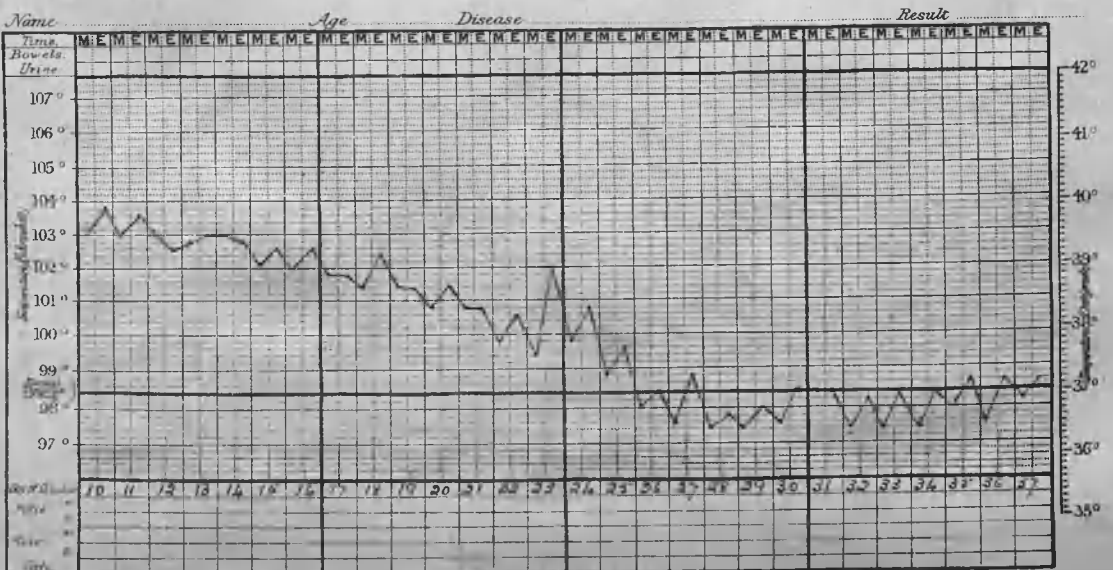
CASE II.—G. S., æt. 17.—Severe and protracted case—almost continued type, steep
curves not well marked. Roseolæ present.   Diarrhœa—spleen only enlarged
to percussion—Widal positive.
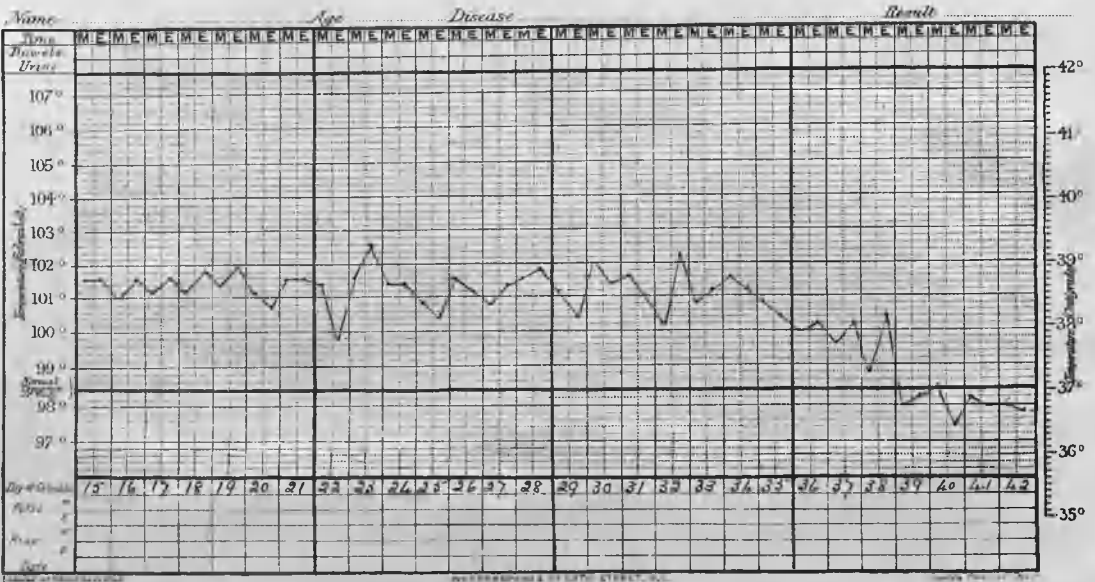
CASE III.—M. J. F., æt. 18.—Case showing marked intermission without corresponding
change in pulse rate.   Defervescence by non-remitting lysis.   Diarrhœa—
splenic enlargement—no roseolæ—Widal positive, but delayed.
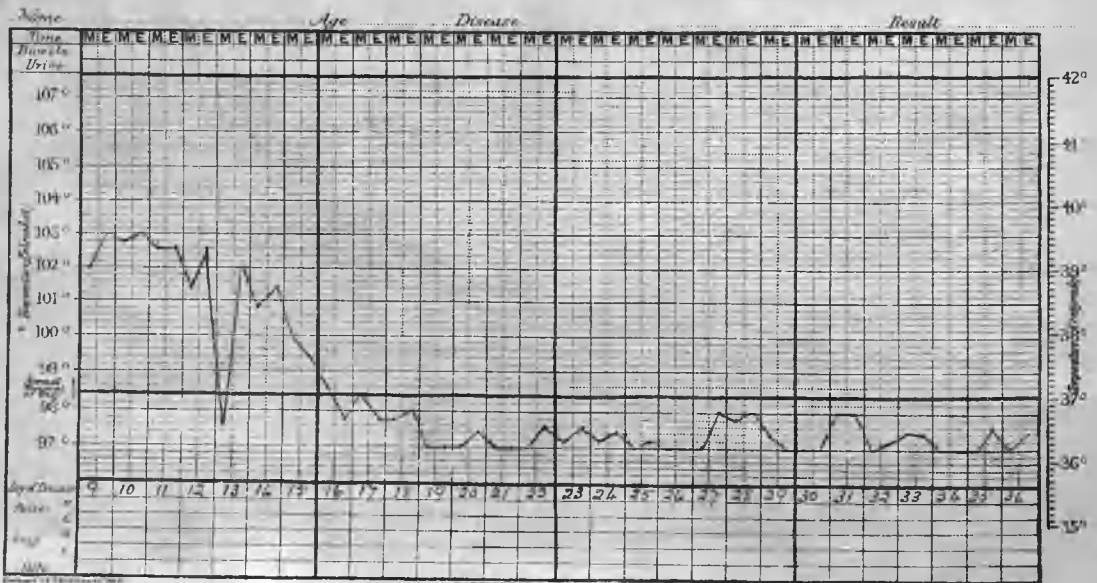
CASE IV.—W. S., æt. 37—Typhoid.—Protracted case. Chart showing irregular temperature curve with remissions and intermissions.
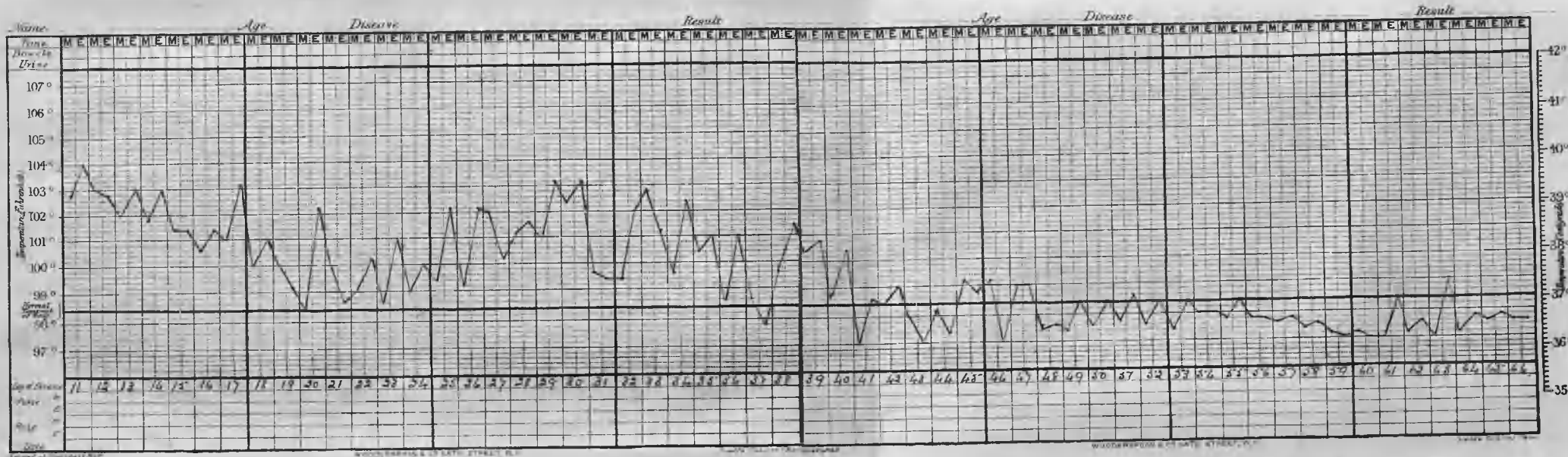
CASE V.—Chart from case of typhoid showing rigors without complication. (Copied from Bolton.)
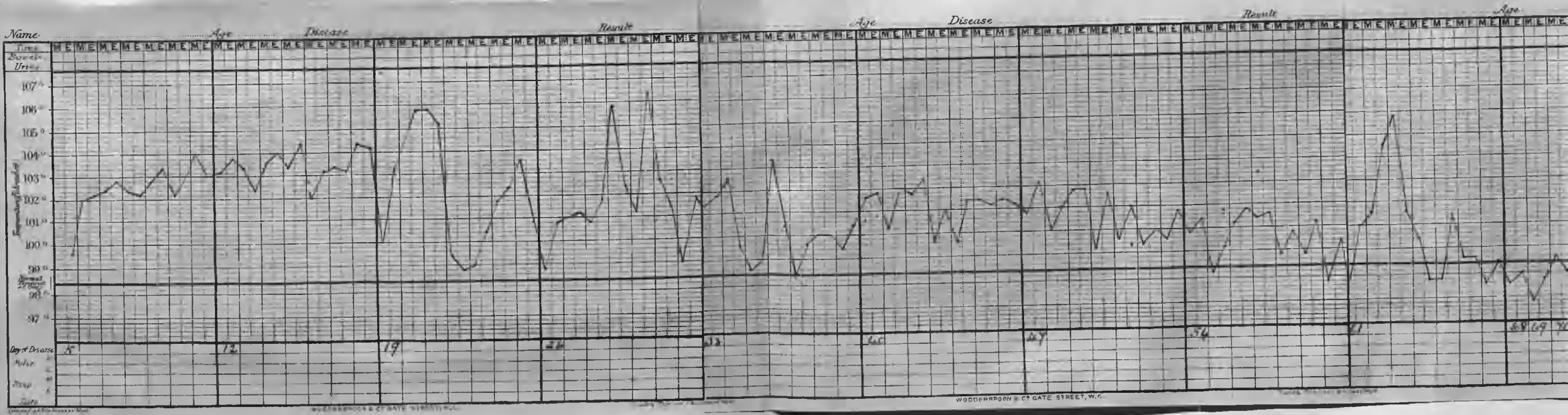
Case VI.—J. M'N.—Chart from case of crypto-genetic septico-pyæmia.
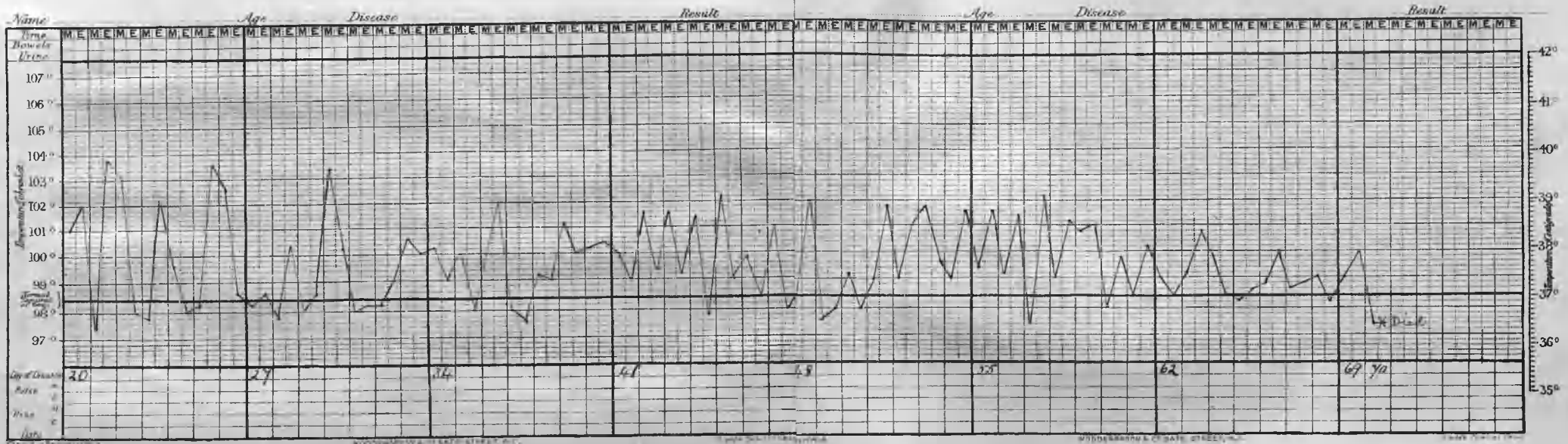
Case VII.—A. M'D., æt. 4.—Mild case of typhoid. Defervescence by non-remitting lysis.
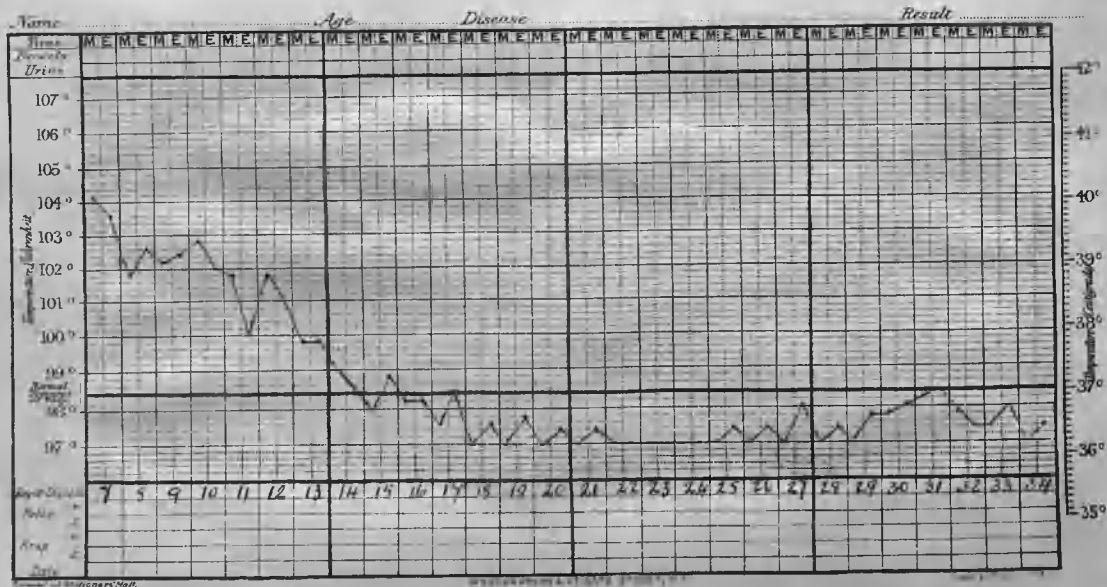
CASE VIII.—J. O.—Abortive case. Defervescence with very slight remissions.
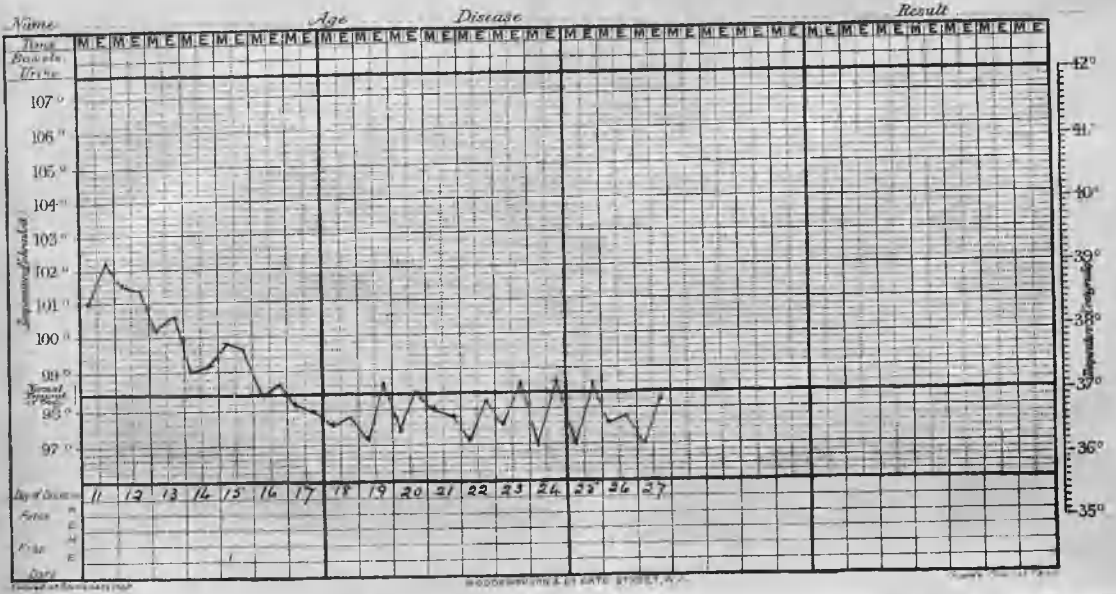
CASE IX.—W. G., æt. 25.—Mild case. Defervescence with slight remissions.
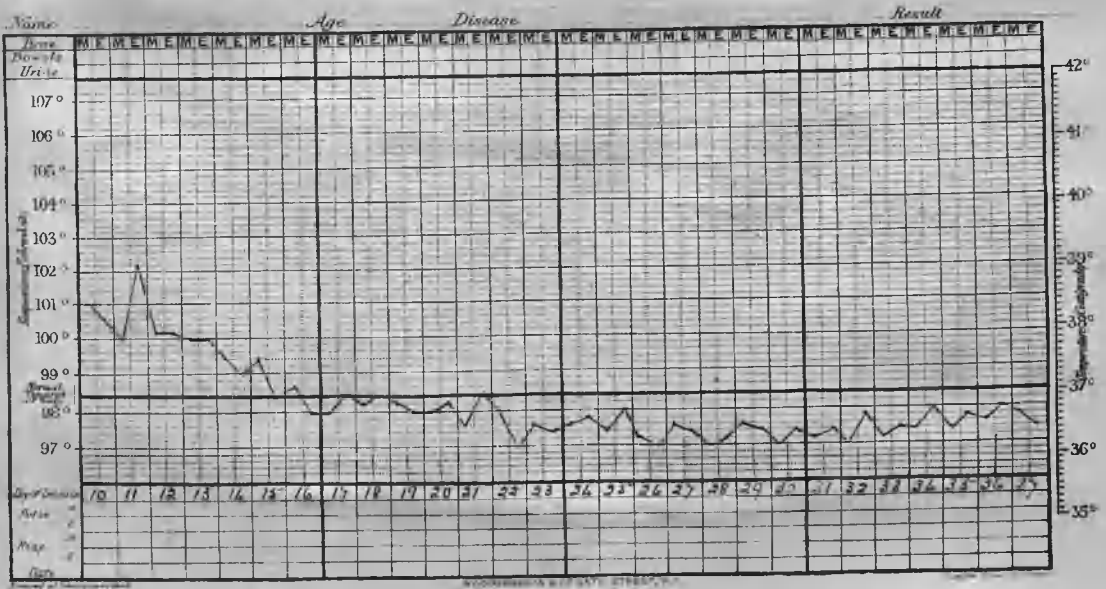
CASE X.—J. S., æt. 13.—Typhoid. Fall by gradual non-remitting lysis for three days, and then remissions for two.
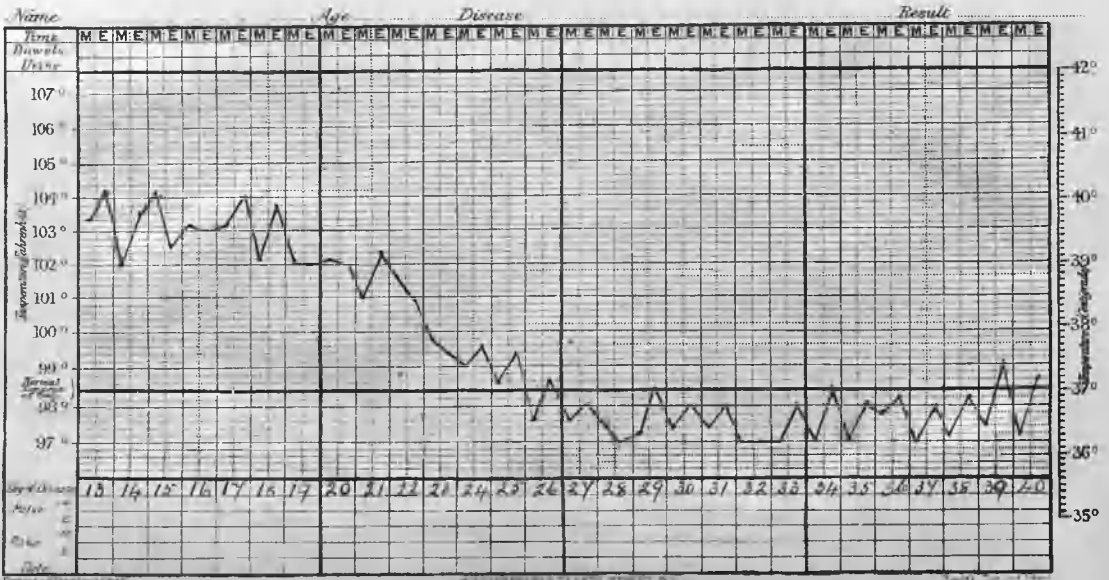
CASE XI.—J. R., æt. 16.—Abortive case. Fastigium not appreciable. Gradual decline from second day.
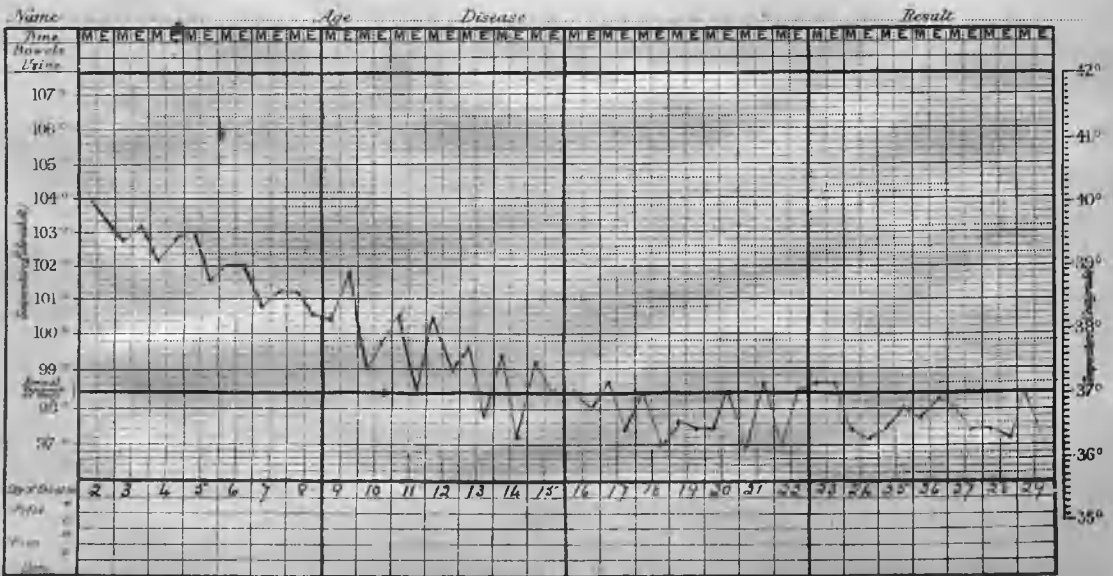
CASE XII.—J. M'M., æt. 9.—Mild case. Temperature declining from seventh day with marked remissions.
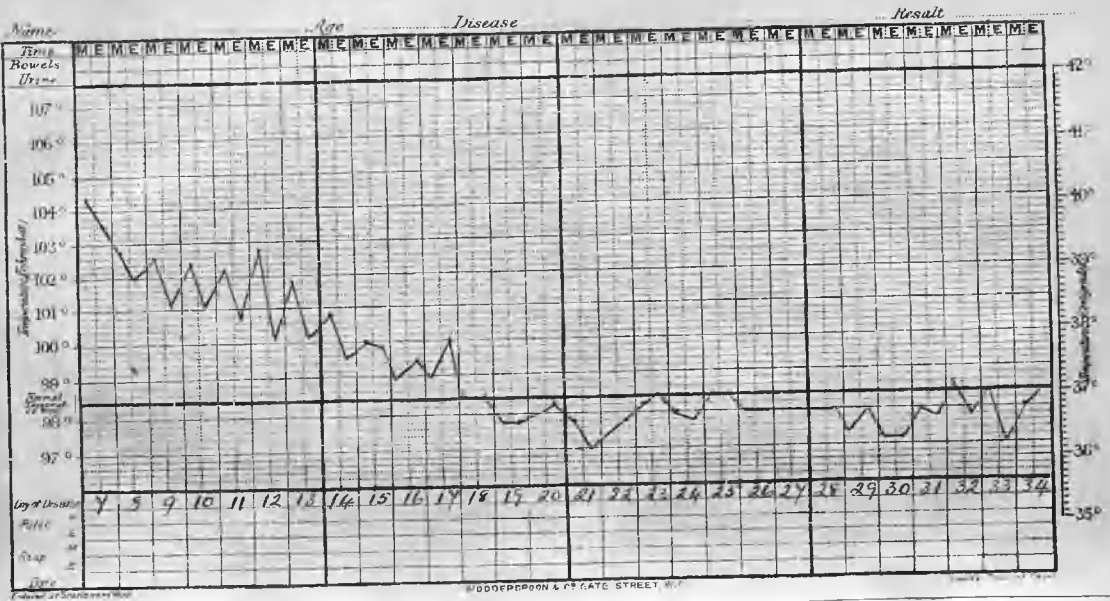
CASE XIII.—Mild case in child, æt. 5.—Irregular and atypical subfebrile temperature curve.
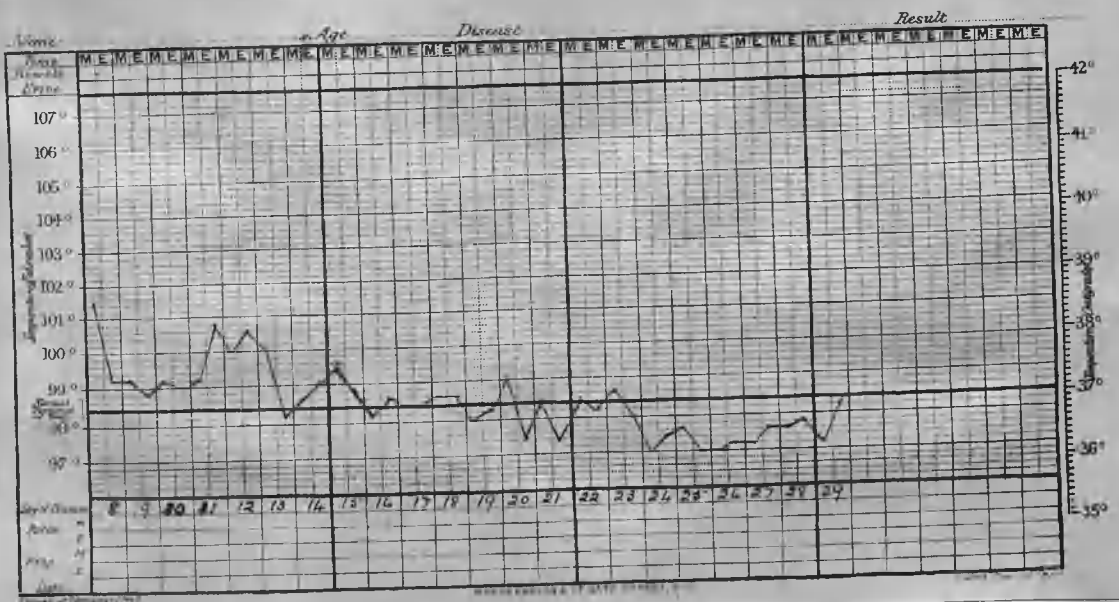
CASE XIV.—Typhoid in man aged 50 (J. B.)—Subfebrile type—remittent and intermittent
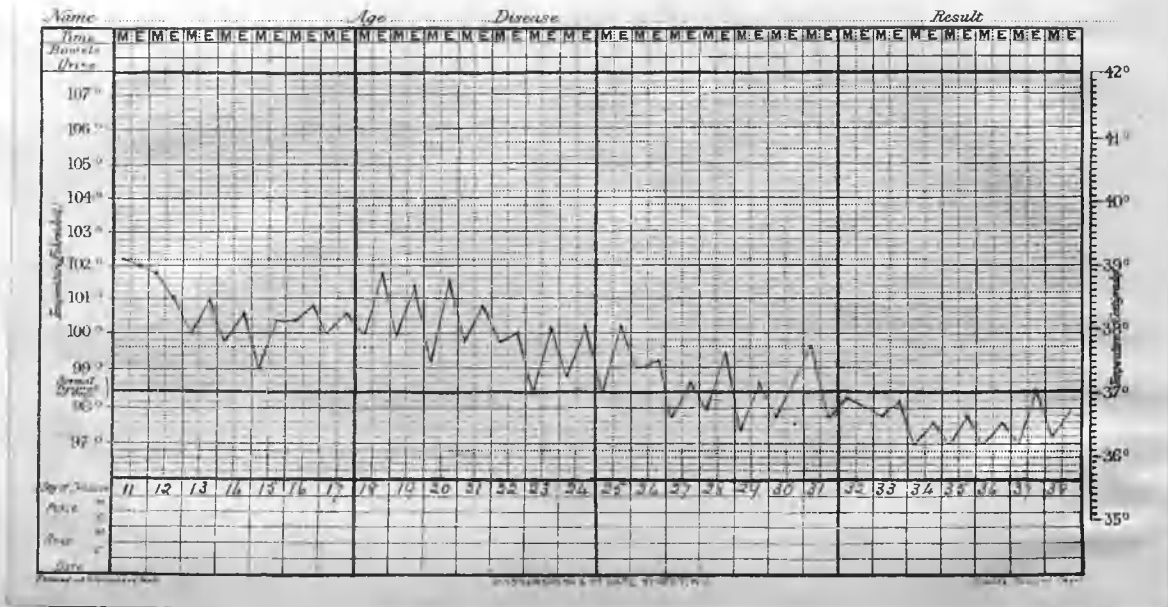
CASE XV.—J.W.—Typical temperature curve.
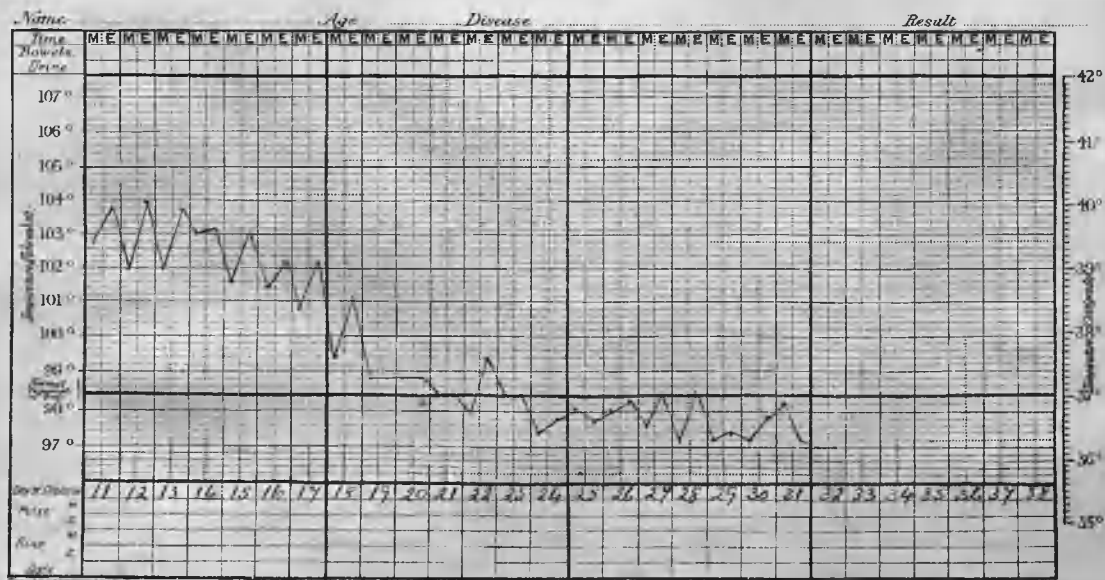
CASE XVI.—N. M'K.—Mild case of typhoid.   Temperature atypical—subfebrile, remittent and intermittent.

CASE XVII.—J. B., æt. 15.—Mild case of typhoid. Fall by remitting lysis to normal on twelfth day, then remissions until twenty-third day.
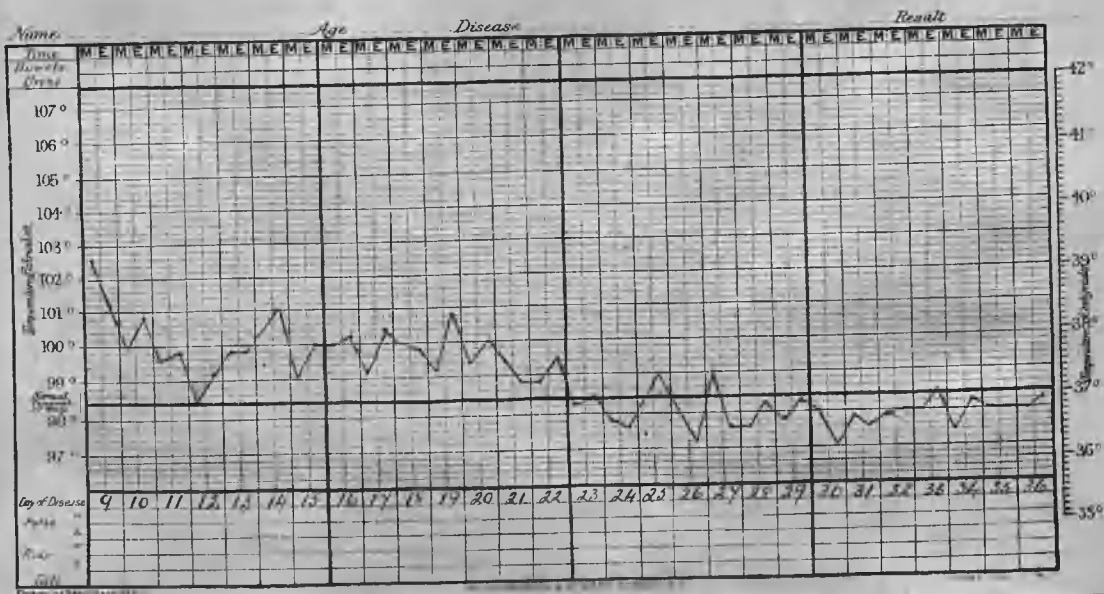
CASE XVIII.—A. C., æt. 34.—Moderately severe case of typhoid. Typical temperature curve, but showing two excursions, with intermissions on the two days following that on which temperature reached normal.
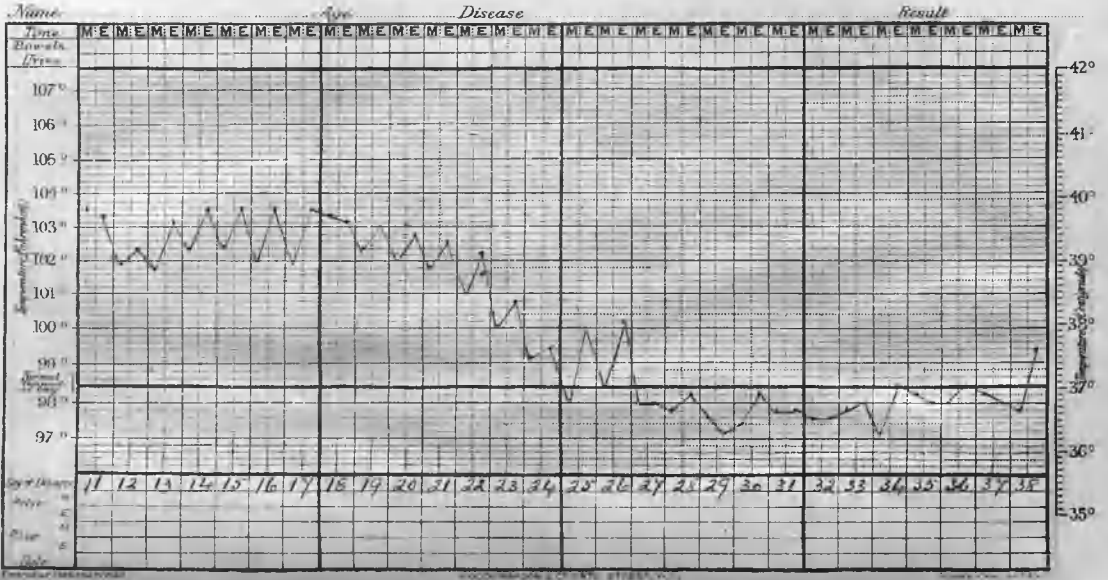
CASE XIX.—J. M‘C., æt. 9.—Severe and protracted case of typhoid—admitted on twelfth day. Remittent temperature for nine days, then higher temperature records reached by step-like ascent—curve finally typical, and defervescence first by remissions, then with elevation preceding non-remitting lysis.
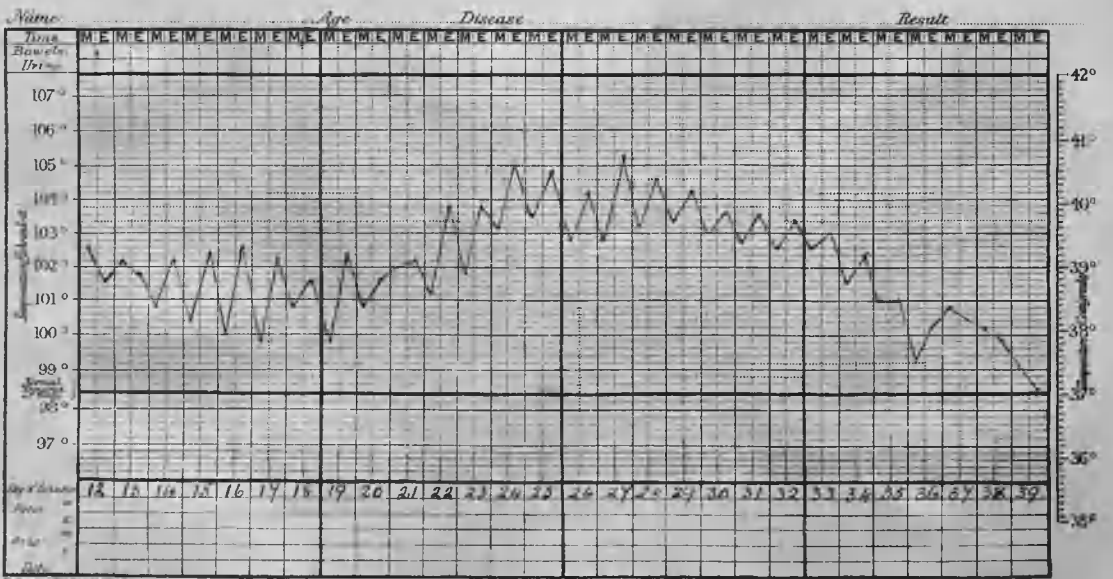
Case XX.—M. M'V.—Moderately severe case, admitted on fourth day—showing step-like rise to fastigium. Interruption of fastigium by lysis lasting three days, then re-elevation of temperature, showing continued remittent type, and finally defervescence by remitting lysis.
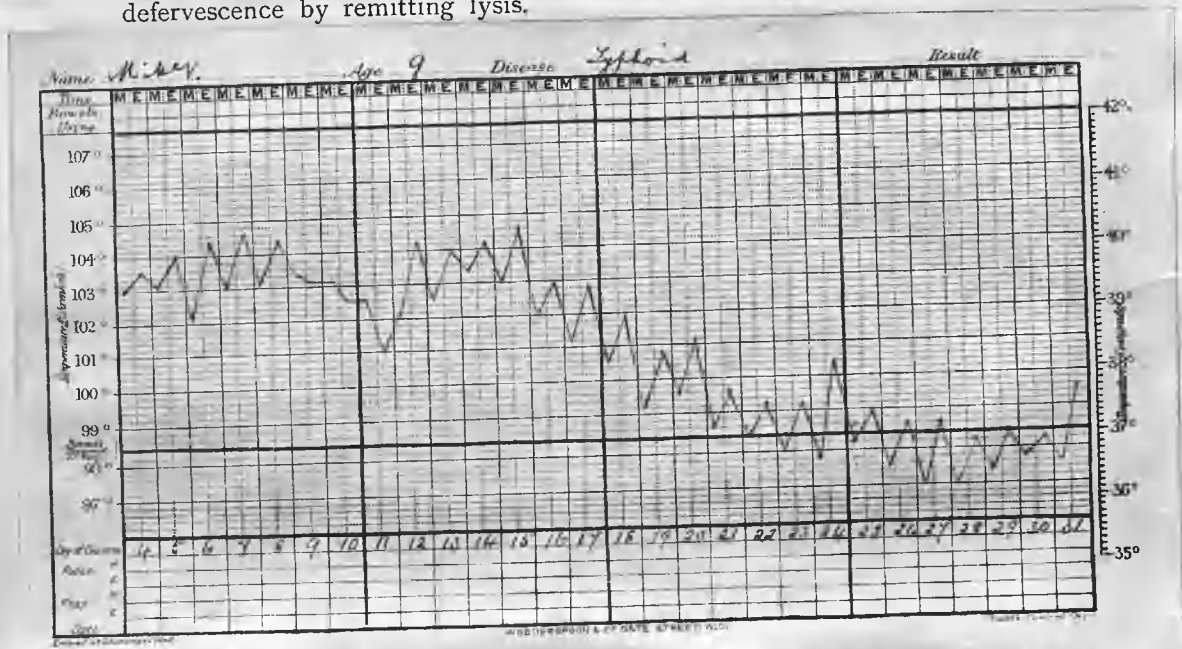
Case XXI.—J. T., æt. 30.—Mild case, with temperature showing wide excursions of 2° to 3½°F. Remittent and intermittent.

CASE XXII.—D. S., æt 7.—Moderately severe case, with fastigium lasting until nineteenth day, then a period of remissions and intermissions lasting until twenty-eighth day, with wide excursions.

CASE XXIII.—J. R., æt. 25.— Mild case of typhoid. Defervescence by non-remitting lysis, followed by two days of intermissions.
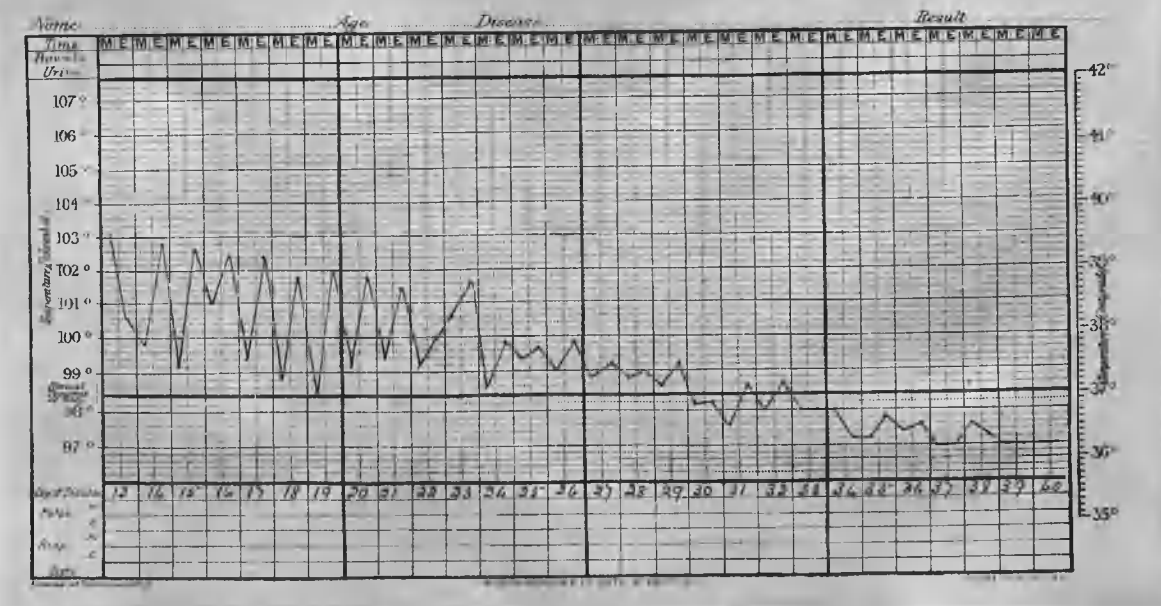
Case XXIV.—J. B., æt. 17.—Mild and abortive case.   Defervescence by marked
remissions and intermissions—temperature being normal on thirteenth day.
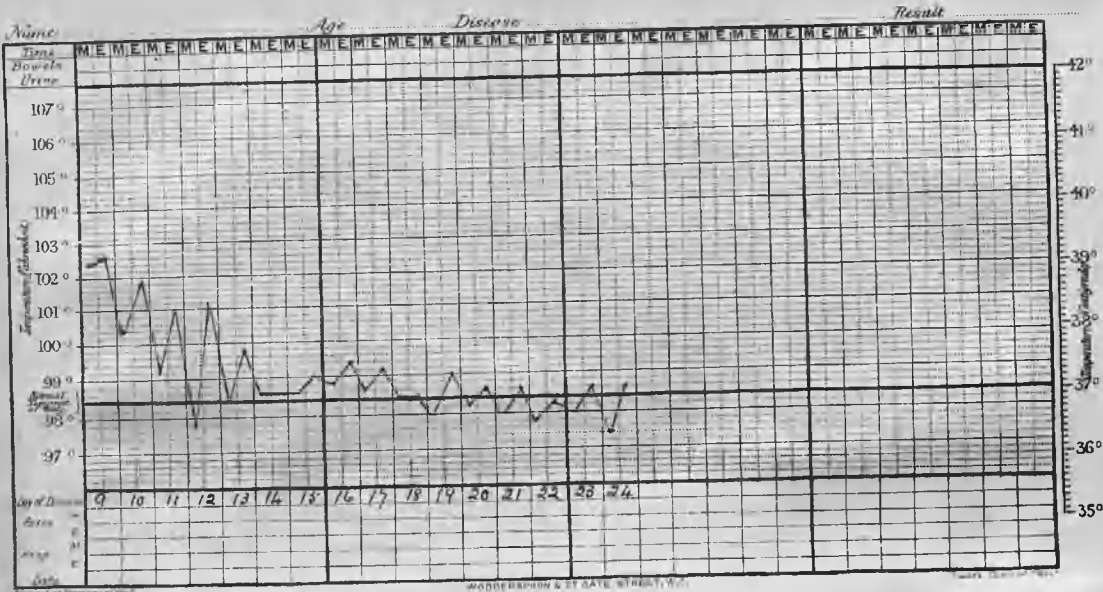
Case XXV.—W. C., æt. 6.—Mild case of typhoid.   Fall of temperature by crisis,
then excursions with intermission for two days.
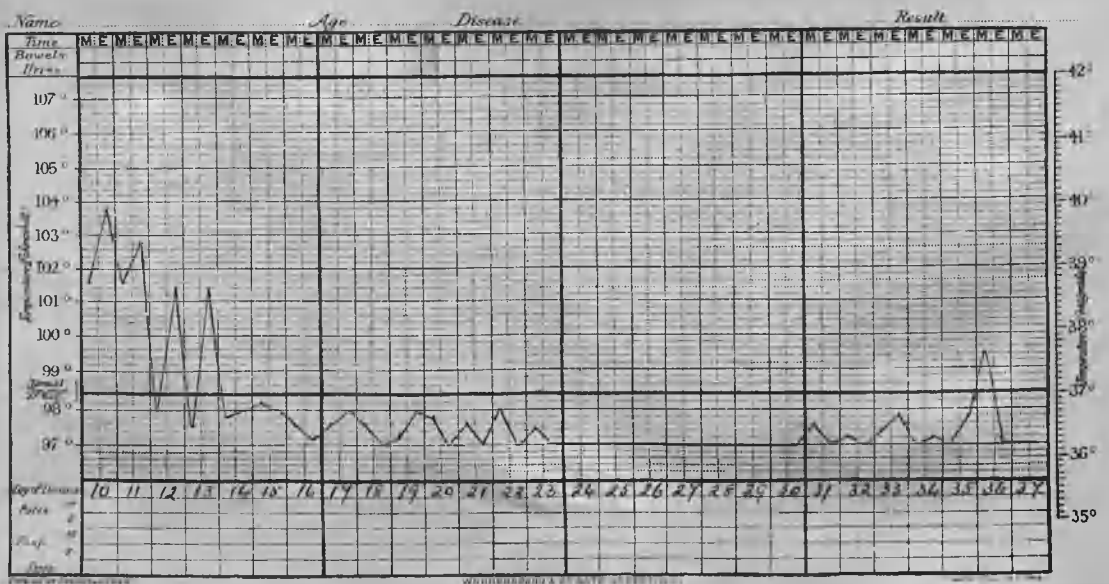
CASE 'XXVI.—J. W., æt. 7.—Typhoid. Defervescence by crisis.
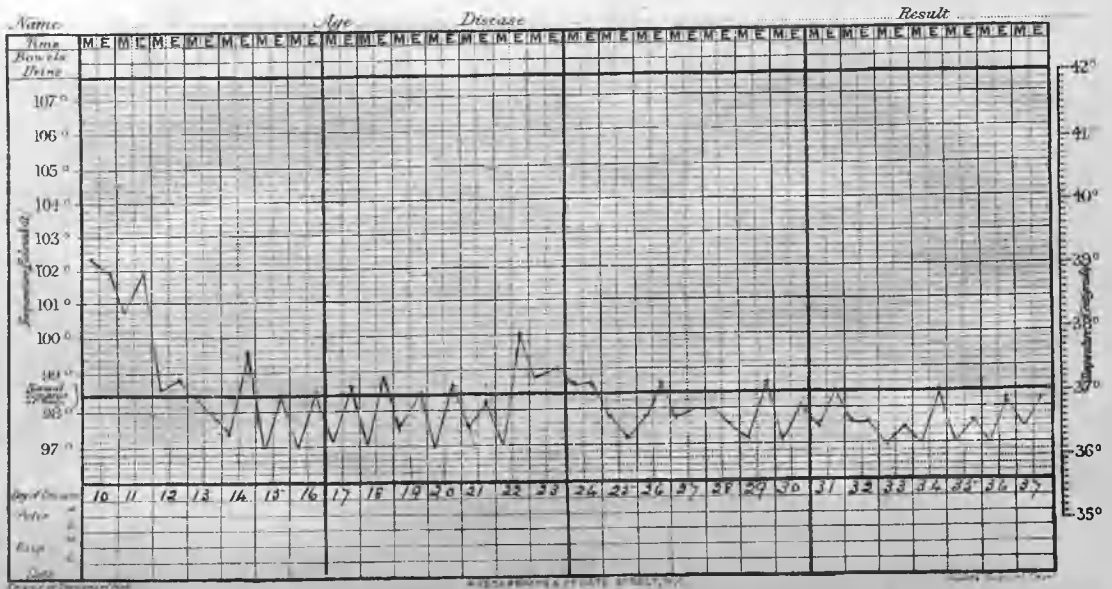
CASE XXVII.—M. M'N., æt. 5.—Typhoid. Defervescence by crisis.
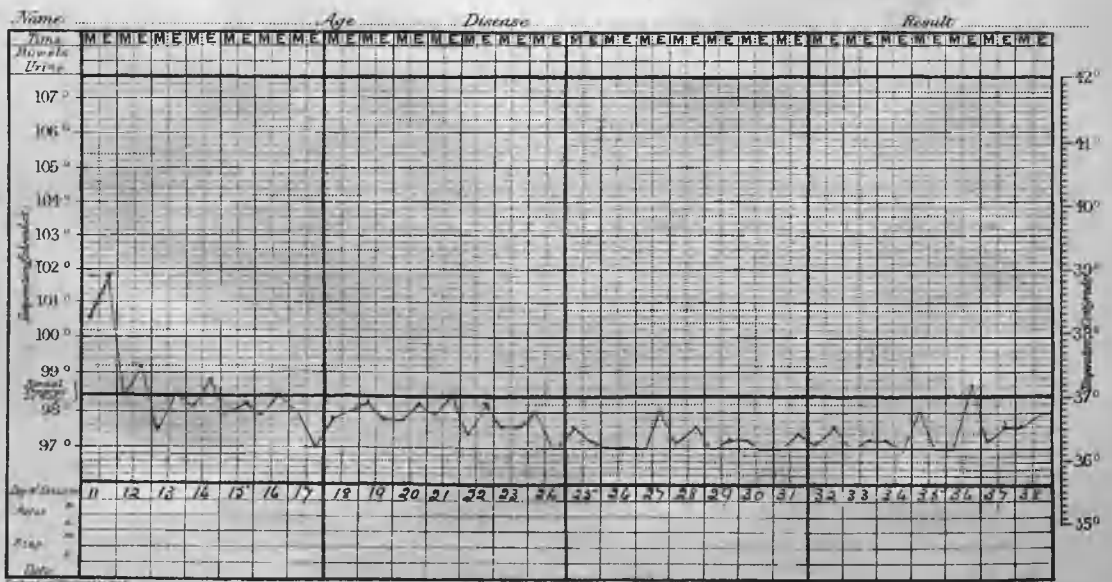
CASE XXVIII.—J. T., æt. 10.—Typhoid. Defervescence by rapid lysis.
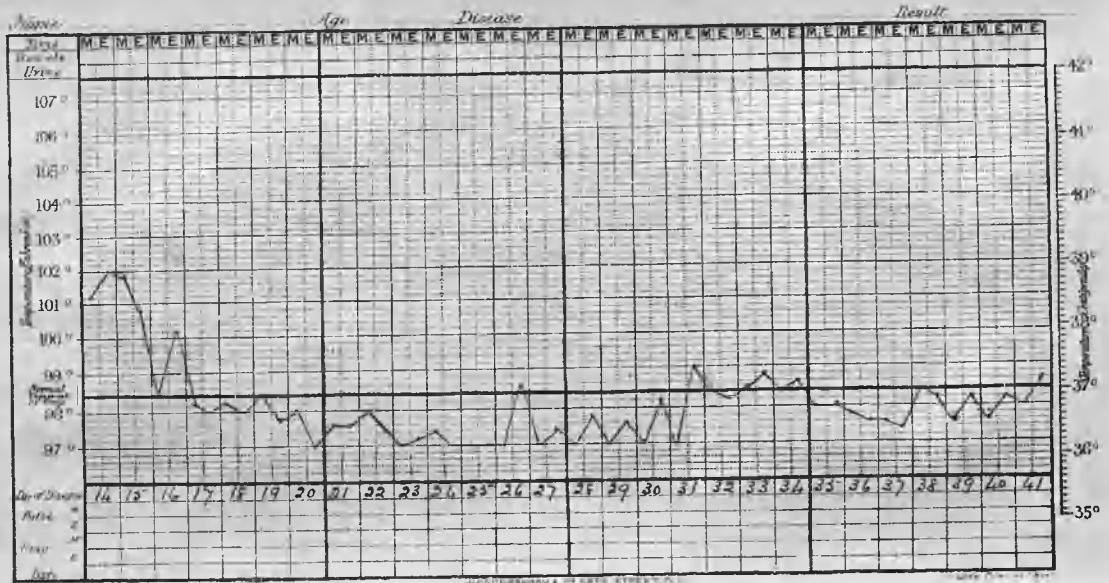
CASE XXIX.—G. M'I., æt. 4.—Typhoid — remittent temperature — finally rapid defervescence.
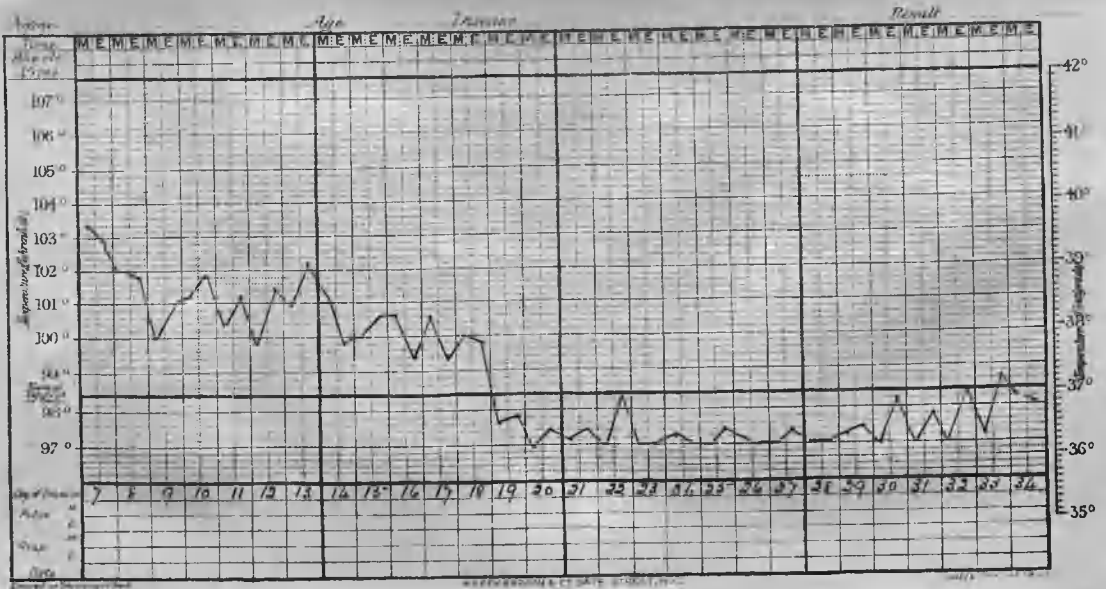
CASE XXX.—A. L., æt. 18.—Abortive case of typhoid. Defervescence by rapid lysis to normal on ninth day.
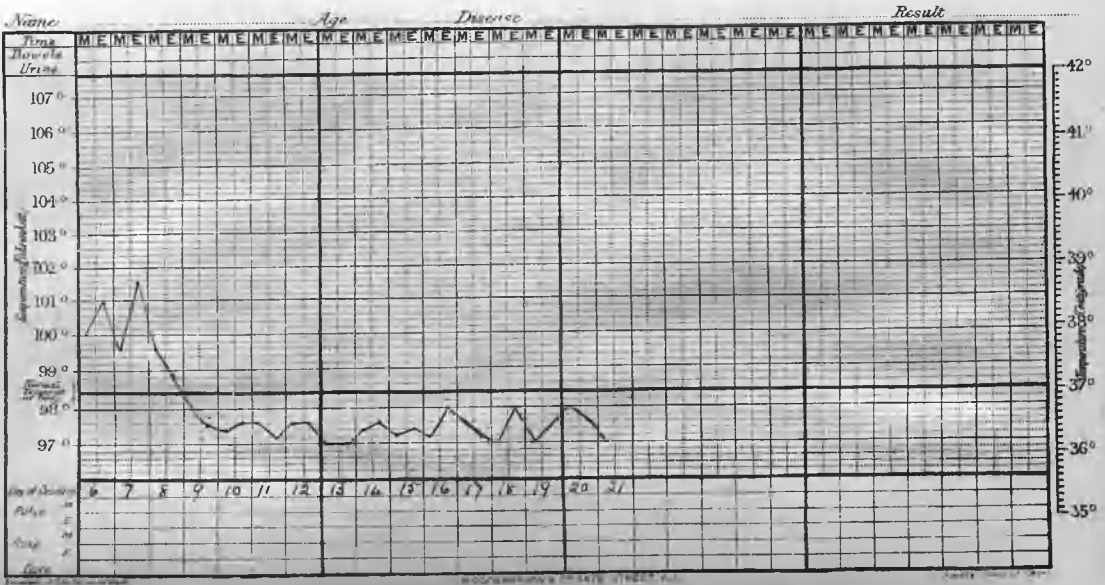
CASE XXXI.—J. S., æt. 14.—Mild case. Defervescence by rapid lysis to normal on twelfth day.
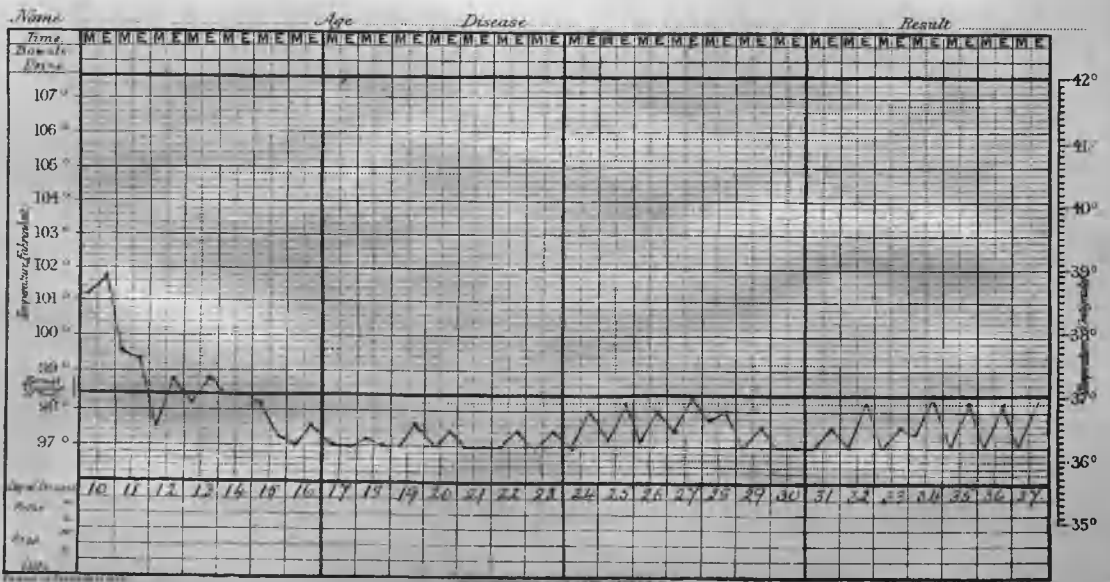
CASE XXXII.—M. F., æt. 4.—Typhoid, with critical decline of temperature on sixth day.
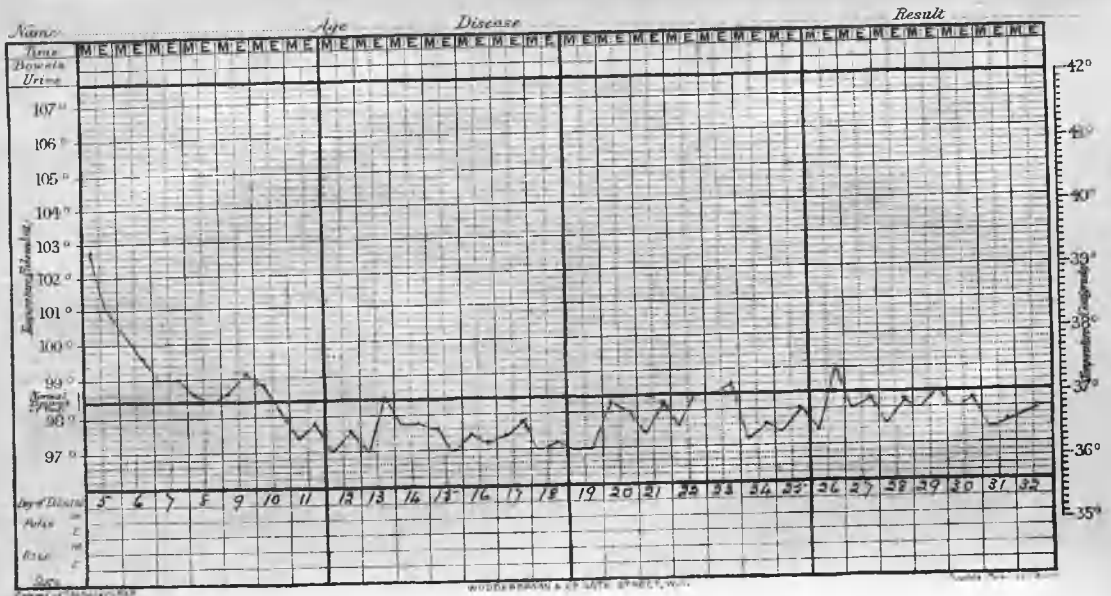
CASE XXXIII.—J. D., æt. 5.—Typhoid, with critical decline of temperature.
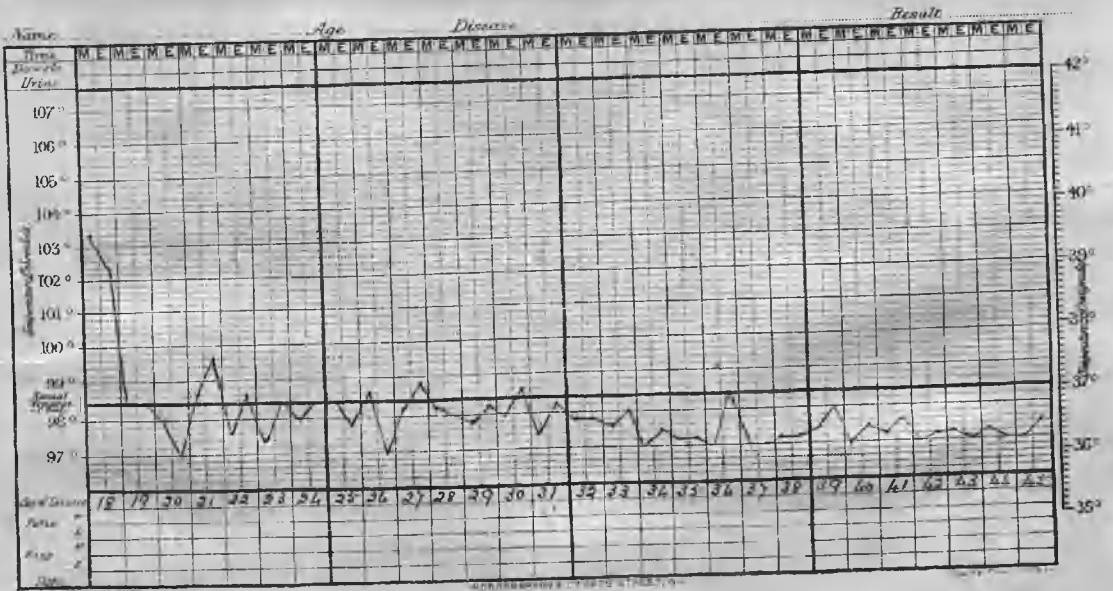
CASE XXXIV.—G. R.—Typhoid in a child of 15 months old—irregular temperature curve with marked fluctuations.
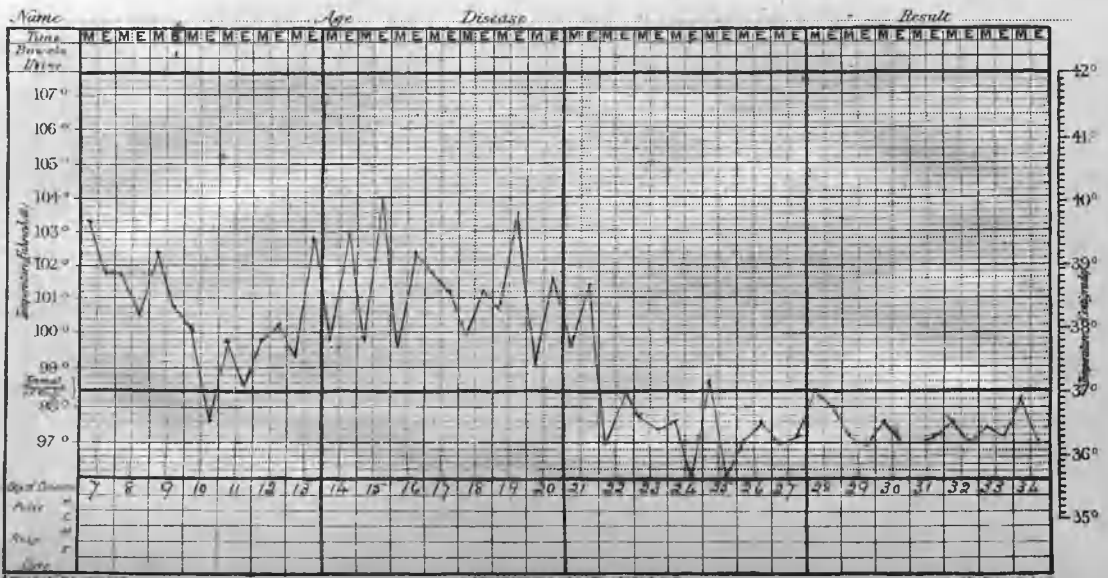
CASE XXXV.—Mrs S. (Pole), æt. 28.—Typhoid with remittent temperature showing wide fluctuations.
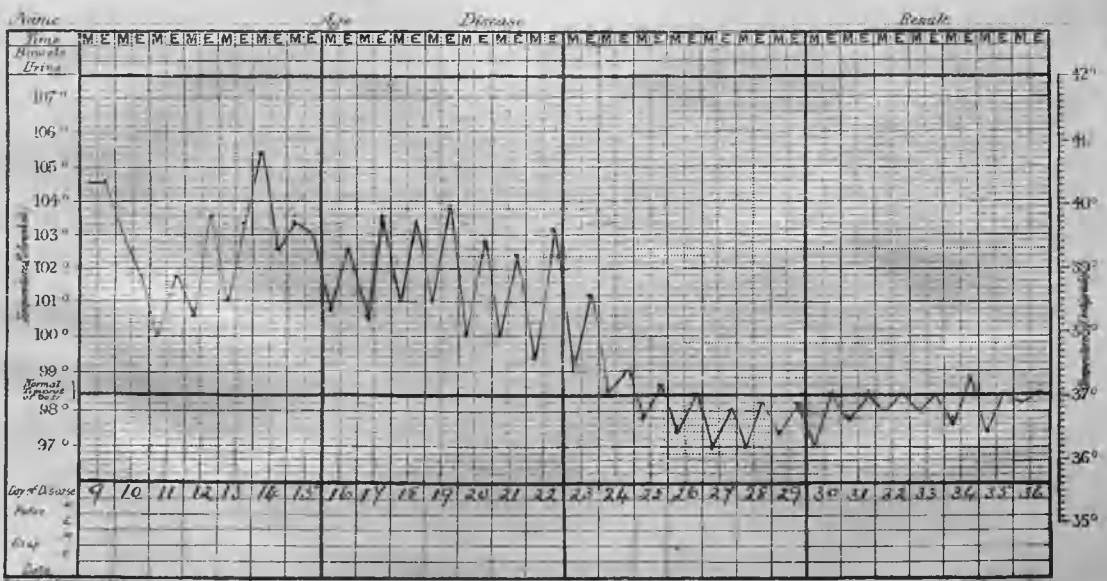
Case XXXVI.—J. C., æt. 21.—Protracted typhoid—intermissions lasting for eleven days.
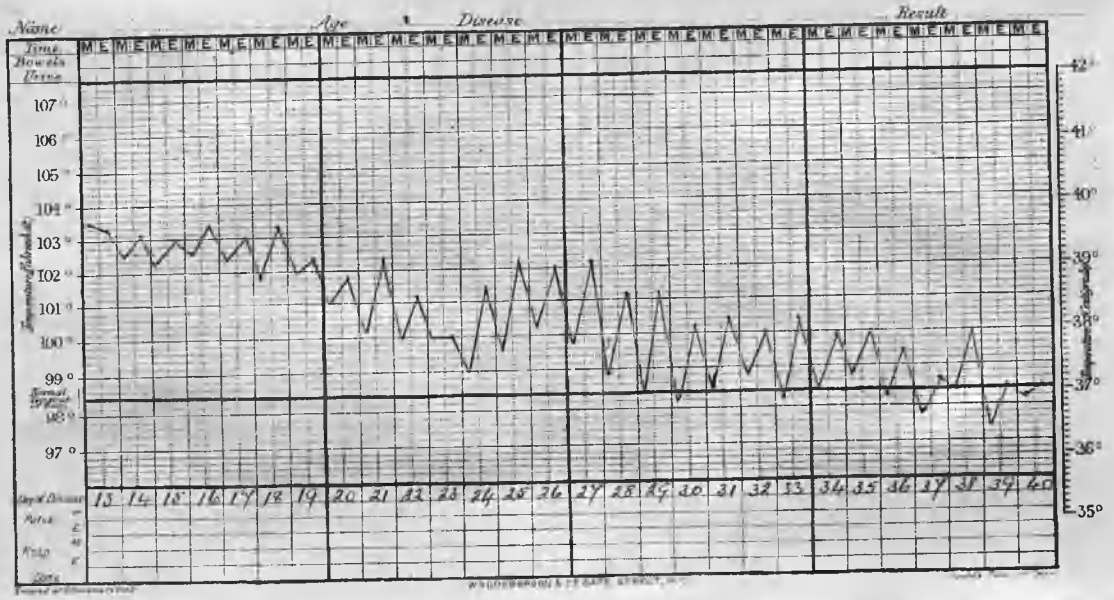
Case XXXVII.—R. B., æt. 30.—Protracted typhoid—very irregular. Four days of continued non-remittent fever, followed by period of remissions and intermissions.
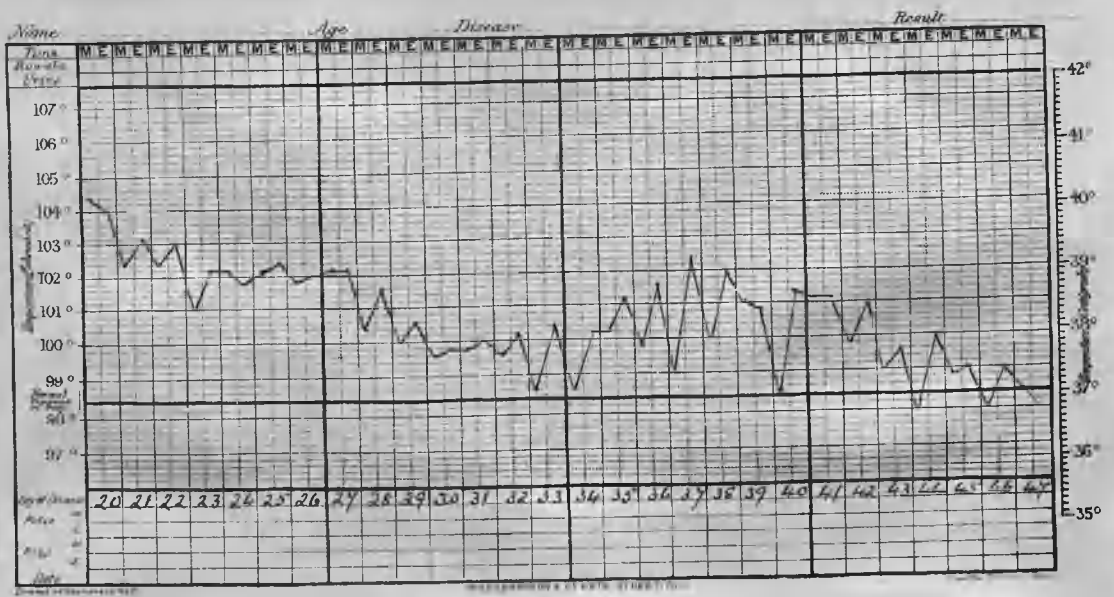
Case XXXIX.—C. P., æt. 29.— Protracted typhoid—well-marked remissions, followed by remissions and intermissions.
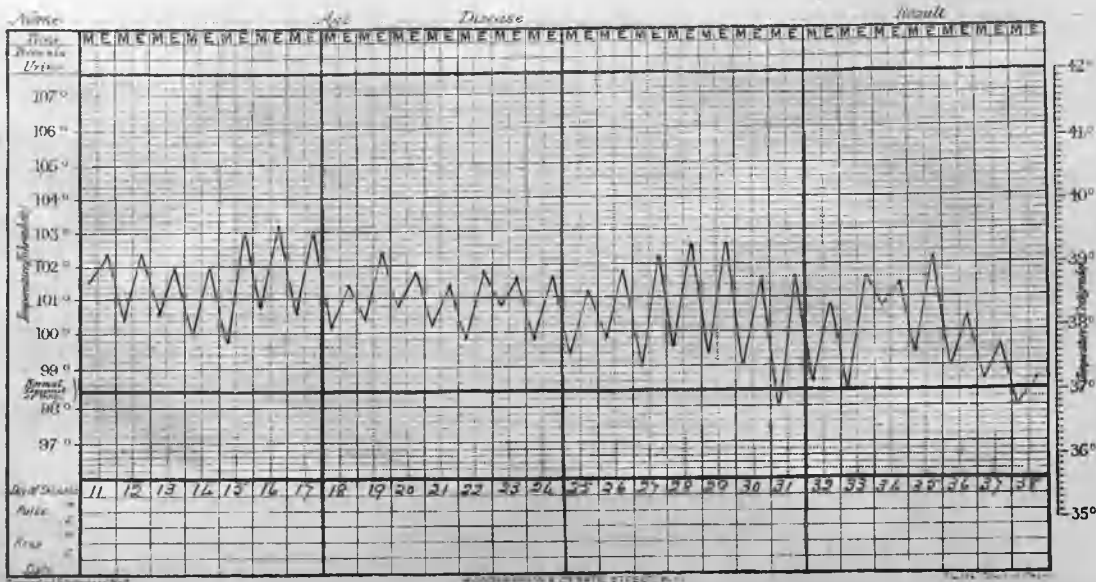
Case XL.—Nurse J. M'A., æt. 22.—Typhoid followed by acute tuberculosis—step-like ascent of temperature towards acme. Interruption of steep curves.
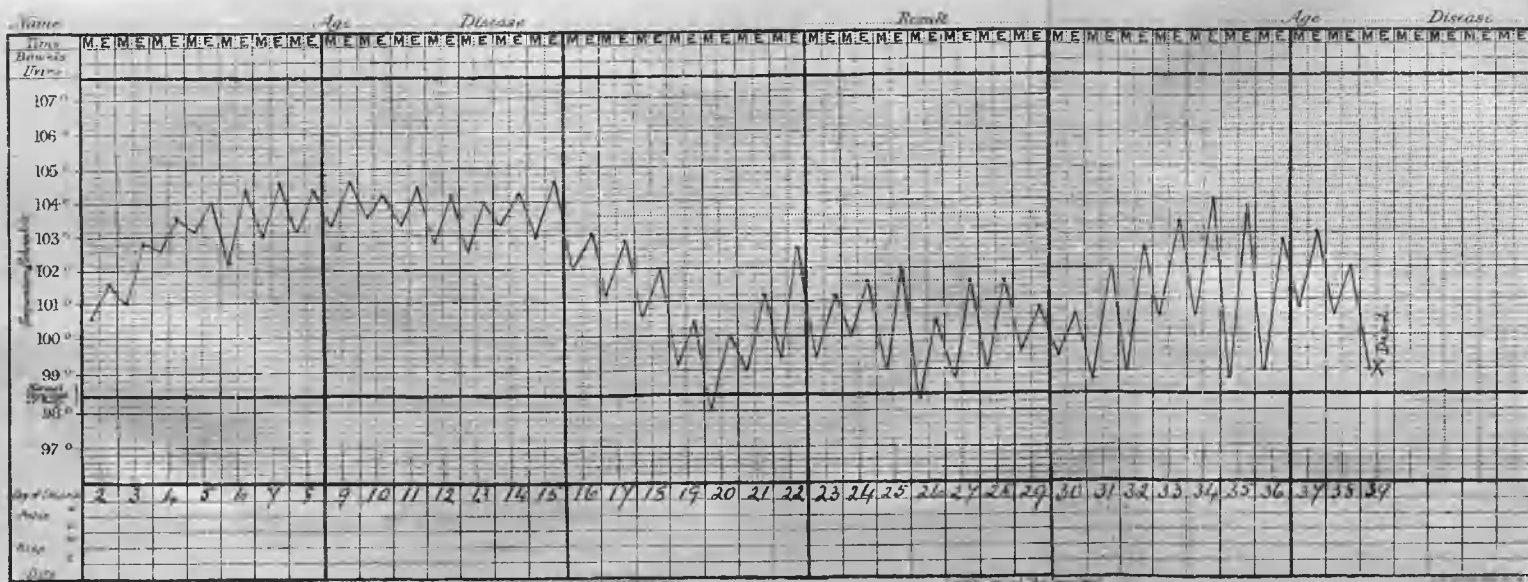
Condition of the pulse.—In most diseases associated with pyrexia the pulse rate is increased, and generally in proportion to the degree of fever or toxæmia. In some, although the temperature may not be exceedingly high, the toxæmia is so great that the pulse rate is disproportionately increased. In most pyrexial conditions the usual increase is at the rate of 15 beats for every 1°F. of temperature. In typhoid, on the contrary, the rate of the pulse and its characters present such constant features that they come to be associated in one's mind with this disease more than with any other. In young, previously healthy persons who are suffering from typhoid, and especially in males up to the prime of life, the pulse rate is *relatively infrequent* compared with the temperature. Thus it is not uncommon to see a temperature of 104°F. with a pulse rate of 80 to 90, and that even in a severe case, with pronounced symptoms. Infrequency of the pulse was, strange to say, considered an exception by Murchison and Louis. In children, down to 12 years of age, we occasionally note this also, but in younger children the rate of the pulse is increased more or less proportionately to the temperature. In studying a temperature chart illustrative of this point, we see the departure from the usual parallelism exhibited by the temperature and pulse curves, the two tending to keep further apart. This infrequency, however, is not observed in the ambulatory cases, nor where there has been pre-existing chronic or wasting disease, or where complications co-exist.

Dircotism of the pulse is well marked in most cases of typhoid. It sets in early and persists for a considerable time, even well into the fastigium. It is not so frequently observed in children, probably on account of the narrowness of the calibre of the arteries, but in middle life it is certainly the rule, and even in old age, if the atheromatous condition of the vessels does not prevent its recognition. Tricrotism may even occur. In very severe or complicated cases, the dicrotism may disappear early, and so not be present when the patient comes under our observation. In my series of cases, it was present in 80 per cent. of patients between 21 and 40 years of age. Of the remaining 20 per cent., one-half were females, a few were fatal cases, and some were admitted late in the disease, probably after it had disappeared. In patients between 12 and 21 years of age it was noted in 66 per cent., while in children under 12 years of age it was only detected in 5 per cent., and not one of these positive cases was under nine years of age. It was also present in an old man aged 57 years.

Value in diagnosis.—The diagnostic significance of the relative bradycardia and associated dicrotism cannot be over-estimated. Relative infrequency alone may lead one at the beginning of a febrile disturbance, especially in young adults, to suspect the existence of typhoid fever; but coupled with the existence of dicrotism, one is almost justified in concluding its presence. In no infectious disease are these two associated qualities so frequently observed. On the other hand, their absence must not exclude the diagnosis of typhoid, for severe toxæmia, hæmorrhage, profuse diarrhœa, or concomitant inflammatory conditions may cause the pulse to become rapid and to lose its dicrotic quality. In children, on the other hand, and in the aged, we rarely expect

to find them.   The chief febrile affections that are apt to lead to difficulty in diagnosis with regard to the pulse rate are influenza and tubercular meningitis.   In the former I have frequently observed both relative slowing and dicrotism, but not occurring with such frequency as in typhoid.   In tubercular meningitis the slowing of the pulse is often extreme, reaching lower records than we commonly find in typhoid, and is rarely or never accompanied by dicrotism.   The bradycardia and instability of the pulse rate during the period following defervescence are also worthy of consideration from a retrospective diagnostic standpoint, as in no other infectious disease are they so marked or so frequent.   I have observed the bradycardia frequently during convalescence from influenza, but not the excitable condition of the pulse.

CHART showing the temperature and pulse curves in a case of typhoid in a young adult.
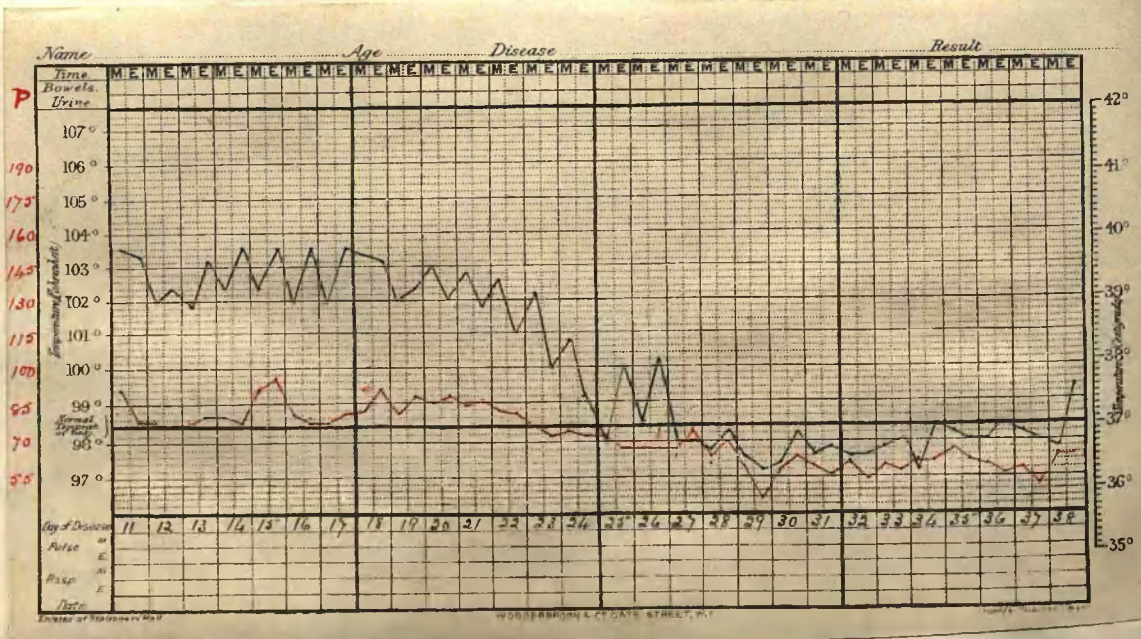
CHART showing temperature and pulse curves in typhoid in child.
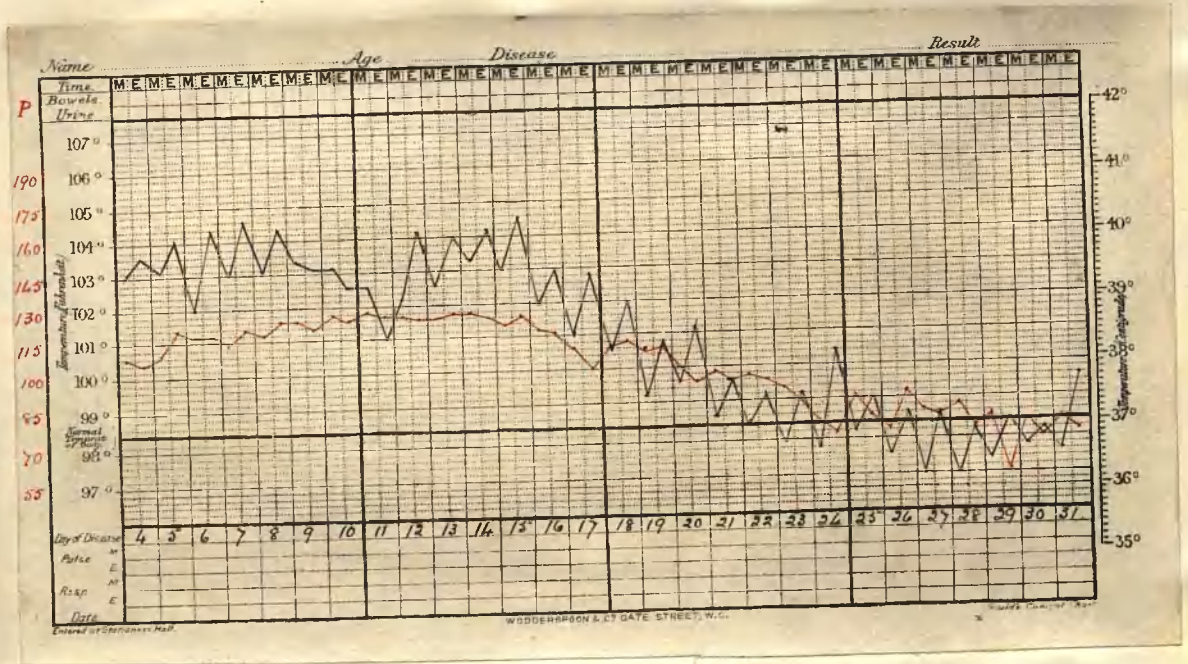
CHART showing temperature and pulse curves in a severe and complicated case of typhoid.
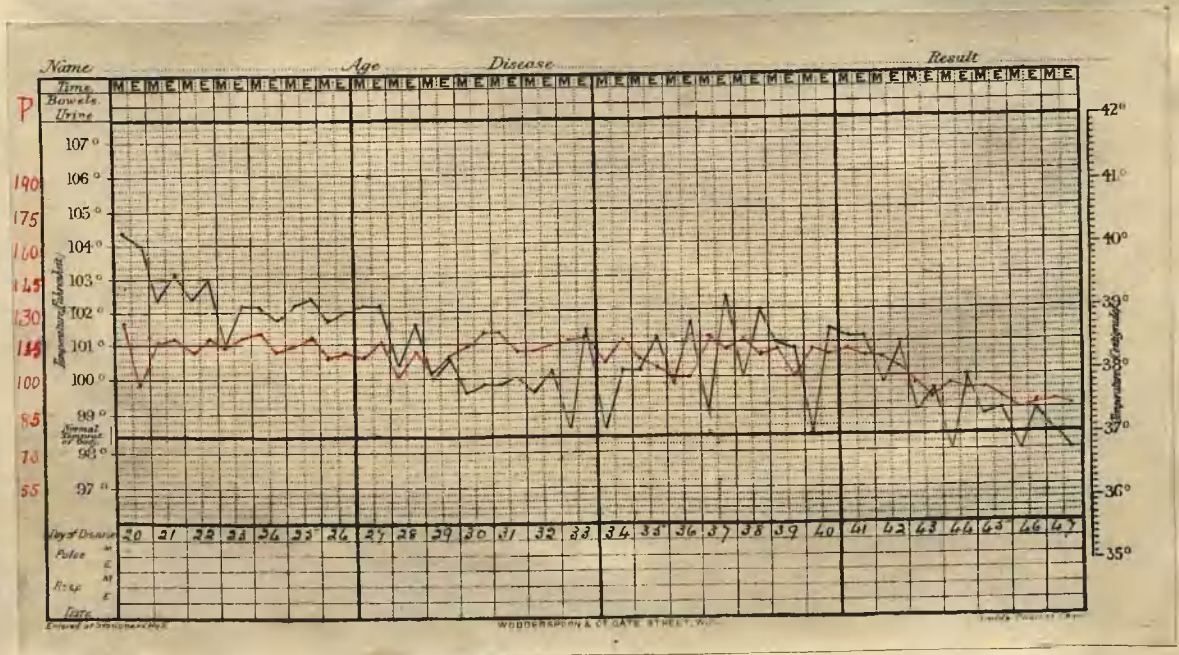
Chart showing temperature and pulse curves in a case of typhus.
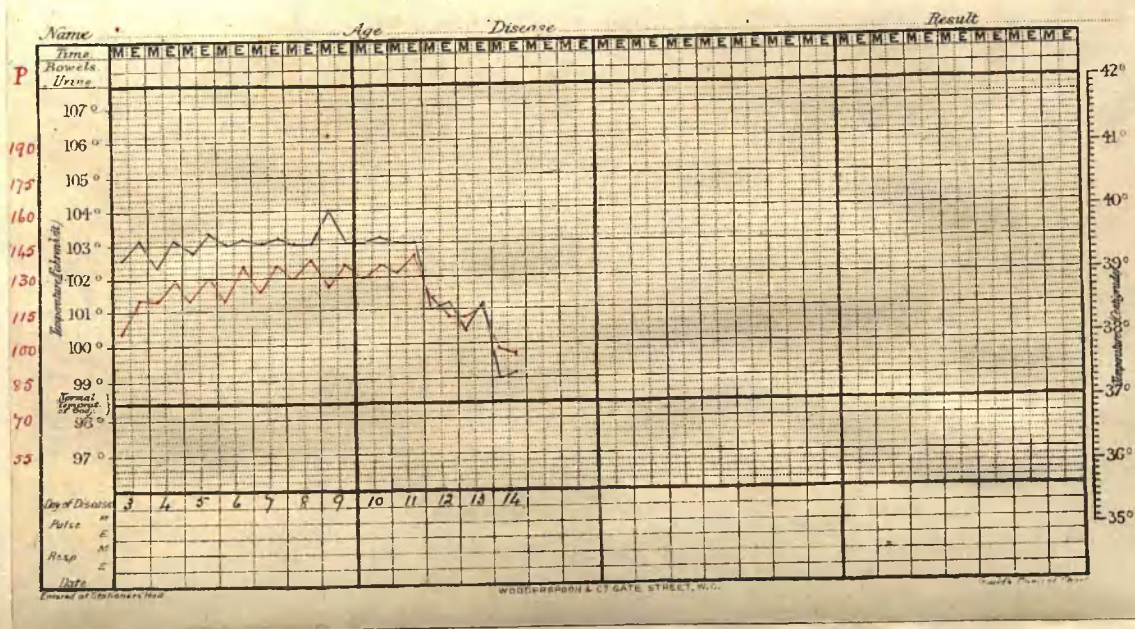
Bowels.—In typhoid fever the condition of the stools is variable. Although Murchison stated that diarrhœa was the rule in typhoid, having observed it in 93 per cent. of his cases, at a later period he added "that it is absent in a greater proportion of cases than he had previously indicated—in fully one-fifth." He also says that "those cases in which it is absent are usually mild, and recover." This latter statement and his percentage of cases with constipation are alike incorrect. Diarrhœa may occur among the prodromal symptoms, and cease at that period, or may continue during the whole illness or alternate with normal motions. It may, however, only appear at the end of the first week after the administration of a purgative, and its appearance may even be delayed until the second or third week of illness. In Osler's cases 34·4 per cent. had diarrhœa before admission, and 17·3 per cent. during their stay in hospital, while 51 per cent. had constipation. Curchmann, in the Hamburg epidemic, noted constipation in 25·3 per cent., while diarrhœa was present throughout the whole illness in 36 per cent. In the Leipsic clinic he noted diarrhœa throughout in 25·6 per cent., constipation in 16·4 per cent., and normal stools in 4·4 per cent. Morse, quoted by Rotch, states that in children, constipation is more common than diarrhœa; while Henoch observed normal motions in 12 per cent. of children. In my own cases, 48 per cent. had diarrhœa before admission; in 42 per cent. the motions were normal or constipated; while in 10 per cent. no definite history could be obtained. During their residence in hospital, 40 per cent. had diarrhœa, while the remaining 60 per cent. had either normal motions, or their bowels were constipated. To the hyperplasia and ulceration of the lymph follicles the diarrhæa

is probably attributable, and in a certain measure also to the associated catarrh. Osler however, is of opinion that the catarrhal process, especially when it affects the large intestine, is much more responsible for the frequent motions than the hyperplasia. To come to the characters of the motions when diarrhœa is present, it was at one time customary to speak of them as the typhoid stools, being regarded as distinctive of the disease. When diarrhœa occurs, the stools are thin, liquid, greyish-yellow, and of the consistency and appearance of peasoup. They are alkaline in reaction, and possess an ammoniacal odour. On being allowed to stand, they separate into two distinct layers—a supernatant serous, containing salts and albumen, but with a deficiency of mucus; and a yellowish-grey sediment containing particles of undigested food, intestinal epithelium, particles of slough, a few white and red blood corpuscles, and crystals of triple phosphate, at one time regarded as being specific. It is probable that the deficiency in mucus favours the separation into two layers. In young children, according to my observations—and this is a point upon which sufficient emphasis is not laid except perhaps by Henoch—the stools throughout often closely resemble those associated with other intestinal ailments in children, being greenish, greenish-yellow, or milk-and-coffee-like in appearance.

Diagnostic value of condition of bowels.—As we have seen, it is only in those cases where diarrhœa occurs that the stools can be of any value in diagnosis, and as this occurs in only about half of the cases, their importance from this standpoint is not by any means considerable. When diarrhœa does occur, the peasoupy motions are only of diagnostic importance when taken in conjunction with other signs of the disease, for, apart from the bacteriological examination of them, there is nothing pathognomonic about them, either as regards their physical or their chemical condition. Certainly we must admit that peasoupy motions are of much more frequent occurrence in typhoid than in any other affection. As hyperplasia of the intestinal lymph follicles and associated catarrh occur in other affections—chiefly measles, diphtheria, and scarlet fever—stools having the appearance and consistency of peasoup are likewise occasionally observed in them. In three cases noted in the appendix, stools of this description were present and persisted for some time. One was H. M'C., a case of scarlatina anginosa, who developed diarrhœa and splenic enlargement; a second was A. S., who suffered from malignant endocarditis, following pneumonia; while the third was Mrs M'V., a case of phthisis. To sum up, then, we may say that peasoupy stools, while *per se* of little diagnostic value, taken in association with other symptoms, and in consideration of their greater frequency in typhoid than in other affections, are an aid to diagnosis.

Eruption.—The roseolous eruption, the tâche rosée lenticulaire of Louis, has often been designated the typhoid roseola, on account of its specificity. It consists of small round or oval pinkish spots, slightly elevated above the surrounding skin, and varying in size from that of a pin-head to a lentil, and always circumscribed. Being purely hyperæmic, they fade on pressure, to return when the latter is removed. They are rarely exceedingly numerous, the average number present at

one time being from five to thirty. The eruption usually makes its appearance for the first time between the seventh and tenth days of the disease, and the individual roseolæ, after persisting for from three to five days, disappear, others making their appearance in other parts, the eruption coming out, so to speak, in successive crops. The total eruption usually lasts from 12 to 14 days. As regards their situation, they usually appear first upon the chest, abdomen, and back, and only when very numerous do they appear upon the legs and arms, but never on the face. In those cases which have an abrupt onset, the rash may appear earlier than the seventh day, and the same is to be said regarding children, in whom it is apt to be more scanty than in adults. In one of my cases, a girl of 16 years, admitted from a house endemic on the second day of illness, the rash was present on the fifth day. In some cases the eruption has to be carefully searched for, as it may readily be overlooked, this being due either to the paucity of the spots, or to the characters of the individual's skin. Thus, in several of my cases, only three to five spots were present at one time, and in three young children one roseola could be detected at once; a second, and later, a third, appearing a few days afterwards. In old age they are not so frequently present as in middle life, although in three males over 40 years of age, under my care, they were noted in all.

Diagnostic Value.—The specific eruption, having all the characters previously portrayed, is undoubtedly of great value in diagnosis, and is, in fact, the only pathognomonic clinical symptom of the disease. Murchison said, and with what truth we know, that an eruption having all the characters mentioned above, is peculiar to typhoid. A little doubt has, however, been thrown on this statement by some competent observers,' Curchmann, for example, stating that in a few instances of acute miliary tuberculosis and of cerebro-spinal meningitis, which were proved on post-mortem examination not to be complicated by typhoid, he had observed eruptions indistinguishable from the typhoid roseola. Osler, also, makes this statement with regard to cerebro-spinal meningitis, and he also affirms that he has met with syphilitic roseola with eruptive fever and splenic enlargement, which caused some difficulty in diagnosis, the roseolæ evidently closely resembling those occurring profusely in typhoid. Waller of Prague, and Barthez and Rilliet make similar statements with regard to acute phthisis. It is questionable, however, if careful attention to all the characters of the eruption, date of appearance, and distribution, could not exclude these cases. In a case, which was under my care— Mrs M., aged 20, suffering from tubercular peritonitis with effusion, and in whose case there was no question to my mind of complicating typhoid, the Widal reaction being after repeated tests absolutely negative—there was an eruption of pinkish spots on the chest and abdomen. They varied in size from a pin-head to a lentil, and some, like some typhoid roseolæ, were capped with a small vesicle They almost, but did not completely, disappear on pressure, and careful inspection showed that they were scarcely so well defined as typhoid roseolæ.

Unfortunately for diagnostic purposes the eruption is not always present, many well-marked cases occurring without any appearance of eruption throughout the whole illness, for, like the fever and splenic enlargement, the amount of eruption does not necessarily bear any direct relation to the severity of the disease. Osler gives his percentage of cases with eruption as 93·2, Louis 90, Murchison 76·9, while in my own series the percentage with eruption among patients, over 12 years of age, was 83·3. On the other hand, in children under this age, I was unable to detect any roseolæ in 60 per cent., but this was in some measure probably due to the fact that many of them were not admitted until the third or subsequent weeks of the disease, and it is quite probable that by that time the rash had disappeared. As a diagnostic element in recent cases, i.e., in patients who have recovered from it, it is valueless, as it leaves no trace after its subsidence. Again, it is of no value during the first week of the disease, for, as we have seen, it is only in exceptional cases that it appears before the seventh day.

Spleen.—The enlargement of the spleen in typhoid is due to distension with blood and to hyperplasia of the cellular elements of the pulp. Although it is observed more or less in all infectious diseases and septic conditions, in no one except malaria is it such a constant symptom as in typhoid. The degree of enlargement varies, sometimes being just appreciable to careful examination, at others increased to twice or thrice its normal dimensions. In the time of its appearance there is also some variation. Although, according to anatomical observations, hyperæmia and splenic enlargement are present by the middle of the first week of illness, the enlargement of the organ is rarely demonstrable clinically before the seventh day. In some cases, however, and especially in those who complain at the beginning of a dragging pain in the left hypochondriac region, the enlargement may be perceived before this date (I had one such case); and some even (Curchmann) have demonstrated it during the period of incubation. These are, however, the exceptions, for it is rare to be able to detect it before the seventh or eighth day. In those cases which begin abruptly (the abortive type, for example) the enlargement may be detectable by the fourth or fifth day. Among my own cases, I was able to detect enlargement on the

Fourth day in 2 cases (æt. 9 years)
Fifth   ,,   in 3   ,,   æt. 20 (fatal), 13½, and 11 years
Sixth   ,,   in 3   ,,   æt. 55 (fatal), 23, and 1¼ years

The enlargement persists during the fastigium, and often well into the stage of defervescence, though in those cases where a relapse is pending, it does not completely subside. The degree of enlargement varies, and bears no relation to the severity of the disease or the height of the temperature. Some cases end fatally at the height of the fastigium without any appreciable enlargement of the spleen being detected, while in some mild cases, pursuing a subfebrile course, the lower border may be felt, during quiet respiration, from one to two inches below the lower costal margin. As regards age, it is most often present in young and middle-aged persons, but acquires a high percentage also during childhood. In old age, on the other hand, it is not nearly so

constant. Henoch gives his percentage in children as 46. Osler found splenic enlargement in 71·6 per cent.; Murchison, quoting Taupin, 90 per cent.; Curchmann 91 per cent.; while in my own series it was present in 80·6 per cent. It must be borne in mind, however, that certain factors may exist which prevent enlargement of the organ. Thus, severe or frequently repeated hæmorrhages, or profuse and watery diarrhœa in the earlier days, may reduce the organ, so that when the patient comes under observation no enlargement can be detected. In my own series I had four fatal cases with intestinal hæmorrhage, in all of whom I failed to detect any enlargement of the spleen. Again, if the patient has been the subject of a severe wasting disease, or a disease attended with extreme emaciation, no enlargement may take place. As regards antecedent disease of the organ itself, any previous condition that may have led to cicatricial changes in the tissue, or to thickening and consequent loss of elasticity of the capsule, may prevent enlargement. Among these are multiple infarctions. In elderly people also, senile atrophy of the organ prevents enlargement, or only allows enlargement sufficient to raise it to normal dimensions. As bearing on the opposite side of the question, it must not be forgotten, before drawing conclusions, that the organ may be enlarged from other causes, such as malaria, leukæmia, pseudo-leukæmia, or be readily palpable and so apparently enlarged, the result of displacement from pleural fluid accumulation, or from congenital mobility. Three cases illustrative of the latter two points came under my own care. One, A. G., an elderly man, who had served in the army in India, and while there had contracted malaria, was admitted to the Middle Ward Hospital notified as suffering from typhoid. He was suffering from influenza, and not typhoid, but examination revealed a considerably enlarged spleen. As he improved, no reduction in the size of the organ took place, and on the day of his dismissal it was of the same dimensions as when first examined. The second was a girl, an Anglo-Indian, who had never had malaria. Palpation revealed a freely movable spleen, which was not tender to palpation nor on bimanual pressure. It was undoubtedly congenitally dislocated. The third was the case of a girl, L. B., whose spleen was readily palpable, as the result of displacement by a left-sided empyema. After evacuation of the pus, the organ receded.

Methods of detecting splenic enlargement.—Perhaps it may not be far out of place to say a few words at this stage on this matter, for, to my mind, the discrepancies in statistics on splenic enlargement from various sources are in great measure attributable to imperfect examinations, or such, in the event of a negative result being obtained at first, not being repeated with sufficient frequency or care. A considerable degree of practice in abdominal palpation is requisite, in order to definitely ascertain enlargement, when present in a small degree. Palpation may be interfered with, in a patient with thick and pendulous abdominal walls, or if there be marked rigidity of them. There is no difficulty in those cases of marked enlargement in children with thin parietes, and where the lower border of the spleen is felt one or two inches below the costal margin ; but in others the degree of enlargement is so slight, that the flat of the fingers require to be pushed well up below the ribs and maintained there until the end of a

deep inspiration, when either the border, well defined, can be appreciated, or only a feeling of increased resistance. If one is unable to detect it in this manner, then it is advisable before resorting to percussion, to try palpation bimanually, with the patient in the right lateral position, the left hand being placed behind in the lumbar region, pushing the organ forward to meet the right hand applied to the anterior abdominal wall under the costal margin. In this manner, I have on several occasions, appreciated splenic enlargement, when not detectable with the patient in the dorsal decubitus, and when undue meteorism prevented accurate percussion of the organ. What was of more importance also, was the fact that in some of these cases the organ never enlarged more, so as to be appreciable by the other methods. Had I not adopted this method as a routine practice when unable to detect it otherwise, I should certainly have missed it altogether. If, on the other hand, failure to perceive the enlargement results from the foregoing methods, then resort to percussion must be had. This is fraught with difficulties, and in the hands of inexperienced clinicians yields untrustworthy results. If reliable results are to be obtained by this method, examination should be carried out from day to day, as the result of a single percussion can scarcely be relied on. The chief difficulty encountered is the encroachment on, or complete obliteration of, the splenic area of dulness, by the tympanicity of a distended colon, meteorism in a varying degree being frequent in typhoid, both in the large and small intestines. Abnormal conditions of the left lung and pleura, if not guarded against, are calculated to give fallacious results.

Splenic enlargement as an aid to diagnosis.—Occurring as it does in from 70 to 80 per cent. of the cases, and making its appearance in the majority of these from the seventh to the tenth days, gradually increasing and persisting during the fastigium, enlargement of the spleen comes to be of considerable diagnostic significance, but in a number of cases must be considered in this light only in conjunction with other symptoms. In no disease does it occur with such frequency, except malaria, and the date of its appearance gives some assistance in separating typhoid from this disease, and from the other acute infectious fevers and septic conditions. We must not forget, however, that its absence does not exclude a diagnosis of typhoid, for as we have seen, severe and even fatal cases occur, in which it is not demonstrable. In others, the enlargement is often delayed, and examination must therefore be made daily before pronouncing it absent. It must always be borne in mind that enlargement may be prevented by several factors, which need not be recapitulated. Of equal importance, too, is our ascertaining, that, when enlargement is present, it is not due to antecedent conditions, or associated inflammatory conditions, or displacement by some other viscus or fluid accumulation therein. Appearing as it usually does on the 7th day, it is of no value in differential diagnosis before that time, unless in those cases with abrupt onset, in which it may appear on the 4th or 5th day, and here, in the absence of other signs, confusion with typhus might ensue. Among the cases which came under my care, notified as suffering from typhoid, but in which other affections

were present instead, and in which splenic enlargement was noted, I might mention several. One was a case of central pneumonia, one suffered from phthisis, one from acute tuberculosis, one from crypto-genetic septico-pyæmia, four from influenza of the gastro-intestinal type, two from malignant endocarditis. In two cases, one of malignant endocarditis, and one of scarlatina anginosa, both splenic enlargement and diarrhœa with peasoupy stools were present.

TABLE I.

Table showing cases in which Enlargement of Spleen was slight or absent.

	Age.	Day of Illness on which Admitted.	Condition of Spleen.	Remarks.
J. B.	9	15	Enlarged to percussion only	Mild case
M. C.	23	13	Palpable in right lateral position only	Severe case—Delayed Widal
T. W.	16	12	Only felt as a feeling of increased resistance—Sensitive	Moderately severe case
A. A.	10	20	Only felt in right lateral position	First appreciated on 24th day—Moderately severe case
J. S.	5½	8	Very slight, scarcely palpable	Mild case
S. M'F.	19	8	Only enlarged to percussion	Fatal on 11th day from toxæmia
T. S.	24		Do.	Severe and protracted—Prolonged fastigium
Mrs H.	30	8	Do.	Moderately severe case
D. M'K.	13	8	Do.	Very severe case
J. R.	55	6	Do.	Fatal on 14th day from toxæmia
W. N.	11	8	Do.	Very severe case—Encephalitis
J. W.	16	10	Do.	Severe
Mrs P.	29		Not enlarged	Fatal on 21st day, osteomyelitis of humerus
A. M.	8		Do.	Retrospective
M. M.	2		Do.	Retrospective
Mrs R.			Do.	Retrospective
J. R.	16	2	Do.	Abortive case
W. H.	29	17	Do.	Moderately severe—Venous thrombosis
M. S.	13	8	Do.	Fulminant case—Death on 9th day.
G. R.	6	22	Do.	Mild
M. H.	6	4	Do.	Mild
G. G.	25		Do.	Fatal—Hæmorrhagic—Admitted in relapse
M. M'C.	9	20	Do.	Severe—Delayed Widal
H. B.	33	16	Do.	Ambulatory—Severe intestinal Hæmorrhage—Fatal
S. H.	30	11	Do.	Severe and protracted—Intestinal Hæmorrhage
J. M.	14	12	Do.	Severe—Profuse diarrhœa
J. A.	6	7	Do.	Severe—Delirium for first two weeks
J. M'C.	9	11	Do.	Severe and protracted
W. S.	34	16	Do.	Severe and protracted

Meteorism.—Among other symptoms present in a considerable number of cases is meteorism. It is attributable, to a slight degree, to local follicular infiltration of the bowel and associated catarrh, but is mainly due to the action of the typhoid toxins on the intestinal wall, causing paralysis of the muscular coat, and consequently varies considerably both in frequency and intensity. Among other causes which

may give rise to it are local peritonitis and imperfect dieting of the patient. In fact, it is noteworthy as bearing on the latter statement, that except in those cases characterized by profound toxæmia, the sooner in the disease a patient is admitted to hospital the less the meteorism. For this reason, statistics on the frequency of its occurrence are somewhat at variance. Murchison noted it in 79 per cent. of cases, Louis in 66 per cent. of cases, Morse in 50 to 70 per cent. in children, while in my own series it was only present in 47·3 per cent. The distension affects chiefly the large intestine, while if it involves the small intestine to any extent, the brunt of it falls on those parts least affected by follicular infiltration, viz., the duodenum, jejunum, and upper part of the ileum. It usually manifests itself during the first week, but may be delayed until the second, or subsequent weeks. In some cases it is only moderate in degree, while in others it is extreme and embarrasses respiration by interfering with the diaphragmatic descent.

Value in diagnosis.—As an element in diagnosis, there is nothing specific about it, and if taken by itself it is of practically little or no significance, as it occurs with considerable frequency in many other affections. It is fairly common in gastro-intestinal affections due to causes other than typhoid, and is present in many cases of chronic indigestion. Likewise it occurs frequently in tubercular peritonitis, in acute miliary tuberculosis, in appendicitis, and in all affections characterized with some degree of local peritonitis, as well as in general inflammation of the peritoneum. I have noted it in several pyæmic cases, in one case of typhus, and, along with diarrhœa, in phthisis.

Abdominal pain and tenderness occur in a number of cases of typhoid, and are, by some, reckoned as important symptoms of the disease. The pain and the tenderness may be general, all over the abdomen, or may be confined to the seat of intensity of the local disease, in the right iliac region or between that and the right hypochondrium. M'Crae, who has made an exhaustive investigation on this point, found it in 60 per cent. of the John Hopkins hospital cases. In my own series it was noted in only 38 per cent. of cases, during their residence in hospital, but if I include those in which abdominal pain was complained of during the earlier days of the illness, i.e., before admission, then the percentage rises to between 90 and 95. As a differential diagnostic sign it is of little value, if for no other reason than that it occurs at the onset of, or during the course of, many other affections, more particularly those affecting the gastro-intestinal tract. Abdominal tenderness is probably of somewhat more value, but in the absence of other symptoms of typhoid, might readily lead one to a diagnosis of appendicular mischief. Again, in tubercular ulceration of the intestine, just as in typhoid ulceration, tenderness may be complained of in palpation over the seat of ulceration. Abdominal pain is frequently complained of by children at the onset of acute pulmonary trouble.

Gurgling in the iliac fossa is a symptom upon which considerable stress was formerly laid, as indicative of typhoid. Attention was first drawn to it by Chomel,

and since then many have noted its frequency in this affection. It occurs pretty frequently in other affections, however, and indicates simply the presence of gas and fluid fæces in the colon and cæcum. I have detected it in a number of cases of gastro-enteritis associated with diarrhœa, and this point has been called attention to by Henoch. Moreover, acting on the advice of one of my teachers, I paid little attention to it and rarely attempted to elicit it, knowing that, particularly during the stage of ulceration, manipulation of the abdomen, however gently carried out, is fraught with danger, as the delicate serous coat of the intestine might readily rupture. I have therefore no statistical evidence as to its frequency, and have given no consideration to it as an agent in diagnosis.

Intestinal Hæmorrhage is an important, though much dreaded, and alarming sympton of typhoid. It may occur at any period of the illness, from the first week onward, but is most common between the end of the second week and the beginning of the fourth, and as this period corresponds with the process of ulceration, the bleeding is usually due to separation of the sloughs, and erosion of one or more arterial twigs. Occurring during the earlier days of the disease, it is to be attributed to the exceedingly hyperæmic and friable condition of the tissue of Peyer's patches, while if it develops during the later days of the disease, it is probably associated with imperfectly thrombosed vessels in the floor of the ulcers, or simply with sluggish ulcers. The amount of blood passed from the bowel varies. In a few instances only small quantities are passed with the motions, and care must be taken not to confound such, with small hæmorrhages from the rectal or anal regions due it may be to hæmorrhoids, in which case the blood is usually mixed with mucus, or is in coagulated masses lying beside the fæcal matter but never intimately admixed therewith. If the amount is slight, the stool has a brownish red or even yellowish red appearance, while if a large amount has been shed into the bowel, and retained for some time, when finally expelled it appears as a reddish black or totally black liquid. If the hæmorrhage occurs quickly and is as rapidly evacuated, the mass appears as coagulated blood, reddish black or red in colour and containing large clots. Examples of all of those forms have come under my care. Though usually occurring in cases of considerable severity this is not always the case, for in my own experience, profuse hæmorrhage occurred in two cases that were, so far as one could judge from temperature and other signs, apparently pursuing a mild course, and in neither was a dietetic error responsible for its development. Statistics bearing on the frequency of intestinal hæmorrhage are more or less in agreement. Osler gives it as three to five per cent. of cases; Murchison, 3·77 per cent.; Homolle quoting Liebermeister and others, 4·65 per cent.; Curchmann, four to six per cent.; Greisinger, 5·3 per cent.; Louis, 5·9; while in my own series it was higher, reaching 6·4 per cent. It is rarer in children, and this is undoubtedly due to the lesser extent and intensity of the lesions. Curchmann noted it in one per cent. Barthez and Rilliet in ·43 per cent. I only observed it once under 12 years of age. In some cases, the expulsion of the blood does not take place, and then the condition of internal hæmorrhage has to be diagnosed. I had one such, the bowels expelling the blood immediately after death.

Value in diagnosis.—True intestinal hæmorrhage is one of the most important diagnostic symptoms of typhoid, though its rare occurrence detracts from its value in this respect. Its late appearance, occurring after the development of splenic enlargement, and roseolæ, causes it to be of value chiefly in those atypical cases in which several of the cardinal signs do not make their appearance. It has, however, on several occasions been the first symptom of typhoid in an ambulatory case, a fact which most clinicians have had experience of. In these cases the patients have gone about with only an indefinite feeling of malaisè, when a sudden, unexpected hæmorrhage revealed the true nature of their illness. In two cases under my care, both of which terminated fatally in hospital, the patients had kept about at their work, until repeated severe intestinal hæmorrhages caused them to seek medical advice.

Name.	Age.	Day on which Admitted.	Day of Illness on which Hæmorrhage first appeared.	Remarks.
H. B.	33	16	12	Ambulatory—Hæmorrhage first sign—Fatal
J. G.	21	18	16	Do.
C. M.	16	8	21	Internal hæmorrhage—Blood expelled at death.
G. G.	25	?	?	Hæmorrhagic typhoid—Admitted in relapse—Fatal
S. H.	30	11	21	Protracted case
J. R.	9	14	37	Death from Perforation on 48th day
B. R.	20	6	15	Fatal—Hæmorrhage and toxæmia
J. S.	26	12	22	Protracted case with frequent hæmorrhages

Perforation of the bowel is another symptom referable to the intestinal tract, and one which is of considerable importance, though fortunately of rare occurrence. It usually occurs in the more severe cases, especially those associated with hæmorrhage, tympanites, or diarrhœa, but may occur in cases in which constipation is a feature. It may, however, occur with startling suddenness in those pursuing a mild course, as I had occasion to experience in one case, a boy of 9 years of age. It usually occurs at the height of the disease, though it may occur later in patients apparently progressing favourably, as the result of dietary indiscretion or sudden movement, and is probably in these cases associated, as is late hæmorrhage, with sluggish ulcers. As the result of perforation, a localized peritonitis may develop, or, what is far more common, unfortunately, a generalized infection of the peritoneum. Statistics from various sources more or less agree as to the frequency of this condition. Osler gives it at 2·7 per cent.; Curchmann, 2·2 per cent (Leipsic), 1·6 per cent. (Hamburg); Greisinger, 2·3 per cent. In my own cases it occurred in 3 per cent.

Diagnostic value.—While of great value as a diagnostic aid when present, its value in the discrimination of typhoid for clinical purposes is diminished by its late appearance in the disease, and by its relative infrequency. Like intestinal hæmorrhage, however, it may be the first indication of the existence of typhoid in an ambulatory case, which has gone about with obscure or indefinite symptoms. Occurring in a patient with an indefinite history of illness, or nothing but a feeling of malaisè, the

question of typhoid should be raised, and examination made for other evidences of the disease. One must not forget, however, that in the absence of other signs of the disease, and especially the Widal reaction, the peritonitis may be due to perforation of some other viscus, conditions which, on the whole, are much more common than ambulatory typhoid perforation.

Bronchitis is one of the most frequent symptoms in the early stage of typhoid. Cough is frequently complained of, though in many instances it does not attract much attention, as it is not troublesome or annoying to the patient. The condition affects usually the medium-sized and smaller bronchial tubes, and as the amount of swelling, in most cases at least, is only moderate in degree, the amount of secretion is not marked, and the expectoration scanty or entirely awanting. It usually sets in during the first week, and careful examination reveals some roughening of the inspiratory portion of the respiratory murmur, or slight prolongation of the expiratory part, and is usually accompanied by râles of the sibilant or snoring type. Though Murchison and others attached no great diagnostic significance to it, yet Curchmann says "that by reason of the constancy of its occurrence, the peculiarity of its symptoms and its course, he believes that it can be definitely looked upon as a specific typhoid symptom, and may be attributed directly to the action of the toxins or of the bacilli." The extent of the bronchitis and the degree of it do not necessarily bear any direct relation to the severity of the disease, but on the whole, the graver cases have the severer degree of bronchitis. I have, however, seen very mild cases, with very pronounced and severe bronchitis. I have not been able to find statistics anywhere, bearing on the frequency of bronchitis. Osler is also of the opinion that it is one of the most frequent symptoms. In my own series, though cough was only complained of by the patient in 9·3 per cent. of the cases, bronchitic râles were detectable on auscultation in no less than 61·4 per cent. Bronchitis was present in varying degree in most of the severe cases, and was absent for the most part in many of the mild cases among children.

Diagnostic value.—Although my experience would not warrant me in being so emphatic as Curchmann, regarding the specificity of bronchitis in typhoid (for from a bacteriological standpoint, I examined the expectoration in ten cases, and failed to detect the typhoid bacillus in all of them), still I am inclined to attach no inconsiderable value to its presence as a diagnostic agent. As an individual symptom it presents nothing characteristic, yet it is present in such a fair proportion of cases (in a higher percentage than diarrhœa), that when the thermometer has shown the existence of some febrile condition, lasting for some days, without the co-existence of signs of another infectious disease, we might feel justified even in the absence of other signs pointing to typhoid, if not in diagnosing this affection, at least, in being suspicious of its existence. The presence of one or more symptoms common in typhoid would be almost confirmatory. It is thus of assistance in differentiating typhoid from cases of protracted intestinal catarrh, in which bronchitis is very rare, from malaria, and appendicitis. It is, however,

a frequent symptom early in the disease in typhus and in influenza, and occurs in acute tuberculosis, before we have physical signs pointing to consolidation in the lung.

Among other symptoms to which importance has been attached by some writers, as diagnostic of typhoid, may be mentioned nervous impairment of hearing, epistaxis, miliaria crystallina, absence of herpes, and parotitis. *Impairment of hearing* is, from my experience, fairly common in typhoid, having been noted in 31 per cent. of my cases, but I have also observed it frequently in other affections, particularly influenza. *Epistaxis* is probably more common at the onset of typhoid than of any other of the acute infectious diseases, although I only got a history of it in eight cases, and only one, a case showing hæmorrhage from all the mucous membranes, developed it after admission. It may occur with almost equal frequency at the beginning of tubercular meningitis, and I have frequently noted it in influenza. *Miliaria crystallina*, small, clear vesicles, usually situated on the abdomen and chest, have been reckoned by some observers as carrying some weight in favour of a diagnosis of typhoid, chiefly on account of their comparative frequency in this affection. In my own series I noted this condition in 42 per cent. of the cases, but I have observed it with almost equal frequency in other conditions, chiefly septic affections, and I have noted it often in influenza and in scarlet fever. It was also present in one case of typhus which was under my care. It occurs late in the disease, though occasionally early, and from my experience is of little importance in differential diagnosis. It simply means that a patient who has suffered for some days from anhidrosis has begun to sweat profusely. *The absence of herpes*, in an acute disease, with fever, has been put forward as being suggestive of typhoid, and my experience certainly points to the rarity of its existence in this condition, as I only noted it on three occasions. As regards *parotitis*, it is usually a symptom of ill omen, as it occurs generally in serious cases, and those passing to a fatal issue, chiefly those who had contracted the disease while in a state of ill nourishment. Statistics show that it occurs only in from ·3 to 1 per cent. of cases. I only observed it in three cases, two of which recovered.

Diazo-reaction.—Since the discovery by Ehrlich that by employing diazo compounds, the existence of aromatic bodies could be demonstrated in certain pathological urines, the so-called diazo-reaction has been employed by many clinicians as a means of differentiating typhoid from other acute affections. The nature of the body, which occurs in certain urines, and which gives the diazo-reaction, is not as yet definitely known, though Späth claims that it is due to an excess of uroproteic acid (a normal urinary constituent). This is disbelieved by others, however. Whatever may be the true nature of the aromatic body, the reaction is regarded as an indication of a pathological decomposition of proteids. For the carrying out of the test, two solutions are required, one containing a saturated solution of sulphonilic acid in a solution of hydrochloric (50 c.c. to 1000 c.c.), and the other a half per cent. solution of sodium nitrite. A few c.c. of urine are put in a test-tube, and an equal quantity of a mixture of solutions 1 and 2, in the proportion of 40 c.c. of the former to 1 c.c. of the

latter, are added and the whole well shaken. One c.c. of strong ammonia is now added, and at the junction of the liquids, if the reaction is present, a deep, brown red ring is formed, but if not, a light brown ring is produced. The real test, however, is to shake up, and the froth is coloured rose-red if the reaction is positive—if not, brownish yellow. Osler observed the reaction in 894 out of 1467 cases, or 61 per cent., while in my own series it was positive in 72 out of 100 cases examined. Curchmann says it can always be obtained at the height of the fever, except in the mild cases. Henoch says he obtained it in all cases in which it was examined for. Butler says he made the test in a number of cases with usually positive results. I observed that the negative result was usually obtained in the mild cases, and especially in this type in children.

Value in diagnosis—Hallowed though it be by association with the name of Ehrlich, the diazo-reaction is only of limited value in the discrimination of typhoid, and has not the important significance formerly attached to it, as a diagnostic agent. Considered in conjunction with other symptoms present, it is undoubtedly an aid. From my own experience of it in 100 cases in which it was examined for, I am of the opinion that it is a better negative than a positive test. It was not present, though tested for on several occasions, in three severe cases, two of which were fatal. In one, A.S., a severe and protracted case, which presented no roseolæ, diarrhœa, or splenic enlargement, it was absent all through the illness. The majority of the cases that gave a negative result were of the mild type, and this shows the limit of its value, for it is especially in those mild and atypical cases, characterized by paucity of distinct signs, that assistance by chemical or other means is usually demanded. Unfortunately also for diagnostic purposes, its almost equal frequency in other acute affections makes it of little value in the differentiation of typhoid. It occurs with considerable frequency in typhus, in malaria (Osler), some cases of pneumonia (Curchmann), scarlet fever, diphtheria, measles, and erysipelas. Sahli gives it as his opinion that a positive reaction is of nearly constant occurrence in typhoid, typhus, and measles. In three cases of typhus which I examined for it, I obtained it in two. In the third it might also have been obtained, but the patient was removed early from my care, and I had not the opportunity of further examination. Sahli calls attention to the fact that a similar reaction may be obtained after the administration of opium, morphine, chrysorobin, heroin, dionin, tannic acid, alcohol in large quantities, phenol, cresol, and guaiacol; and this must be borne in mind when applying the test, before coming to any diagnostic conclusions. Pini and Benini obtained positive results in grave forms of maniacal excitement, in severe melancholics, and in 10 cases of general paralysis. Most important of all to be remembered, is its frequency in another disease, which has, perhaps, more than any other, to be considered in arriving at a diagnosis in doubtful cases, viz., acute miliary tuberculosis. In four cases of this affection which came under my care in hospital, having been notified typhoid, I obtained a positive reaction in three, and in three cases of tubercular peritonitis, also notified typhoid, a positive reaction was present in one.

Leucocytes.—The morphology of the blood has formed the basis of much study during recent years, and especially so in the infectious diseases, both with a view to diagnosis and prognosis. Much has consequently been written on the subject, and the results obtained in the study of typhoid are fairly well in accord with each other. In typhoid, the red corpuscles and hæmoglobin present nothing distinctive during the course of the disease, the former showing a slow progressive reduction in number during the febrile period, while the latter also shows a gradual decline, with a slow regeneration during convalescence. The most important of the blood elements from a diagnostic view point are the leucocytes, and their condition in this disease is very remarkable. Among those who have devoted much attention and study to this matter may be mentioned Türck, Rieder, Naegeli, and Thayer, the observations of the last-named being those usually quoted in the literature, as they are probably the most exhaustive and comprehensive on the subject. I will deal with this subject in two sections:—(1) the total number of leucocytes present in the peripheral blood (absolute count), and (2) the relative proportions of each type of leucocyte (differential count). In enumerating the leucocytes I adopted the method advocated in the text books of Cabot and Da Costa, selecting the lobule of the ear by preference, as the site for the withdrawal of the blood, having first cleansed it with methylated spirit without rubbing violently, to avoid inducing a local transient hyperæmia. The pipette and counting chamber used were those of Thoma-Zeiss and the dilution (1 in 20), the diluting fluid being ·5 per cent. acetic acid tinged with a few drops of an aqueous solution of methyl blue to render the leucocytes more conspicuous. In counting, I always used a narrow aperture of the diaphragm, as this enables one to delineate the leucocytes even better than with wide open diaphragm. I was careful also, in counting those leucocytes lying on the lines, to adopt the method advocated by Cabot, viz., only to include those lying on two sides of the square. To avoid error, although it occupied a good deal of time, I made three separate counts, and took the average, by this means eliminating, to a certain extent at least, an error which occasionally cropped up, in getting a difference between the first and second counts. In order to avoid errors creeping in, due to physiological leucocytosis, I avoided counting after cold sponging in those cases where hydrotherapy was being carried out. The leucocytosis of digestion, however, I could not avoid, in the case of those at the height of the fever, or before convalescence was established, on account of the irregularity and frequency of administration of their diet (milk).

In most infectious diseases and inflammatory processes generally, there is a decided increase of leucocytes circulating in the peripheral blood, in other words, a leucocytosis, but in typhoid fever this is not the case. Virchow, strange to say, in his "Cellular Pathology" assumes that a certain amount of leucocytosis must follow the hyperplasia of the lymphatic tissues in typhoid, and he quotes Allen Thomson, who says that in a dozen cases of an epidemic fever occurring in Edinburgh he found a distinct leucocytosis. It is probable, however, as recent investigations show, that the cases referred to were typhus, and not typhoid. Most

observers, however, are of opinion that no leucocytosis occurs in typhoid, but that on the contrary, a distinct reduction from the normal actually takes place, a leucopenia or hypoleucocytosis. Durozier, Halla, Sorensen, Tumas, Ouskow, and Khetagurow all note the absence of leucocytosis, and Thayer's observations are in accord with these. The leucopenia is not to be explained by any destruction of the white corpuscles, but is rather attributable to a decreased influx, which in the case of the polymorpho-nuclear elements at least, is to be referred to the presence in the circulation of negatively chemiotactic substances. The fall in the number of leucocytes continues during the course of the disease, reaching its lowest point towards the end of defervescence, and beginning again to ascend towards normal during convalescence, more slowly in debilitated individuals than in those more healthy. As regards the degree of leucopenia, Ewing says that " the more profound the typhoid intoxication, the lower the count." This, from my own experience, is not by any means an absolute rule. Undoubtedly, generally speaking, leucopenia is usually well marked in the severe or moderately severe cases, but from my own observations I do not think the degree of leucopenia necessarily corresponds to the severity of the disease, any more than does the degree of splenic enlargement or the number of roseolæ. I have had fatal uncomplicated cases with only a moderate degree of leucopenia, and others of the mild type with pronounced leucopenia. In fact the lowest count I ever recorded, 938, was in a mild case. Taking as the normal number of leucocytes 6000 to 8000 per c.mm. (average 7500) we usually find this number unaffected during the first days of illness, but by the end of the first week or beginning of the second a reduction to 6000 takes place, and following this, a steady diminution throughout the illness, depending on the individual case, to 4000, 3000, and even to 1000 as I have occasionally observed. In children, the leucopenia is usually apparently not so well marked, as the normal count is higher, a point which must be borne in mind. On the other hand, there are certain factors which may diminish the degree of leucopenia, or actually lead to leucocytosis at one stage of, or it may be throughout the whole disease. These may be considered under two heads :—(a) physiological and (b) pathological.

Physiological.—In the new-born or in very early life the leucocytes are above the normal for the individual in later years, and in pregnancy they are increased, as also after exertion, cold baths (this being of special significance where hydrotherapy is resorted to in the treatment of hyperpyrexia). Lastly, we have the leucocytosis of digestion. In two pregnant women under my care, the lowest leucocyte counts were 8125 and 8438 respectively, while in a third there was a decided leucopenia.

Pathological.—Conditions may occur during the course of typhoid, or may precede the development of it, which are associated usually with leucocytosis, and which may either raise the leucocyte count to normal or cause an actual leucocytosis. Among these, the following are the most common, viz. :—hæmorrhage, profuse diarrhœa, cachexia, malignant disease, phthisis ; while of the inflammatory complications, the undernoted are of most frequent occurrence :—perforation followed by peritonitis,

boils, venous thrombosis, pleurisy, pneumonia, bronchitis (severe), periostitis, otitis media, parotitis, glandular abscess, pericarditis, bedsores, conjunctivitis, cholecystitis, cystitis.

From Thayer's statistics, it is seen that counts in excess of 10,000 (in uncomplicated cases) are met with in 10 per cent. of cases. In my own cases, I have several records of high counts, and careful examination failed to reveal any complication.

The following table shows my results obtained in the different weeks of the disease, up to the sixth, inclusive. Comparison with those of Thayer's, Table II., shows a slight difference :—

AUTHOR'S TABLE.

First week	16 cases	...	...	7670 leucocytes per c.mm.
Second ,,	60 ,,	...	...	6279 ,,
Third ,,	54 ,,	...	...	5811 ,,
Fourth ,,	22 ,,	...	...	5375 ,,
Fifth ,,	15 ,,	...	...	4886 ,,
Sixth ,,	7 ,,	...	...	5491 ,,

THAYER'S TABLE.

First week	14 cases	...	...	8026 leucocytes pe rc.mm.
Second ,,	30 ,,	...	...	6713 ,,
Third ,,	13 ,,	...	...	7076 ,,
Fourth ,,	6 ,,	...	...	4400 ,,
Fifth ,,	6 ,,	...	...	5766 ,,
Sixth ,,	2 ,,	...	...	6250 ,,
Seventh ,,	2 ,,	...	...	4500 ,,
Eighth ,,	1 ,,	...	...	8000 ,,

The following table shows counts **in my cases**, irrespective of the week in which they were taken (150 cases.)

Under	1000	...	...	in	1 case
Between	1000 and	2000	in	4 cases
,,	2000 and	3000	in	9 ,,
,,	3000 and	4000	in	18 ,,
,,	4000 and	5000	in	32 ,,
,,	5000 and	6000	in	23 ,,
,,	6000 and	7000	in	19 ,,
,,	7000 and	8000	in	15 ,,
,,	8000 and	9000	in	14 ,,
,,	9000 and 10,000		in	8 ,,
Over 10,000	...	...	in	7 ,,

Highest count 12,180
Lowest do. 938

Reference to the foregoing tables shows that in only a small percentage of the cases are the leucocytes raised above 10,000, while in the greater proportion a distinct

hypoleucocytosis or leucopenia is manifest. Moreover, many of these high counts above 7500 were made during the first and second weeks of the disease, while later in the febrile period a reduction in the total amount took place. Again, some of those should properly be excluded from the table, as there was some co-existing inflammatory lesion, and the increase in the leucocyte count was undoubtedly attributable thereto. Still, after all those have been taken into account, there remain a few cases characterized by a slight increase in the number of leucocytes, all through the illness, from what cause it is difficult to say. It might be presumed that there is some occult complication, which even the most careful search may fail to detect, or it may be due to profuse sweating, which occasionally occurs, or to profuse diarrhœa causing concentration of the blood. The following table gives a list of cases which showed leucocyte counts over 7000.

TABLE II. (A).

Over 12 Years of Age.

Name.	Day of Illness.	Leucocyte Count.	Remarks.
Ovaliski	13	8,125	Abortive case
Bowbell	9	12,186	Severe—Fatal—Acute Ascending Myelitis and Cystitis
J. S.	18	8,438	Phlebitis
A. C.	18	7,800	Protracted—Fatal—Severe Intestinal hæmorrhage—Bronchitis—Icterus
Mrs W.	7	8,125	Pregnancy
H. B.	16	7,812	Ambulatory—Fatal—Severe intestinal hæmorrhage—Profuse diarrhœa
M. S.	8	12,600	Fulminant case—Marked cerebral symptoms—Fatal on 9th day.
G. S.	16	8,438	Mild—No complications
A. S.	14	9,600	Do.
Mrs S.	12	8,438	Pregnancy
B. R.	7	7,500	Fatal—Profuse intestinal hæmorrhage—Profuse diarrhœa
H. T.	15	11,875	Scarlatini form rash present—Leucopenia later
H. M'V.	17	7,188	Labial abscess
M. B.	13	10,000	Severe case—Severe bronchitis—Leucopenia later
S. H.	14	8,125	Protracted—Intestinal hæmorrhage—Profuse diarrhœa—Abscess over thyroid leucopenia later
D. M'K.	14	8,438	Very severe bronchitis

TABLE II. (B).

Under 12 Years of Age.

Name.	Day of Illness.	Leucocyte Count.	Remarks.
W. M.	12	7,187	Mild
J. S.	15	11,875	Mild
R. M'K.	19	9,800	Severe bronchitis
A. M'D.	8	12,000	Abortive
J. M'C.	13	10,000	Severe and protracted—No complications
W. O.	20	7,500	Mild
R. B.	15	10,312	Severe case—Extreme bronchitis—Death from perforation
T. T.	19	11,000	Mild
M. M'C.	24	8,438	Mild—Delayed Widal
M. W.	13	8,438	Mild

Examination of this table, containing a list of my cases, whose leucocyte count was never below 7000, shows, with few exceptions, an explanation for the absence of leucopenia, or the presence of actual leucocytosis, in the existence of some physiological factor, as pregnancy, or some inflammatory or septic process. Several of the cases are in children under 12 years of age, in whom the normal count is above that of the adult, so that we may regard the leucocyte count in them as practically normal for those cases, or if raised, only slightly so. Still, there are a few which maintained a leucocyte count above normal all through their illness, and no complication could be detected.

Qualitative changes in leucocytes.—Differential count.—Much attention has of recent years been given to the qualitative changes in the leucocytes, both as a diagnostic and prognostic factor. The different forms of leucocyte bear certain relations to each other in normal blood, and in certain diseases there is a departure from this, one variety being increased at the expense of the others, it may be, or totally increased. Thus in most inflammatory affections with leucocytosis, the polymorphonuclear cells are increased relatively to the others. In other conditions the eosinophylls are increased, while in lymphocytosis the lymphocytes are raised in number. In polymorphonuclear leucocytosis we have an excessive production and output of these cells by the bone marrow, due to the influence of positive chemiotactic bodies, while leucopenia is regarded not as a destruction of white corpuscles (leucocytolysis), but is due to a lessened influx, which in the case of the polymorphonuclears is to be referred to the presence of negatively chemiotactic substances in the circulation. In lymphocytosis, which accompanies leucopenia, due to negative chemiotaxis, we have a relative increase of the lymphocytes, upon which the repellant action is not exerted. Ehrlich regards lymphocytosis "as due to local irritation of certain areas of lymphatic glands, which produces an increased circulatory activity in these situations, in consequence of which large numbers of lymph elements are swept mechanically from the lymphatics into the general circulation."

Before going on to detail the changes that take place in the leucocytes in typhoid, it may be as well to refer briefly to the different forms which mainly concern us as being most affected by the infectious process.

(1) **Polymorphonuclear leucocytes** are the ones which are present in greatest number in normal blood, forming from 70 to 75 per cent. of the total number. They are usually about twice the size of a red blood cell, but vary often, some being little larger than a red corpuscle. The nucleus is very irregular in shape, appearing to consist of several parts, which careful focussing, however, shows to be connected with each other. The protoplasm contains a large number of fine granules, which on account of their staining properties are called neutrophile. These cells are amœboid, and are, according to Ehrlich, formed in the bone marrow. In all cases of leucocytosis they are increased in number, but in the leucopenia of typhoid they undergo a steady diminution in number until the end of defervescence, when they gradually return to the normal. Should any inflammatory complication occur, however, they are increased, or if already diminished, may be raised to the normal number.

(2) **Small lymphocytes** are about the size of the red blood corpuscle, and form in normal blood about 20 per cent. of the leucocytes. The nucleus stains deeply and almost occupies the whole cell, being surrounded by a narrow rim of protoplasm. They are not amœboid, and are derived from lymphatic tissue in the different parts of the body.

(3) **Large mononuclear cells.**—These are the largest of all the leucocytes. They are usually of round or oval shape, and the nucleus, which may be also round or ovoid, is situated towards the periphery of the cell. The amount of the protoplasm is relatively greater than in the small lymphocyte. Both nucleus and protoplasm stain faintly, and no granules are evident, unless Wright's stain be used, which shows often red granules. Another cell which is usually, in counting, included with the above, is the transitional cell, which differs from the former in having a nucleus which is indented or kidney shaped. Both are developed in the bone marrow, and both are amœboid.

Large lymphocyte.—Another cell present is the larger form of lymphocyte. These cells are increased in typhoid fever.

There is another type of cell, which is increased considerably in typhoid, and to which I have given the name of the "indeterminate lymphocyte." This is the cell which Thayer and Ouskow have found to be present in considerable numbers in typhoid, and which both of these observers place among the large lymphocytes and large mononuclears. This cell occupies a position intermediate between the small lymphocyte proper and the large mononuclear cell. Some of these resemble the small lymphocyte in having a relatively large nucleus, but are larger, some being as large, others larger than the polymorphonuclear, and do not take on the stain so deeply as the true lymphocyte. Occasionally the nucleus is eccentric. Occasionally, also, we see one as large as a polymorphonuclear cell, but with a deeply staining small nucleus.

Eosinophyll.—These cells are also marrow-bred elements, and possess amœboid movements. They vary in size, some being as large as the large mononuclear, others as small or smaller than the polymorphonuclear cells. The nucleus is more or less polymorphous, and does not stain so deeply as the polymorphonuclear. The granules in the protoplasm, however, are much coarser than those in the poly-morphonuclear. In typhoid fever, during the course of the disease they undergo a steady reduction, rising again towards normal during convalescence. They form from ·5 to 5% of the normal number of leucocytes.

Myelocytes, also marrow-bred cells. They are larger than the polymorphonuclear and the nucleus is spherical or ovoid and usually lies towards one side of the cell. The nucleus does not stain so intensely as that of the polymorphonuclear cell. The protoplasm contains either neutrophile or eosinophile granules.

They are present in typhoid blood in small numbers—from ·1 to ·3 or ·5, and do not undergo any special changes during the disease. In cases passing to a fatal termination I have observed them more frequently than in the milder cases.

Technique of staining the blood films. — In preparing blood films for staining purposes, I always prepared several, and selected the best specimens, usually submitting these to different staining agents. Among the stains which I used were the following :—

(1) Ehrlich's triple stain, followed by methyl blue for two seconds. I adopted this method at first, but on account of the difficulty in estimating the requisite degree of heat in fixation (I simply passed the film, face upwards, held in forceps, through the Bunsen flame several times), I did not always get well-stained specimens, and so always stained others by one or other of the following means :—

(2) Eosin and Methylene blue.

(3) Jenner's stain.

(4) Leishmann's modification of Romanowsky's method.

(5) Wright's stain.

I certainly, after adopting the last method, got by far the most regular and best results for detail.

In counting, I employed a Watson's microscope, eyepiece D, and oil immersion $\frac{1}{12}''$ lens, using the mechanical stage, and counting from 400 to 500 leucocytes.

In normal blood, the following are the percentages of the different forms of leucocytes as given by Da Costa :—

Polymorphonuclear	75
Small Lymphocyte	20
Large Mononuclear and Transitional	4·8
Eosinophyll	·5-5
Basophyll	·5
Mast Cell	·5

In leucopenia, the lymphocytes are relatively increased owing to the reduction in the polymorphonuclears. In typhoid, after the first week, or during the later days of this week, the polymorphonuclears undergo a reduction in number, which becomes more marked as the disease progresses, until the onset of convalescence, when the number gradually increases again until normal is reached. The eosinophylls likewise become reduced in number, and may even disappear entirely, to reappear during convalescence. The small lymphocytes usually show a slight but steady increase from the first week onward, but in quite a number of cases no such increase is noted. In children, however, in whom slight intestinal irritation is followed by an increase in the small lymphocytes, the increase in this type of cell is more marked.

The large mononuclear and transitional forms show a gradual but steady increase in number from the first week onwards. However, there is one point to which I would like again to draw attention, a point to which attention has been called by Thayer, but of which no notice has been taken by others, except Ouskow. Thayer

says that the varieties which Ouskow and himself found to be particularly increased in typhoid are the transparent and faintly staining mononuclear leucocytes which closely border upon the line separating the small mononuclear from the large. In both of these writers' counts, such cells are placed among the large cells. This has been my experience, and I had been struck with the relative numbers of such cells, and had difficulty in deciding how to classify them before I came across Thayer's monograph. After perusal of the latter, I surmounted the difficulty by adopting his advice, in classifying them as large or small, according to their size relatively to that of the polymorphonuclear cell.

In studying Türck's tables, one is struck by the diminution in the percentage of large mononuclears and transitionals combined, compared with other writers' percentages, especially those of Thayer. This is probably accounted for by his placing these cells among the small lymphocytes. In my tables, therefore, the group entitled " large hyaline cells" includes large lymphocytes, large mononuclears and transitionals, and these doubtful cells.

TABLE III.

(A) AUTHOR'S TABLE.

Week.	Polymorpho-nuclear.	Small Lymphocytes.	Large Hyaline.	Eosinophyll.
1st week	69·6 per cent.	19·8 per cent.	9·8 per cent.	0·4 per cent.
2nd ,, ...	64·3 ,,	23·7 ,,	10·4 ,,	0·28 ,,
3rd ,, ...	58·8 ,,	26·2 ,,	14·9 ,,	0·1 ,,
4th ,, ...	54·6 ,,	28·0 ,,	16·6 ,,	0·3 ,,
5th ,, ...	49·2 ,,	30·3 ,,	19·6 ,,	0·6 ,,
6th ,, ...	44·1 ,, –	34·0 ,,	20·7 ,,	0·9 ,,

(B) THAYER'S TABLE.

Week.		Polymorpho-nuclear.	Small Lymphocytes.	Large Hyaline.	Eosinophyll.
1st week	12 counts	74·0 per cent.	12·9 per cent.	12·4 per cent.	0·5 per cent.
2nd ,,	39 ,,	70·9 ,,	14·6 ,,	13·4 ,,	0·8 ,,
3rd ,,	34 ,,	66·3 ,,	21·5 ,,	11·6 ,,	0·3 ,,
4th ,,	19 ,,	65·0 ,,	20·1 ,,	14·4 ,,	0·4 ,,
5th ,,	8 ,,	61·7 ,,	18·2 ,,	19·7 ,,	0·3 ,,
6th ,,	4 ,,	57·7 ,,	22·6 ,,	13·5 ,,	6·0 ,,
7th ,,	1 ,,	37·3 ,,	23·7 ,,	34·4 ,,	4·6 ,,
8th ,,	1 ,,	56·9 ,,	24·2 ,,	16·8 ,,	2·1 ,,

Inspection of these tables, while showing by no means an absolute uniformity in results (probably owing in part to the difficulty encountered in arriving at the correct day of the disease), at least make out with sufficient clearness, certain points which

are worthy of special attention.   We see that at no time in the disease, if uncomplicated, is there a polymorphonuclear increase, but the reverse, the diminution from the normal being evident during the first week of the disease (at least towards the latter end of it). On following the differential count throughout the first six weeks of the disease, certain striking changes are evident.   The polymorphonuclears undergo a steady reduction, dropping as low in my series as 44·1 per cent.   Thayer, however, maintains that qualitative changes are absent, or inconspicuous during the first two weeks of the disease.   My results, on the contrary, showed decided changes, and are to some extent at variance with those of this careful observer.   I found, as the table shows, a decided diminution in the polymorphonuclears, during the first week, my average at this stage for 17 counts being 69·6 per cent.   There is also a corresponding diminution in the eosinophylls, which in many cases, disappear entirely, not one being noted among the 500 leucocytes counted.   The small lymphocytes undergo a steady increase from the second week onwards, though in several individual cases, they remain at the normal percentage. The most distinctive feature, however, is the gradual increase of the large hyaline cells, and transitional forms, the latter, however, not being so well represented in the increase as the others.   In a few cases, however, I found the transitionals very much increased. These large mononuclears and large lymphocytes undergo a steady increase throughout the illness, this increase being, according to my observations at least, manifest, though not to a great extent, during even the first week.   Thayer got them as high as 19·7 per cent. in the 5th week, and 34·4 per cent. in the 7th week.   In my own cases, the average for 17 counts during the first week was 9·8 per cent, but during the 6th week the average for 6 counts was 20·7 per cent.   I can strongly endorse Thayer's observations when he says that "the mononuclear cells, which are most markedly increased, are elements containing nuclei, not much larger than those of lymphocytes and often presenting the general appearance of a lymphocyte nucleus, with the exception of the slight affinity for colouring matters.   The size of these cells is usually about that or but little larger than that of the ordinary polymorphonuclear neutrophile."   In most of my films these cells were undoubtedly most in evidence.   My counts of lymphocytes are somewhat higher than Thayer's, and so are Türck's, this being probably due to my inclusion among the small lymphocytes, of some of those cells, closely resembling the latter in size, but which Thayer includes among the larger forms of lymphocytes.   I had great difficulty frequently in saying to which class these belonged, and I am inclined to doubt if Thayer adhered rigidly to the rule laid down by himself.   I have not included, in these tables, the counts from cases in which there was any inflammatory or suppurative complication, causing a distinct polymorphonuclear increase, as such would have materially interfered with the accuracy of any deductions to be made from the enumerations.   Several of these cases occurred.

CHART illustrating leucocyte changes in an uncomplicated case of typhoid.

CHART illustrating leucocyte changes in a case of typhus.   M. B., æt. 24.

——— Polymorphonuclear   ——— Small Lymphocytes

                                          ——— Leucocytes

——— Eosinophyll   ——— Large Hyaline
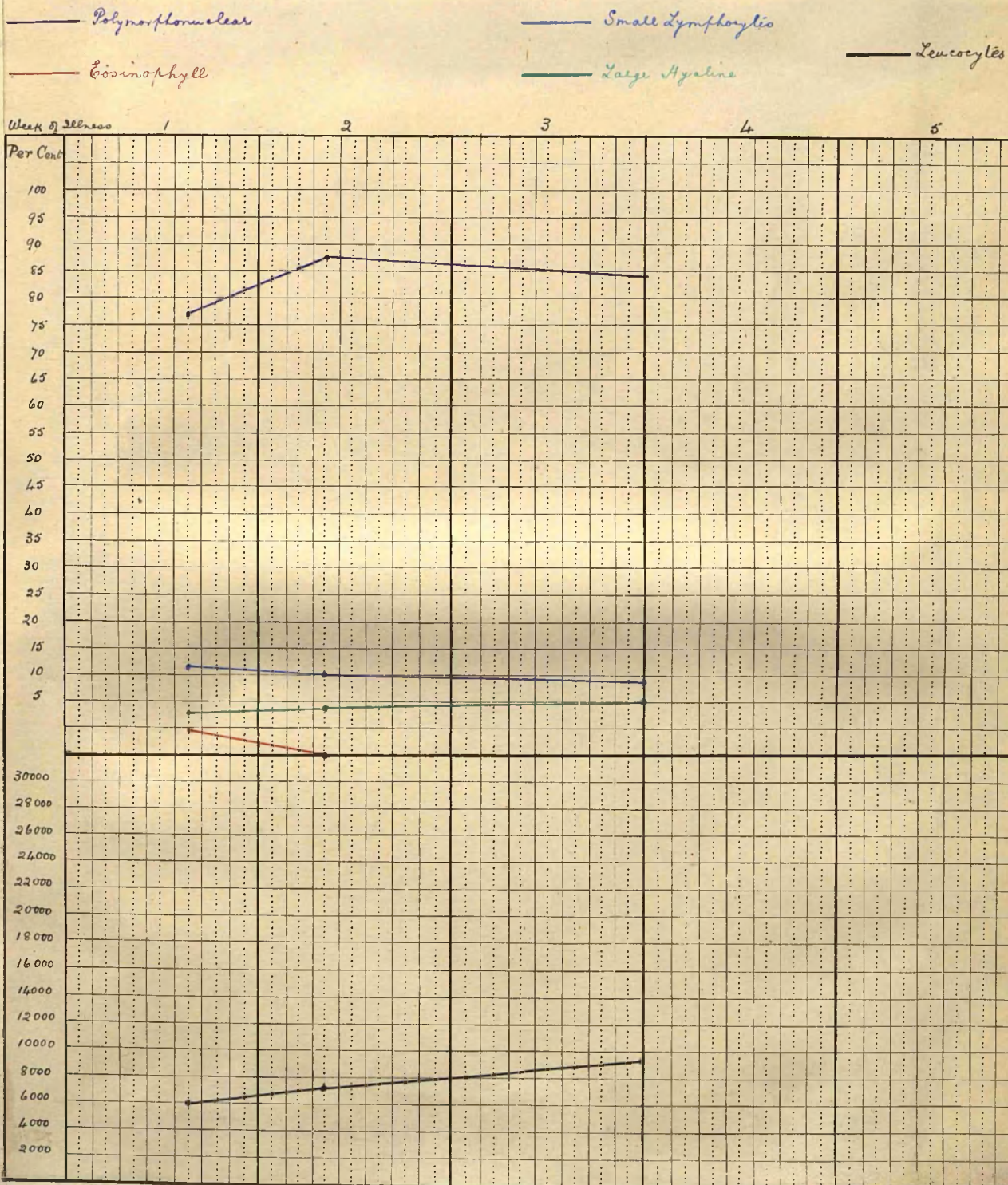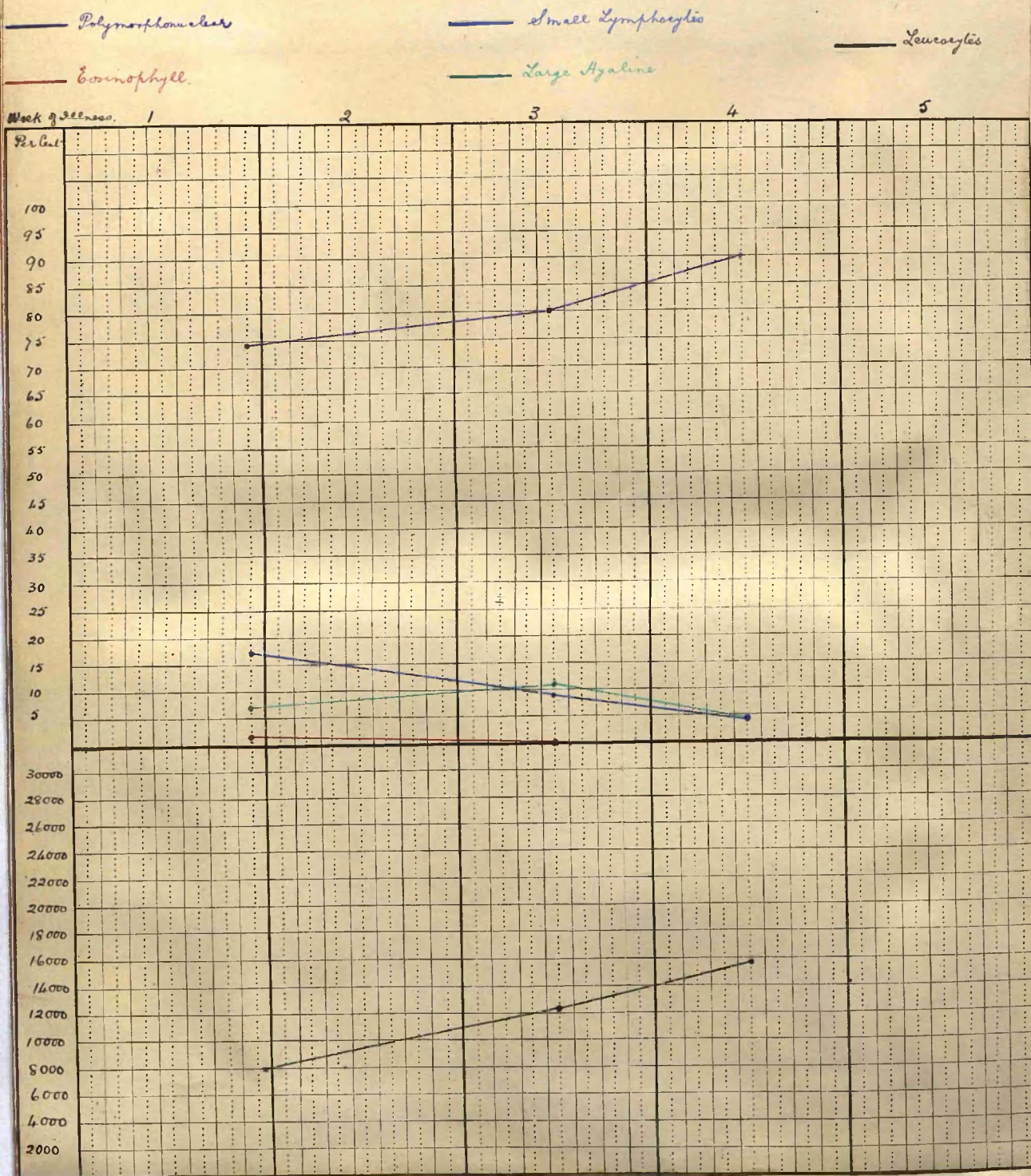
CHART illustrating leucocyte changes in a case of typhoid complicated with acute myelitis. T. B.

TABLE IV.

Table showing total and differential counts in cases admitted to hospital notified Typhoid. Some were not suffering from this affection.

Name	Age	Day of Illness	Evening Temperature	Total Leucocyte Count	Polymorpho-nuclear	Small Lymphocyte	Large Hyaline	Eosino-phyll.		Remarks
J. B.	9	15	102·6	5937	56·0	32·3	9·6	1·3	Mast 0·6	Severe—Fatal on 31st day, Diarrhœa, 3-6 motions daily—Bronchitis
Mrs W.	30	26	102·8	3437	67·8	20·2	10·7	0·6		Hypostatic Congestion, Lactation
G. G.	25	14?	103·4	3750	60·2	26·6	13·1	...		Fatal, taken 5 hours after arrest of Profuse Hæmatemesis and Epistaxis
D. M.	6	25	100·6	0250	58·7	26·4	14·9	...		Encephalitis
M. M.	8	14	101·8	4688	66·0	20·7	12·3	...		
Ovaliski	27	13	100·8	8125	67·8	18·8	11	2·4		Very mild case (Note existence of round worms)
C. M.	16	18	102·6	2500	58·4	26·8	14·7	...		Bronchitis—Very severe case—delirium, Fatal on 22nd day from hæmorrhage
A. R. {	13½	7	103	5625	78·3	14·7	6·9	...		
		15	100·8	3500	51·8	30·2	17·9	...		
J. B. {	15	10	101	7000	70·2	16·7	8·6	0·7	Myelo 0·5	
	10	18	98·6	6875	65·4	32·2	14·2	...	Mast 0·2	
Mrs T.	26	13	103·4	4063	61·6	30·5	6·9	0·3	Mast 0·3	
Mrs B.	25	16	102·6	1875	48·8	28·6	20·6	1·9		Severe case—Great prostration (Note existence of Tapeworms)
		15	103·4	5000	74·6	17·2	6·7	1·4		
T. B.	48	19	102·6	12,188	89	8·9	11·0	...		Fatal—acute Myelitis and Cystitis
		32	101·8	15,625	88·8	4·8	4·8	...	Myelo 1·3	
M. M'C.	9	24	98·	8438	70·2	19·6	10·2	...		Mild case—Widal reaction negative at first
H. M'V.	13	17	102·8	7188	68·7	19·7	11·3	·3		Labial abscess
		25	100	5600	52·9	28·9	18·1	...		
J. G.	37	15	101·	6600	63·2	26·2	10·6	...		Count probably taken during relapse
M. R.	17	31	100·8	3750	49·4	31·2	19·3	...		Venous Thrombosis (left leg) during convalescence
J. S.	23	18	100·8	8438	59·4	28·9	10	...	Myelo 0·5	Profuse Diarrhœa at first
W. M.	10	12	102·2	7188	67·9	23·7	8·3	·1		
W. H.	5	25	101·6	6562	59·2	29·7	12·1	...		
J. M'M.	9	7	102·6	2813	61·7	26·4	11·8	...	Myelo ·7 / Mast ·7	
M. H.	15	8	103	7000	68·7	22	7	...	(	Severe case—delirious—profuse diarrhœa
		15	104·6	6875	59·5	19·8	19·8	0·7		
T. S.	15	26	103·6	3125	63·7	21·7	14·5	...		Admitted in relapse—severe—delirious
J. L.	29	7	103·4	17,500	88·6	7·9	3·3	...		Central Pneumonia
J. R. (Pole)	25	18	103	2813	55·4	29·2	15·2	·2		Abortive case
Mrs B.	32	15	101·6	3750	48·9	32·4	18·7	...		Mild
S. M.	16	10	102	3750	65·9	23·1	10·9	...		Mild
J. H.	13	16	103·2	4063	67·7	23·7	7·5	·6	Mast ·3	Moderately severe
Mrs M.	18	14	101·8	8750	76·2	16·7	12·3	·5		Tubercular Peritonitis, &c.
		35	102	6250	70·2	17	7	...		
Mrs R.	47	15	104·6	3125	51·4	17·1	28·5	2·8		Endocarditis? Relapse developed
M. C.	3	22	102·6	2812	51·6	32·1	18·2	...		Severe—delirious—Delayed Widal
J. B. (Pole	20	10	103·4	6875	62·1	16·7	20·5	0·6		Hypostasis, right lung—Severe case
J. R.	16	3	103·2	5625	69·5	22·2	8·5	...		
M. M.	2	40?	98·4	8125	68·1	22	11·9	...		Continued profuse diarrhœa
M. F.	12	16	100·6	15,000	82	18·5	5·7	...		Not enteric—Influenza
		17	98·4		75·5	17·3	5·3	1·7		
A. G.	50	13	97	9375	68·4	24·2	7·2	·2		Not enteric—Influenza
		20	98	7500	70	23·1	6·6	·2		
R. W.	17	16	103·6	11,875	78·2	17·1	4·6	...	Myelo ·1	Not enteric—Malignant Endocarditis
		18	103	7800	74·2	19·7	5·8	·2		
A. C.	30	24	102·8	5960	61·9	24·1	13·9	...		Psoriasis, Hæmorrhage? Bronchitis—Icterus—Protracted—Fatal
		32	102·4	7000	64·2	22·6	13·1	...		
J. G.	11	28	101	5938	55·5	30·5	13·8	...		Mild—melœna
A. M'L.	34	14	102·8	6213	62·1	25·2	12·7	...		Abortive (sharp)
R. B.	30	—	102·2	2813	63·5	27·7	01·1	0·6		Ambulatory—Profuse diarrhœa
T. W. {		12	102·8	7000	85·1	10·1	4·7	...		Mild
		15	102·8	6563	77·8	19·7	2·3	...		
H. R.	7	16	100·2	6250	66·5	17·8	15·2	...		Severe—delirium
R. C.	12	14	101	4688	66·2	24·1	9·7	...		Mild
M. F.	9	6	103	4375	69·4	21·2	9·2	·2		Fatal—perforation—Hyperpyrexia, also Parotitis
T. M.	9	13	103·2	4063	54·1	32·6	13·2	·1		
		29	101·8	5000	50·9	33·7	15·3	...		
Mrs W.	23	8	102·6	8125	70·1	19·1	10·7	·1		Pregnancy (5 months)
S. M'F.	19	13	104	3125	75·5	16·5	7·9	...		Fatal case—Toxæmia
Mrs P.	29	16	104	2188	60·7	24·1	14·2	...	Myelo ·2	Bronchitis, severe—chronic ulcers on leg (left)
		21	104·2	1255	49·8	28	20·4	...	Myelo 1·7	Death—see notes—Osteomyelitis humerus (right)
J. B.	9	21	102·6	5938	50·7	33·2	16·1	...		Very mild
J. S.	5½	15	98	11,875	63·7	21·7	14·5	...		Double venous thrombosis during convalescence
W. H.	29	20	101·8	4375	51·7	28·4	19·9	...		Mild
J. S.	12	22	100·8	5937	57·9	26·8	15·3	...		Mild
H. B.	33	13	102·6	7813	76·9	13·5	9·6	...		Ambulatory case—Fatal—Had had several large hæmorrhages before
Mrs C.	17	22	103·6	4688	49·8	31·6	18·5	...		[admission. Profuse diarrhœa (6-10 per day
A. A.	10	35	97·8	4375	44·8	43·2	10·5	·8		Mild
R. M'K.	5	19	99	9600	70	22·7	7·3	...		Mild
		8	100·8	6875	77·1	18	4·7	...		Mild
G. R.	1½				72·2	19	8·7	...		Diarrhœa
					22·2	16	10·2	·2		
J. C.	21	15	103	2813	57·8	27·5	14·6	...		Severe and protracted case
J. M.	28	26	103·6	3438	49·9	29·0	20·2	...		Probably admitted in relapse
Mrs H.	30	12	100·8	4375	77·2	14	8·8	...		
		18	101·2	4000	00·1	22	6·4	...		
J. M'G.	21	33	99	3125	39·9	30·7	19·4	...		Mild
S. D.	6	17	100	5938	62·2	29·9	7	·8		Mild
					63·8	29·3	6·2	...		
M. H.	6	11	103·6	1875	50·8	34·5	14·6	·1		Mild
A. S.	17	33	102	4500	59·7	27·1	21·0	...		Moderately severe
		8	102·6	12,000	87·9	11·1	4·5	...		Abortive
A. M'D. {	4	14	98·4	9600	70·6	20·1	9·3	...		
W. O.	7	20	102	7500	59·4	29·8	16	...		
J. M'C. {	9	13	102·4	11,873	65·2	23·7	11·5	...		
		21	102·2	10,000	56·5	22·9	20·4	...		
J. S.	25	16	103	5000	58·2	28·4	13·2	...		
M. M'A.	12	21	102	3750	58·2	29·4	11·7	...		
J. M'A.	6	13	102·6	6250	50·4	33·1	16·5	...		
J. D.	20	19	102·8	4060	51·8	30·3	17·8	...		
C. B. {	10	10	102·8	9365	70·2	22·1	7·5	·2		Nosocomial infection
		20	99·2	6250	64·2	23·9	11·9	...		
W. R. {	18	21	100·8	5700	54·8	30·9	14·3	...		
		25	102	5900	49·7	33·6	16·7	...		
D. F. {	6	20	103	5625	62·5	28·1	9·4	...		
		17	102·8	4375	59·1	31·8	9·1	...		
J. M'V.	17	10	103·8	8750	74	19·1	11·4	·6		Fatal—fulminant—Pronounced cerebral symptoms
M. S.	13	13	105·2	12,600	65·9	20·4	13·6	...		
M. B.	21	13	101·6	10,000	73·7	21·1	6·1	·1		
		18	102·6	8125	69·5	24·0	9·7	...		
R. T.	3	24	102·8	10,00	78·7	15·0	5·4	...		Not enteric—Gastro-enteritis
G. O.	7	13	99	16,312	85·3	8·7	4·4	·6		Not enteric—Gastro-enteritis
C. M.	6	11	97	15,312	70·1	15·5	7·2	·8		Not enteric—Gastro-enteritis
G. S.	17	16	101·8	8437	67·3	21·5	10·7	·2		Mild
A. S.	42	14	102·4	9600	55·9	33·1	11·2	...		Moderately severe
		17	102·8	5937	64·7	22·6	12·7	...		
Agnes S.	9	23	102·3	5000	59·3	26·8	16·8	...		
J. S.	11	11	99·6	6562	62·7	27	10·2	...		
M. C.	4	14	100	3437	73·6	18·4	7·9	...		Typhoid—mild
				5937	73·6	18·4	7·9	...		
R. A.	8	11	101·2	10,000	82·7	9·2	7·9	...		Scarlet fever
N. E. H.	7	10	99	12,250	70·9	21·3	5·3	2·5		Enteric fever. Later acute miliary tuberculosis
M. M.	8	33	101·4	18,000	76·3	19·1	4·6	...		This count was taken after 2 very large hæmorrhagic motions, which
		11	99·8	7188	65·4	24·8	9·7	...		almost caused collapse. Perforation occurred on evening of 30th
		10	99	9687	69	17·9	11·9	·7	Myelo ·3	October
J. R. {	9	27	100·8	5625	60·3	32	7·6	...		
		39	98·2	7500	70		10	...		
J. B.	10	7	102·6	938	45·3	40·5	13·9	...	Myelo ·2	3 hours after sponging—severe protracted—Diarrhœa (7 per day) Hæmor-
J. S.	13	18	103·8	3438	57·9	26·4	15·7	...		rhages, 3 on 18th day
S. H.	30	14	104·6	8125	63·2	27	9·7	...		Abscesses opened after this (Boils, one large over thyroid)
		34	101·4	4688	48·7	28·9	22·3	...		Tubercular Peritonitis
A. S.	19	33	102	4500	89·7	9·3	·7	...		
S. A.	28	32	103·4	3785	46·7	29·4	23·9	...		
S. M'C.	9	13	101·8	11,873	56·5	22·9	20·4	...		
					65·2	23·7	11	...		
J.S.(Pole)	25	16	103	5000						
		18	104	6562	47·9	33·6	16·8	1·6		Empyema
		30	102	5625						
L. B.	8	16	100·2	28,000	79·8	14·9	5·3	...		Influenza
J. D.	45	9	98·4	3450	54·7	36	9·1	·2		Malignant endocarditis, &c.
M. H.	21	31	100·8	34,500	84·9	10·9	2·1	...	Myelo 2·1	Not enteric
Mrs H.	21	16	98·4	9375	63·8	30·5	13·2	2·5		
F. M'N.	20	11	100	9062	70·2	19·1	10·7	...		
M. J. F.	18	11	102·6	6562	58·8	24·9	15·5	...		
B. M'G.	10	20	99	7188	46	36·1	17·4	·3		
				6875	43·7	38·7	21·7	...		
M. W.	12	13	104	8437	66·2	24·3	9·4	·1		Very severe case—Extreme bronchitis—Pronounced nervous symptoms—
M. M'V.	9	7	104·6	6250	68·4	23·2	8·4	...		Perforation?
R. B.	9	8	104·4	13,125	71·5	20·7	7·3	·2		
		15	104·8	10,313	60·3	28·1	11·6	...		
J. W.	7	10	102	6250	59·4	29·3	11·9	...		Pregnancy
MrsS.(Pole)	28	12	103·6	8438	82·9	9·3	7·1	·1		Very severe bronchitis
N. M'K.	11	11	100	4375	47·4	34	18·5	·1		
D. M'K.	13	14	103·4	8438	61·5	28·6	8·9	·5	Myelo ·2	
T. T.	13	19	103	11,250	79·8	12·9	6·9	...		Severe case—Fatal
J. R.	55	8	101	3438	48·1	26·8	24	·9		Alveolar abscess
L. D. {	13	33	98·8	7500	79·9	16	3·9	...		Gastro-enteritis
R. B.	11	8	99	18,750	64·6	29·6	5·8	...		Moderately severe
J. H.	38	23	98·4	5025	49·1	42·6	8·3	2·2		
					43·1	45·4	9	...		
		42	97·8	3750	43·8	39·8	0·9	1·8		Severe—Encephalitis
W. N.	11	11	104·6	4062·5	72·8	20·4	6·7	·3		
D. S.	7	12	104	4062·5	60·7	32·1	7·1	·1		Moderately severe
A. L.	18	7	101·6	5937·5	68·2	22·1	9·7	...		Mild case—abortive
B. R.	20	7	102·2	7500	64·3	25·4	9·1	...	Myelo 1·2	Fatal—Diarrhœa—Profuse hæmorrhage
H. T.	30	15	102·6	11,375	79·5	13·5	6·4	·3		Scarlatini form, rash present
		29	99·2	8437·5	64·5	25·8	9·3	...		
		48	102·8	4062·5	64·3	34·2	10·8	·6	Mast ·3	Otitis media present, as a complication
J. A.	6	12	102·6	6250	58·7	30	11·3	...		
J. M.	14	17	104·6	7500	77·0	14·5	7·8	...		
					68·1	13·1	6·3	...		
H. M'C.	8	19	101·6	13,132	72·5	21	5·3	·8	Mast ·2	Scarlatina anginosa—see appendix
		26	103·8	20,875	79·9	13	3·7	3·2	·2	
J. M'K.	13	8	103·2	4375	73·4	19·5	7	...		Moderately severe
		20	101·8	2500	49·5	35·6	17·8	·5		
H. D.	13	12	101·6	1876	67	21·7	7·9	1·2		Mild
J. G.	28	12	102·2	18,000	80·2	14·2	5·6	...		Appendicitis
A. M.	9	12	102·8	5625	50·4	36·2	10·4	·5		Moderately severe
J. T.	11	16	102	5800	55·8	28·2	12	·1		Moderately severe
W. C.	12	12	102·6	6875	41·9	37·2	19·9	·9		
J. K.	12	10	102·4	5938	62·8	20·9	14·7	1·2		Phthisis (Latent)
		16	103	4375	42·4	34·4	20·0	1·2	Mast ·9	
J. M'B.	16	16	102·2	6875	60·3	26·3	5·8	...		Protracted
		34	102·2	4062						
W. S.	37	15	103·2	4062	53·9	30	14·7	1·2		
		22	102·6	2812	51·8	31·2	18·2	1·2		
M. B.	24	7	102	5940	75·2	11·3	3·2	·3		Typhus
		14	102·8	7500	85·5	10·5	3·9	...		
J. R., Junr	23	6	103	10,937	79	15·1	5·8	...		Very severe
		13	103·2	5312	75·4	14·8	9·3	...		
		19	103·6	4062	56·1	28·7	14·0	·3		
R. R.	30	20	101·2	4875	63·5	27·7	11·1	·6		Severe case
Mrs M'V.	22	12	102·8	9000	61·3	31·1	4·6	...		Phthisis
A. S.	40	16	101·6	23,750	74·9	17·8	4·6	3·7		Malignant Endocarditis
		14	102·6	20,875	64·6	27·1	5·1	1·1		Mild case
B. G.	10	13	102·6	6500	66·4	27·1	5·1	1·1		
Mrs D.	24	12	102·8	8750	69		7·7	6·2	...	
		19	103·2	7000	72·5	14·6	10·7	·5		Severe case
M. B.	9	16	102·8	4687	57·2	23·9	14	...		
		25	99	3125	54·2	34·6	10·6	...		
H. S.	11	16	102·4	4062	44·9	44·1	17·1	...		
		16	99	5625	51·7	36·9	9·3	...		
M. M'V.	9	5	104	5400	60·2	32·7	7	...		Severe case
		8	104·6	4738	51·6	30·4	17·7	...		
		10	103	6500	54·6	31·6	13·1	·2		
J. M'K.	16	14	102·8	4036	49·6	34·8	13·4	1·3		
		23	102·4	7000	48·5	31·6	13·4	·2		
		14	100·4	5000	55·7	29·3	15·0	·8		
D. H. S.	6				81·3	13·3	4	...		
M. M'L.	13	12	103	5635	47·1	35·1	16·3	·4		Gastro-enteritis
Mrs R.	60	7	98	8750	82·7	8·0	9·0	...		Typhoid—Retrospective diagnosis
M. R.	5	20	101·2	5600	60·4	27·4	10·1	1·6		Acute miliary tuberculosis
M. D.	6	18	102	14,000	57·2	30·9	15·0	2·3		Gastro-enteritis
A. B.	4	14?	102	3593	66·4	18·8	11·1	·3		Acute miliary tuberculosis
T. B.	8	20	104	3125	64·6	18·5	13·0	...		Acute miliary tuberculosis
T. P.	24	10	98	4500	35·3	58·1	5·4	...		Influenza
J. G.	17	19	103·4	7500	42·2	34·5	21·2	...		Typhoid—Mild
A. M.	9	8	14	102·6	7188	63	21·6	14·4	·9	Typhoid—Mild
J. B.	14	13	102·2	4375	45·7	41·9	12·3	...		Typhoid—moderately severe

There is a distinction which is noteworthy, between the differential counts in children, and those in adults. Probably on account of the irritation of the lymphoid tissue in the intestine (according to Ehrlich's view), the lymphocytes are considerably increased; and this is, I may add, another reason for my relative increase in lymphocytes as compared with Thayer's results, as almost one-fifth of my cases were in children under 12 years of age.

We see then that the examination of the blood in uncomplicated typhoid fever gives the following results :—

I.—A leucopenia, manifest during the latter days of the first week, and progressive, and bearing on the whole a relation to the severity of the disease, though this is by no means absolute.

II.—A diminution in the percentage of the polymorphonuclear cells, evident during the latter days of the first week, and becoming more marked as the disease progresses.

III.—A diminution in the eosinophylls—which cells may entirely disappear.

IV.—A slight though decided increase in the small lymphocytes.

V.—An increase in the large hyaline cells, beginning from the first week and becoming more marked during the subsequent weeks of the disease.

VI.—A decided increase in the indeterminate form of leucocytes.

VII.—In children, a pronounced increase in the small lymphocytes.

Value of the examination of the leucocytes in the diagnosis of typhoid.— My experience in this matter, though limited compared with that of others, enables me to endorse the sentiments of those who attach considerable importance to the leucocyte count, absolute and differential, as a means of discriminating typhoid from other affections which clinically bear a close resemblance to it. Thus, the existence of leucopenia serves to distinguish typhoid from many of the infectious diseases and from inflammatory and septic conditions, which are usually accompanied by a degree of leucocytosis. It must be remembered, however, as bearing greatly on this matter that leucopenia may exist in diseases usually associated with a leucocytosis, where the infection is great and the vital resistence low. In typhus which, early in the disease may be confounded with typhoid, there is a distinct leucocytosis, which increases as the fever progresses (Love), while the leucopenia of uncomplicated typhoid becomes more marked with the further progress of the disease. In typhus, in septic conditions, in pneumonia, and in cerebro-spinal meningitis, we have likewise a decided increase in the polymorphonuclear cells, with no increase in the lymphocytes or large hyaline forms. Unfortunately, however, in some other affections which bear a close resemblance clinically to typhoid, we have a leucopenia. Chief among these are measles, diphtheria, influenza, malarial fever, acute miliary tuberculosis, and tubercular peritonitis. The differential count, however, enables us to differentiate typhoid from some, if not from all of these. In malaria, we have a diminution in the polymorphonuclears with an increase in the large hyaline forms, but there is no increase in the lymphocytes. I have appended a table showing the absolute and differential counts in some cases which were admitted to hospital under my care, having been diagnosed and notified typhoid, but which further clinical observation, coupled with other diagnostic guides, proved not to be.

TABLE V.

Table showing absolute and differential leucocyte counts in cases notified typhoid, but which subsequent examination proved not to be due to this affection.

Name.	Age.	Day of Illness.	Leucocyte Count.	Polymorpho-nuclear.	Small Lymphocyte.	Large Hyaline.	Eosinophyll.	
J. L.	29	7	17,500	88·6	7·9	3·3	......	Central Pneumonia
M. F.	12	16	15,000	82	12·5	4·7	·7	Influenza with severe bronchitis
A. G.	50	13	9375	77·4	18·2	4·4	......	Influenza
C. B.	12	10	9365	78·2	17·6	3·8	·3	Influenza
D. B.	14	7	8750	70·8	22·7	5·5	1 Mast cell ·5	Influenza
J. P.	24	13	4500	35·3	58·1	5·4	5	Influenza, giving positive Widal
Mrs M. {	18	14	8750	70·2	16·7	12·3	·5	Tubercular Peritonitis with effusion
"	18	35	6250	76·2	17	6·6	......	
D "S. {	19	28	4250	81·3	14·3	4	·2	Tubercular Peritonitis with effusion
	19	33	3785	89·7	9·5	·7	......	
R. T.	3	24	10,000	71·9	18·6	9·2	·3 Myelo. ·3	Acute Gastro-enteritis
G. O.	7	13	16,250	85·3	8·7	4	·6	Do.
C. M.	6	11	15,312	76·1	15·5	7·2	·8	Do.
R. A.	5	11	10,000	82·7	9·2	7·9	......	Do.
R. B.	11	8	18,750	72·6	16·1	11·2	...... Mast ·2	Do.
H. M'C. {	8	19	13,125	72·5	21	5·3	·8 Mast ·2	Scarlatina Anginosa, with splenic enlargement—Peasoupy stools, &c.
H. M'C.	8	26	26,875	79·9	13	3·7	3·2	Acute miliary tuberculosis
M. R.	4	16	8750	81·6	13	5·4	......	Do.
A. B.	4	20	3593	81·4	15·1	3·5	......	Do.
T. B.	3	24	8125	66·6	18·8	11·1	3·3	Gastro-enteritis
M. D.	5	12	14,000	51·2	30·9	15·4	2·3	Empyema
L. B.	8	16	28,000	80·2	14·8	4·9	......	Malignant Endocarditis
R. W.	17	12	11,875	79·8	15·1	4·7	·4	Malignant Endocarditis
A. S. {	40	21	23,750	74·9	12·6	11·1	·6 Myelo. ·7	
A. S.	40	30	26,875	82·1	7·5	4·6	......	Malignant Endocarditis
M. H.	21	31	34,500	86·9	10	3·1	......	Appendicitis
A. G.	30	14	23,800	75·2	19·3	5·1	·4	Cryptogenetic Septicopyæmia
J. M'N. {	46	21	21,250	80	16·4	3·6	...... Myelo. ·6	
		30	39,375	86·2	10·1	3·1	·6	Typhus
M. B. {	24	6	6000	72·6	19·5	6·1	1·8	Typhus
		13	8750	85·5	10·5	3·9	...... Myelo. ·7	
Mrs M'V. {	23	28	7000	81·3	13·1	4·6	Myelo. ·6	Phthisis
		40	10,000	80·9	14·4	4·1	Mast ·9	
J. M'B. {	16	18	6875	42·4	34·4	20·9	1·2 Basoph. 2·2	Influenza—later, incipient Phthisis
		30	7500	66·4	24·1	5·8	1·1	
S. D.	3	33	18,000	70·2	19·8	10	......	Acute miliary tuberculosis

It will be noticed that in those diagnosed as tubercular peritonitis, there is a leucopenia, but the differential count is not the same as we find in typhoid. In one case, in the first count, taken on the 14th day of illness, the percentage of polymorphonuclears is slightly below the normal; while the large hyalines are slightly increased. Later, on the 35th day of illness, with a more marked leucopenia, the differential count approaches to normal, and is in fact normal. In the other case, A. S., as the patient was removed from hospital, only one count was taken, and while a leucopenia was noted, the differential count showed a slight increase in the polymorphonuclears, with a marked diminution in the large hyaline forms, not a single transitional or large lymphocyte being noted among the 400 cells examined, the small percentage present being made up exclusively of large mononuclear forms. Turning to the cases of acute miliary tuberculosis, all of which proved fatal, we see in two of them a distinct leucocytosis; while in the remaining two, there was a normal count in one and a slight leucopenia in the other. In three of these, the differential count shows a slight increase in the percentage of polymorphonuclear cells; while in the fourth the percentages bear a close resemblance to those found in typhoid, except that the eosinophylls are little, if any, diminished. Unfortunately, this child died before opportunity was afforded of making another blood examination. The four cases of protracted influenza are worthy of more than passing notice. In one, M. F., a girl of 12 years, the affection was complicated with severe bronchitis, and there was a total leucocytosis of 15,000. The differential count here showed, in the first instance, an increase of polymorphonuclears; while the second count, taken on the day after the temperature had reached normal, showed a condition which was practically normal. In the case of J. P. only one count was obtained, which showed a very marked diminution in the polymorphonuclears, a marked increase in the small lymphocytes, but no increase in the large hyaline forms. In the third case, J. M'B., two counts showed a leucopenia, the differential count in the first instance resembling that of typhoid; while in the second, taken a fortnight later, while the temperature was still slightly elevated, showed a slight increase in the polymorpho-nuclears, though still subnormal, but a marked reduction from the previous count, in the number of large hyaline cells, a condition contrary to that found in typhoid. The fourth case is even more interesting. Two brothers, C. B. and D. B., were admitted notified typhoid, but both were found to be suffering from influenza—one with the febrile type, the other with the gastro-intestinal form, the respective leucocyte counts being 9365 and 8750; while the differential counts showed in the one a slight increase of the polymorphonuclears, in the other a normal count, but in neither was there any increase in the large hyaline forms. Later, C. B. contracted typhoid in the ward, and blood examination showed a reduction in the total count at the end of the first week, but more marked in the second, and with a diminution in the poly-morphonuclears, and an increase in the large hyaline form and small lymphocytes. In the cases of gastro-enteritis in children, it will be noted that all show a leucocytosis, and only one shows a count suggestive of typhoid. The blood examinations of three cases of typhus, notified typhoid are also given, and it will be seen that all show a

leucocytosis after the first week, and a decided increase in the polymorphonuclear forms. One case, H. M'C., in the table, is of considerable interest also. He was in the scarlet fever pavilion suffering from the anginose type of the disease. After his temperature had reached normal it began to re-ascend in staircase fashion, and with it diarrhœa and peasoupy motions, and later splenic enlargement. Suspecting that it was a case of nosocomial infection with typhoid, his blood was examined, and in addition the Widal test was applied, but with a negative result, on several occasions. A leucocytosis, however, was noted, and the differential count showed first a normal condition, and later an increase in the polymorphonuclears. The diazo-reaction was also negative.

My own observations thus enable me to come to the conclusion that in the examination of the leucocytes we have a most valuable diagnostic aid. The absence of a leucocytosis or actual existence of a leucopenia, with a diminution in the percentage of polymorphonuclears, a slight increase in the small lymphocytes, and a decided increase in the percentage of large and intermediate lymphocytes and large mononuclears, gives us two valuable points which, while neither may be absolutely pathognomonic of typhoid, are of considerable diagnostic value, and in the presence of one or more of the cardinal symptoms would place the diagnosis beyond doubt. Repeated examinations at intervals, showing a steady reduction in the polymorphonuclears and a steady increase in the large hyaline forms is, in my experience, distinctive of typhoid. Unfortunately there are some cases which throughout the disease do not show such changes, without any obvious reasons, and there are others which give a different relative percentage of the leucocytes, as the result of inflammatory or suppurative complications. Unfortunately, my list of cases of protracted influenza, and acute miliary tuberculosis and tubercular peritonitis, is too limited for any very definite results to be drawn therefrom, but in not one of them is there a progressive diminution in polymorphonuclears, coupled with a slight increase of small lymphocytes, and a progressive increase in large hyaline forms and intermediate forms, a condition which I am of opinion exists only in typhoid.

Blood film from typhoid case, A. R., showing mast cell, and large lymphocytes. (Romanowsky stain.)
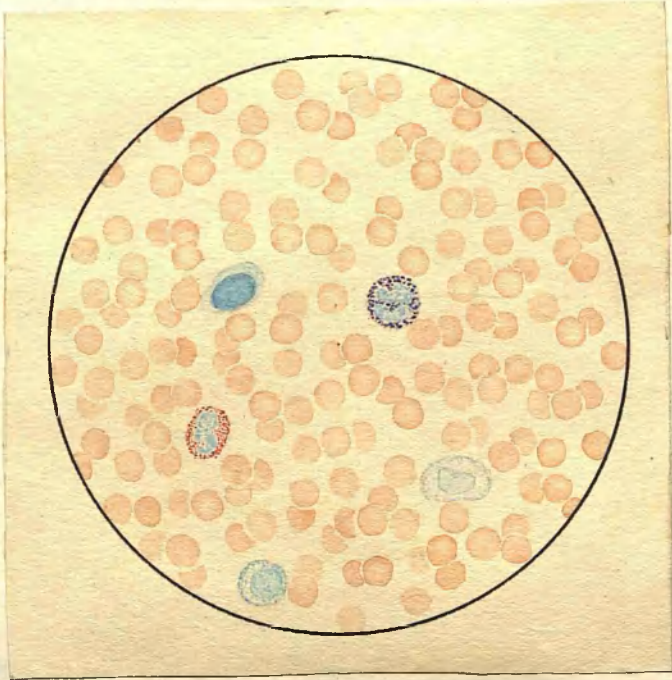
Blood film from typhoid case, G. M'I., showing large forms of lymphocytes. (Romanowsky stain.)
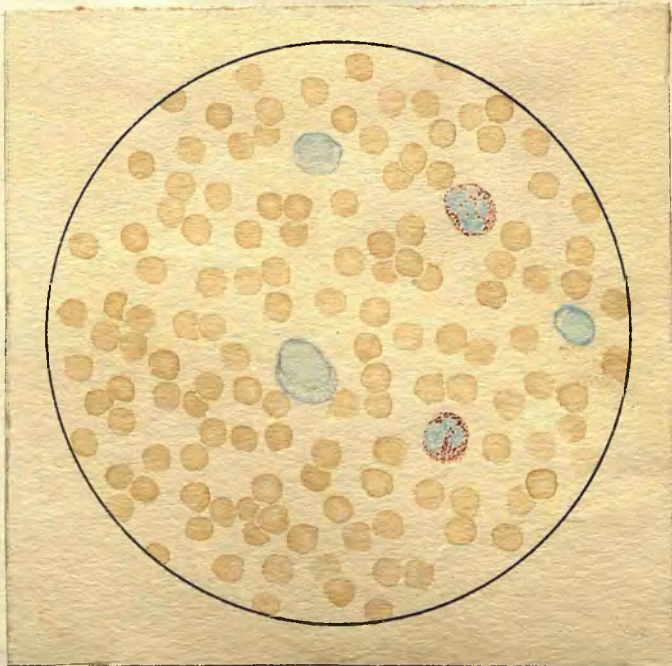
Blood film from typhoid, L. D., showing one eosinophyll, two small lymphocytes and four larger lymphocytes. Two "fields" are shown. (Romanowsky stain.)
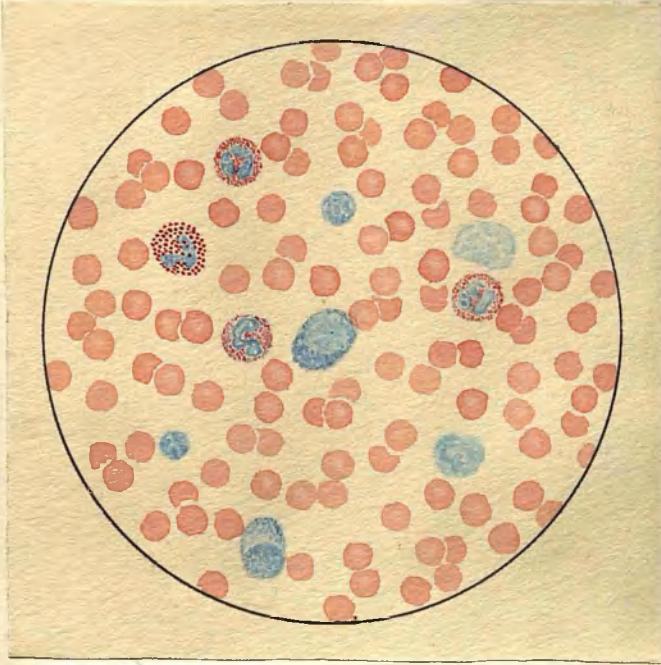
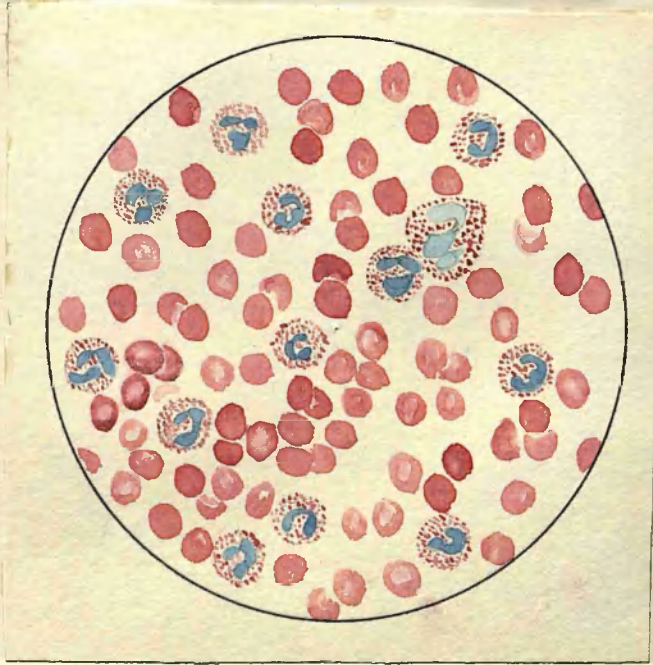Blood film from typhoid, H. S., showing large lymphocyte forms. (Triacid and methyl blue.)
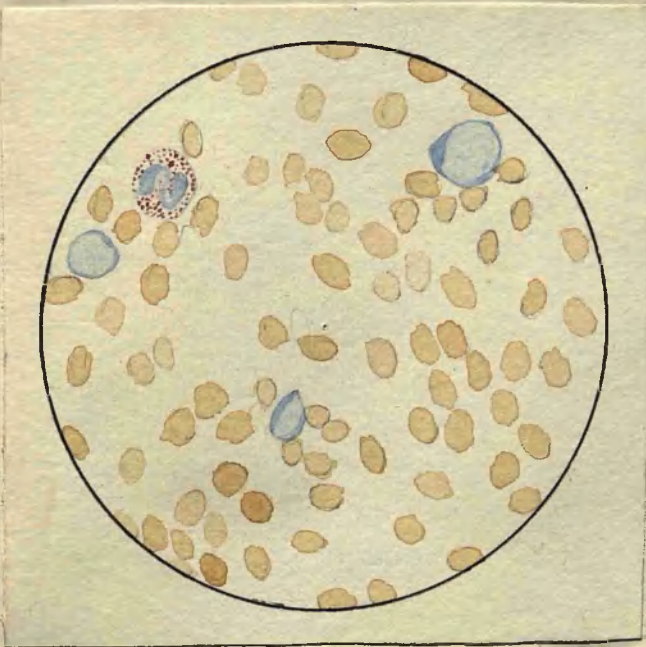
Blood film from typhoid, T. B., complicated by acute ascending myelitis, leucocytosis, one myelocyte seen. (Triacid and methyl blue.)
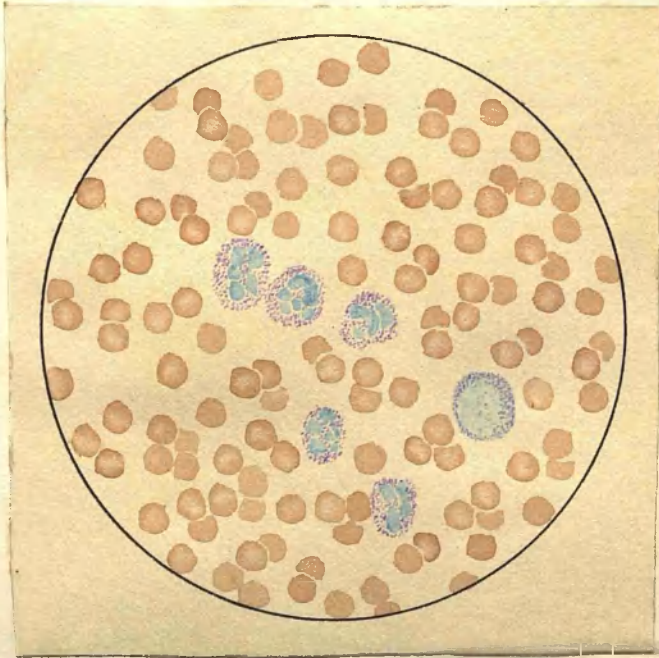
Blood film from J. M'N., case of cryptogenetic septico-pyæmia (leucocytes 35,000), showing leucocytosis. (Eosin and methylene blue.)
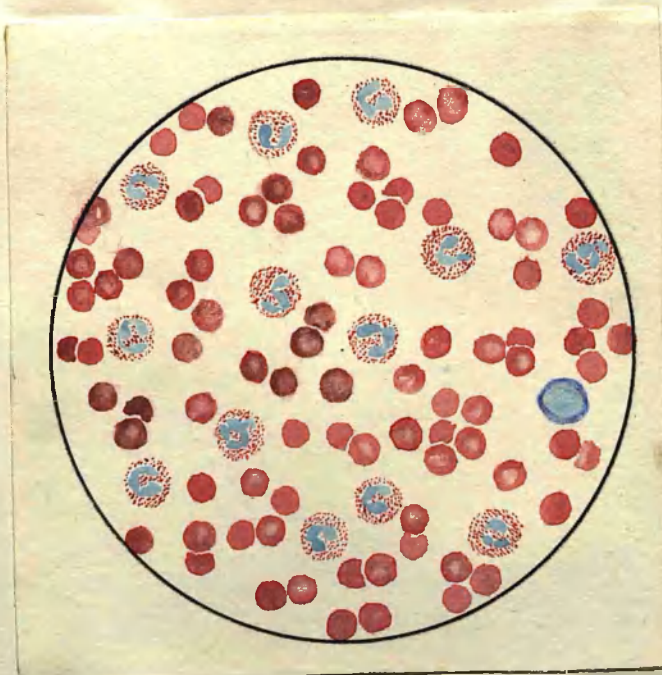
Blood film from H. M'C., case of scarlatina anginosa, with diarrhœa, splenic enlargement, simulating typhoid ; leucocytosis, one eosinophyll seen. (Eosin and methylene blue.)

Blood film from J. M'B., case of influenza, with later development of tubercle, leucopenia, showing large lymphocyte forms, one small lymphocyte seen. (Wright's stain.)
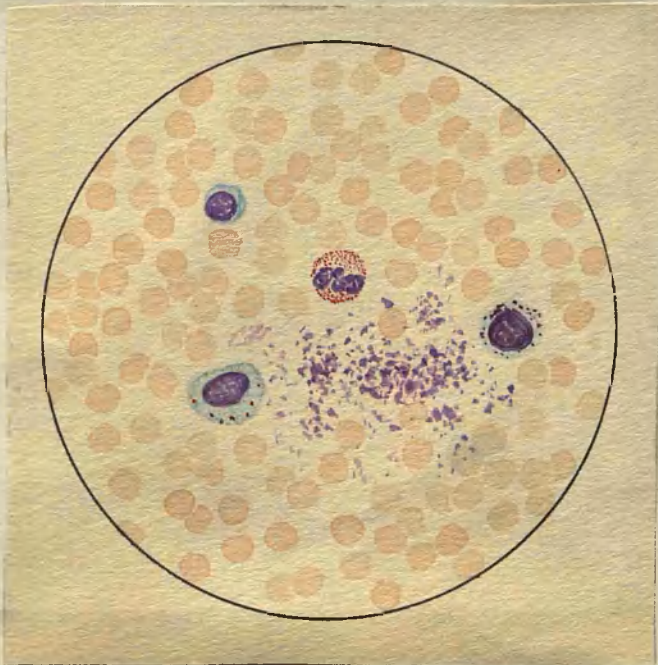
Blood film from case of influenza, J. P., with lymphocytosis, three small lymphocytes seen. (Triacid and methyl blue.)
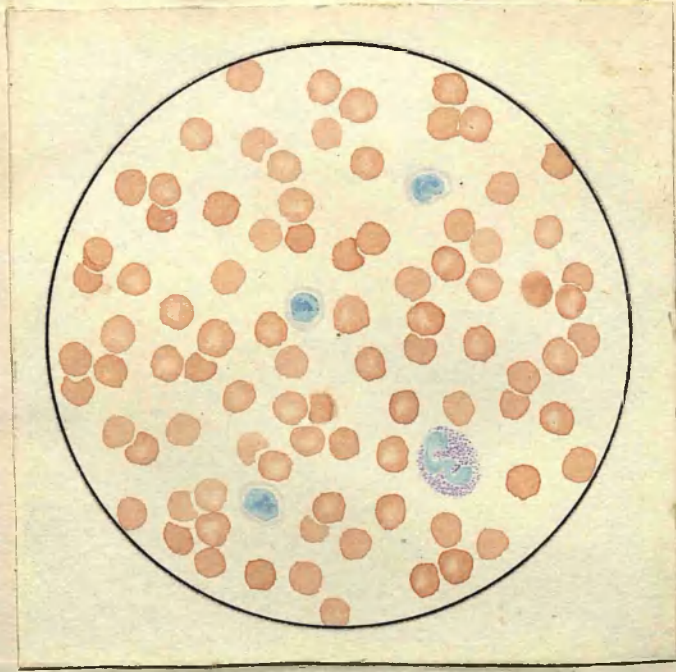
Blood from case of typhus, M. B., showing leucocytosis. (Eosin and methylene blue.)
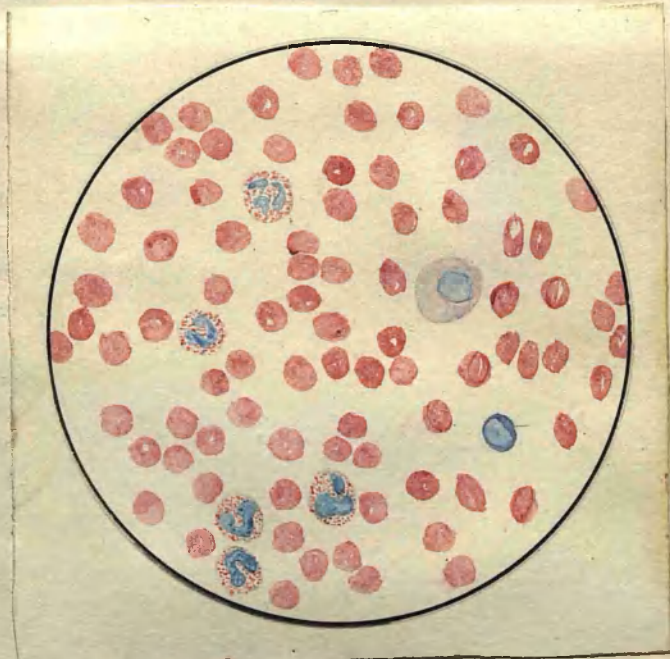
Blood film from Mrs M'V., case of phthisis, leucocytosis. (Wright's stain.)
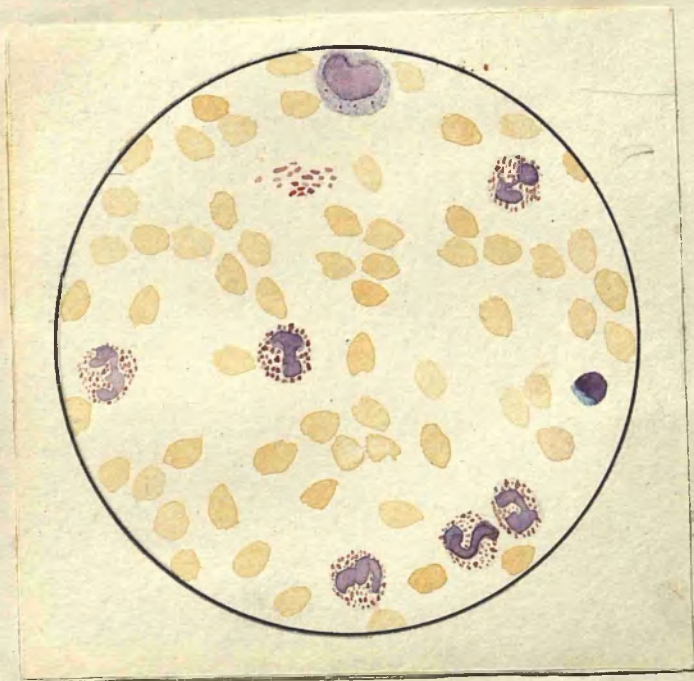
Serum-agglutination reaction.—This test, known as the Gruber-Durham-Widal reaction, or Widal's reaction, is based on the fact that if the diluted serum of a patient suffering from typhoid fever be mixed with a culture of typhoid bacilli, the latter lose their motility and become agglutinated or gathered together into masses varying in size. It is not my intention to give here a detailed historical survey of the discovery, but suffice it to say that as long ago as 1889, the first step in this direction was taken by Charrin and Rogers, who, working with bacillus pyocyaneus, showed that if the culture be made in the serum of an animal immunized against this bacillus, the resulting growth did not produce a diffuse turbidity such as occurs when it is grown in normal serum, but instead formed a mass at the bottom of the tube, the supernatant liquid remaining quite clear. Later, in 1891, Metchnikoff showed similar phenomena with the pneumococcus, and the vibrio Metchnikovi. In 1895 Bordet showed that cultivation was not necessary, and that agglutination occurred as well if the serum from an immunized animal were added to a culture already developed. In 1894, Pfeiffer, working at the subject of immunity, studied the action of the serum of animals immunized to typhoid upon the bacilli, and demonstrated what has since been known as Pfeiffer's phenomenon. If the serum of animals immunized against typhoid be placed in the peritoneal cavity of a

guinea-pig, along with more than a lethal dose of typhoid culture, not only does the animal recover, but the bacilli become converted into granular masses, and finally disappear as the result of the lysogenic and solvent action of the serum. Then followed Gruber, Durham, and Grünbaum, who showed that the serum of a patient convalescent from typhoid could accomplish this as readily as the serum of an immunized animal, if the bacilli were added to the serum placed in tubes. The bacilli fell to the bottom as a sediment, remaining there. But to Widal, in 1896, was left the honour of demonstrating the applicability of the test at the bed-side. He showed that the reaction was not one of immunity, as Gruber had thought, but was one solely of infection, and could be obtained by using the blood from the patient at the height of the disease. It could, therefore, he pointed out, be used as a means of diagnosis. Of the two methods of applying this test, (a) the macroscopic or slow, and (b) the microscopic or rapid method, I will confine myself to the description of the technique of the latter, as it is the one which I exclusively employed, since, as experience has shown, it is the more rapid and reliable. The blood or blood serum is the fluid almost always used, though the other body fluids also show the reaction, but the first is always selected because it possesses the most marked agglutinating power.

Technique.—Blood from the ear is drawn into an ordinary capillary tube, and if not to be used at the moment, the ends are closed by heating. When required, the ends are broken off, and heat applied by spirit lamp or Bunsen to one end, when the serum will be expelled. Occasionally a little blood-clot is simultaneously expelled, but this is more often an advantage than otherwise, as the red blood corpuscles enable one the more easily to recognise the bacilli. Many use an ordinary slide and cover-glass, but I prefer to use a hollow slide for the hanging drop. The blood serum or blood having been expelled on to the end of a slide, one or more drops are removed to a cover-glass held in forceps, and diluted thereon, by mixing with the requisite quantity of the bouillon culture of the bacillus. In diluting, I simply employed the platinum loop, though others, for purposes of greater accuracy, employ a graduated pipette, such as that for blood counting, but I found that with some experience the loop method gives accurate dilution if carried out with care. The cover-glass having been inverted and placed on the slide, I employed the high power dry lens, and the narrow aperture of the diaphragm, for examination. In addition, I always placed, beside it, under another microscope, a control, with culture diluted with ordinary sterile bouillon, or more often with a drop of my own blood equally diluted, thus avoiding false clumps.

Certain points, in connection with this test, call for a little consideration, as inattention to them may lead to error in result. Among these may be mentioned the following :—(a) race of typhoid culture used, (b) state of culture, i.e., as influenced by growth on media, (c) dilution employed, (d) time limit. The race of typhoid employed is important (Muir). All races do not give uniform results, some being more sensitive than others. Durham, Widal, and Bensaude deny this, having

found little difference in the clumping power of many races, obtained from different parts, but Van de Velde, after examining twenty cultures got marked differences, having one which scarcely reacted at all. Some authorities maintain that these differences only exist in old bouillon cultures, and that if solid (agar) media be used, no such differences exist. I cannot, however, from personal experience venture an opinion on this matter, as I only employed two stock cultures, one of which was obtained from the Public Health Department in Glasgow, and the other from the Pathological Department of the Western Infirmary (Dr Ferguson), and both were equally sensitive and did not react in the slightest to my own blood. Certainly, I found some differences in the sensitiveness towards the blood of typhoid fever patients, of bacilli isolated from the blood or urine of others, but this is scarcely comparable.

State of culture used.—Undoubtedly the sensitiveness of a culture may be altered by the conditions under which it is grown. If a bouillon culture be kept in the incubator at 37°C. for several days, and then a drop examined under the microscope, it will be observed that the majority of the bacilli are sluggish involution forms. Daily transplantation in bouillon prevents this, but the motility becomes gradually impaired if kept at 37°C. I therefore followed the plan recommended by Muir and by Wyatt Johnston, of keeping the stock culture on agar at room temperature, and making subcultures therefrom, at least once a month, though I preferred every fortnight. Then, previous to applying the test, I made a subculture in bouillon, which I kept in the incubator at 37°C. for twelve hours and then used. Some maintain that excess of alkalinity in bouillon may cause false clumps to be formed : calcium carbonate may be precipitated, which, according to Malvoz, has agglutinating properties of itself.

Dilution.—The proper dilution to be used has been a vexed question ever since the discovery of the reaction, and has caused much controversy. Widal originally used a dilution of (1-10), but found that if allowed to remain for some time, other sera than those of typhoid patients caused agglutination. In St. Bartholomew's Hospital, the dilution which has been employed has been (1-20), Muir advocates (1-30). In the Johns Hopkins Hospital (1-50) is used, while Durham advocates (1-100). I have always used a (1-50) dilution, but in the event of a negative result being obtained, I tried (1-30) and (1-20), repeating the (1-50) later.

Time limit.—The allowance of time for a complete reaction cannot be considered apart from the dilution. Thus, if a low dilution be used, a short time is usually allowed, and vice versa. Most observers, however, consider a dilution of (1-10) too low, irrespective of the time limit, and insist on a minimal dilution of (1-20), with a time limit of fifteen to twenty minutes for a complete reaction. Others believe in (1-30) with time limit of half-an-hour, and many do not work with a dilution under (1-50), and time limit of one hour. The chief objection to a high dilution, for practical purposes, is the correspondingly long time limit. With a dilution of (1-10) other sera than typhoid may clump the bacilli, while on the other hand a dilution of (1-100) is too high, as many typhoid sera never clump in this dilution

(Grünbaum and Gruber).   Horton-Smith says that a dilution of (1-20), with time limit of one hour, is quite satisfactory; and he adds that twenty per cent. of typhoid sera never reach an agglutinating limit of (1-100).   Cabot says that a dilution of (1-10) for fifteen minutes is equally satisfactory with a dilution of (1-40) for one hour.   I always, as previously stated, employed a dilution of (1-50), and allowed a time limit of an hour for a complete reaction.

Date of appearance of the reaction—Most authorities are agreed that the reaction usually makes its appearance for the first time about the end of the first week or the beginning of the second.   Bensaude, however, has reported three positive results on the third day, while Johnstone and M'Taggart (*British Medical Journal,* December 5th, 1896), report positive cases on the second day.   Some of these results are, however, open to dispute, chiefly on account of the difficulty of fixing the exact day of illness in many cases.   Elsberg says it is present in 8 per cent. during the first week, in 78 per cent. during the second week, and in 14 per cent. during the third and subsequent weeks.   Courmont says that 93 per cent. react within the first nine days.   For my own part, I had not much opportunity of testing this point, for most of my cases were admitted during the second week of the disease, and the reaction was present on admission.   In the case of two nosocomial attacks, however, it was present in one on the 6th day, and in the other on the 10th day of illness.   In two other cases, admitted early in the disease, from house endemics, the reaction was present in one on the 5th day, and in the other on the 8th day.

Percentage of cases giving the reaction.—Statistics show that the reaction is present in about 97 per cent. of cases, only three per cent. showing a total absence of it throughout the disease.   In my own experience, I failed to get a positive result in only five of my cases (200 examined) which were clinically regarded as typhoid. Of these five, two responded to other organisms (B. Gaërtner and B. paratyphoid), and the remaining three were all fatal cases, so that they may have been examples of a delayed reaction, and not evidences of a total absence.   Cabot says that a positive result is to be obtained in 97.2 per cent. of cases of typhoid.

Delay in appearance of reaction.—This is probably responsible for a number of the negative results reported from time to time.   Cases have been frequently reported, in which the reaction did not appear until the third or subsequent weeks of the disease, and Widal, Eshner, and Thoinot have noted its absence until the relapse.   In my own series, ten cases showed no reaction until the third and subsequent weeks,

Early disappearance of the reaction.—The reaction may be present and disappear early, and so may be absent by the time the patient comes under our observation. Widal noted its disappearauce on the 18th day, Breuer on the 17th day, and Fraënkel on the 25th day.

Duration of the reaction.—The reaction usually disappears during or shortly after convalescence, though cases have been recorded in which it has persisted for months, and even years.   Renaud noted its presence in cases from 23 to 30 years after the attack.   In my own cases, I got a positive reaction from antecedent typhoid in two

cases, four and six years respectively after the typhoid illness. Negative results in most cases are to be attributed to one or other of the following causes:—(a) delayed reaction ; (b) early disappearance of the reaction ; (c) intermittency of the reaction ; (d) non-existence of typhoid. On the other hand, positive results are frequently recorded in conditions other than typhoid, and these are to be attributed to (a) inattention to dilution and time limit ; (b) old bouillon culture containing pre-formed clumps ; (c) previous attack of typhoid ; (d) pseudo-reactions being mistaken for positive reactions. A positive reaction is only present when, at the end of the time limit for that particular degree of dilution, most of the bacilli are clumped into masses, and the unclumped bacilli show complete cessation of motility. In pseudo-reactions only small clumps are formed, and the majority of the bacilli remain quite active. Positive results have been reported in typhus, malaria, septic conditions, pneumonia, tuberculosis, acute osteomyelitis, influenza, Weil's disease, and infectious due to the bacillus proteus. Careful enquiry has proved, however, the existence of an error in technique, usually an old bouillon culture with pre-formed clumps being used, and no control, or a too low dilution with too long time limit, or returning a pseudo-reaction as a positive one. In most of those cases where a positive reaction has been reported it is noteworthy that the reaction was evanescent, and did not increase in intensity, and was probably attributable to some chemical agent in the blood, for as Malvoz has shown, safranin, vesuvin and other bodies have quite marked agglutinating properties. In my own series of cases, in those which were not typhoid, I never obtained anything but partial reactions, and only when a dilution of (1-20) was employed.

Some writers have attached great importance to the presence in the blood of agglutinins of organisms other than the bacillus typhosus, which, they maintain, are liable to lead to errors in the reaction. The most common are the agglutinins of the bacillus coli. According to my own experience, these are never present in great quantity in typhoid. With a view to ascertaining to what extent these were present, in the blood of patients suffering from typhoid, I tested the blood of thirty cases, in different dilutions from (1-20) to (1-100) with bacillus typhosus, bacillus coli, bacillus enteritidis (Gaërtner), bacillus paratyphoid A and B, the last three being obtained for me by the Medical Officer of Health, from Kral. In several cases I obtained some clumping, but only a partial reaction, with bacillus coli, but never in dilution over (1-20), while in all these cases the bacillus typhosus was completely clumped in higher dilutions. With bacillus Gaërtner, I got one positive reaction in a well-marked degree, but in this case the bacillus typhosus was not agglutinated. With paratyphoid A, I got a few partial reactions in low dilutions, but more with Paratyphoid B, but only one gave a positive result with the latter bacillus, and in this case the bacillus typhosus was not clumped at all. In one case of appendicitis with abscess, which did not agglutinate bacillus typhosus, the bacillus coli was clumped in dilution (1-50) in an hour. A week after the abscess was opened, the reaction had all but disappeared.

Value of the serum agglutination reaction in the diagnosis of typhoid.—Most clinicians are of opinion that the Widal test, if properly carried out, constitutes a very valuable diagnostic aid, being present in about 97 per cent. of cases of typhoid fever, and my own observations are very much in accord with these. I applied the test to every case that came under my care, notified as suffering from typhoid, in all, over 200 cases. Of that number 200 were clinically typhoid, and only five gave a negative result. Two of these agglutinated paratyphoid organisms, and were regarded as cases of paratyphoid fever, while the remaining three were fatal cases, dying on the 9th, 18th, and 21st days of the disease respectively, and it is just open to question whether or not these might be regarded as examples of delayed reaction. Several cases came under my care in which the reaction was delayed, as the following table indicates.

TABLE VI.

Table showing Cases in which the Widal Reaction was delayed.

Name.	Age.	Day on which Reaction first appeared.	Remarks.
R. M'K.	5	24	Mild case
G. R.	1¼	21	Severe case
M. C.	23	25	Severe case
S. M'F.	19	20	Severe case, fatal, toxæmia
W. S.	34	35	Severe and protracted, few clinical symptoms, hæmorrhage
M. M'C.	9	24	Mild case
W. N.	11	26	Severe, encephalitis
H. T.	30	22	Moderately severe
J. R.	21	21	Very severe case
S. H.	30	19	Protracted and severe

Table showing Cases Clinically Typhoid in which no Reaction was obtained with B. Typhosus.

Name.	Age.	Result.	Remarks.
M. S.	14	No attempt at clumping	Fulminant case, fatal on 9th day
J. R.	55	No clumping	Profound toxæmia, fatal on 14th day
B. R.	20	Slight clumping	Profuse hæmorrhage, toxæmia, fatal case on 21st day
A. C.	30	No clumping	Paratyphoid, clumped by paratyphoid B
F. M'N.	20	No clumping	Paratyphoid, clumped by B. Gaërtner

Table showing Cases, not Typhoid, in which a Positive Reaction was obtained with B. Typhosus.

Name.	Age.		Remarks.
M. B.	24	+(1-100) in 2¼ hours	Typhus fever, typhoid 4 years previously
J. P.	24	+(1-50) complete in 1 hour	Influenza, typhoid 6 years previously

In the case of R. M'K., the reaction with the bacillus typhosus was not complete in one hour, while with the bacillus coli an equally good result was obtained. A week later, the reaction with the bacillus coli was still present, though slightly less pronounced, while the bacillus typhosus was clumped in a dilution of (1-100) in one hour. The case of G. R., æt. 15 months, is equally interesting. He was admitted with other three members from a house endemic. On the 7th day, the bacillus coli in dilution (1-20) was clumped in 1½ hours, while the bacillus typhosus only gave a partial reaction in that time, and with the bacillus Gaërtner very little clumping was observed. There was no attempt at clumping with paratyphoid bacilli A and B. On the 14th day of the disease, the bacillus coli and bacillus typhosus gave an equally good reaction, but would not clump in a higher dilution than (1-20). On the 18th day, the reaction was still incomplete, and equally well marked with bacillus coli and b. typhosus. On the 21st day, however, while the bacillus coli would only give an incomplete reaction in an hour in dilution (1-20), the bacillus typhosus was clumped completely in that time in a dilution of (1-100). In the case of the others no partial clumping from other agglutinins was observed, the reaction with the bacillus typhosus being absolutely negative until the day mentioned in the table. We see, therefore, that in the event of a negative result being obtained at first, we must re-examine the blood, at intervals thereafter, before concluding that the reaction is negative. It appears often suddenly, and is liable to intermit. With the technique which I employed, and dilution (1-50) with time limit of one hour, I never got a positive reaction in any case which, clinically, was not typhoid, except in two, one of influenza and one of typhus, in both of which the reaction was due to agglutinins retained in the blood from antecedent typhoid. The former case gave a positive reaction with dilution (1-50) in an hour. She had had typhoid six years previously, having been confined to bed with it for six weeks. In the latter case, the patient had all the symptoms of typhus, but her blood gave a positive reaction in dilution (1-50) in an hour, and in (1-100) in 2¼ hours. She had had typhoid fever four years previously in Edinburgh.

As bearing on the value of the reaction in diagnosis of doubtful cases, I might mention three cases which are of some interest :—

Case I.—Two brothers were admitted to hospital, notified as suffering from typhoid fever, but neither presented any clinical symptoms suggestive thereof, and the Widal reaction, examined for on several occasions, was negative in both cases. As the father, the only parent alive, had met with an accident, it was decided to keep the lads in hospital for the time being. Owing probably to laxity on the part of the nursing staff, one of them took ill with what proved to be typhoid, and a positive Widal's reaction was obtained on the 10th day of the illness in a dilution of (1-100).

Case II.—A little girl and her father were simultaneously admitted, notified as suffering from typhoid. The father was undoubtedly suffering from this disease. The child had been ill for at least four weeks prior to admission to hospital. On admission, the child, beyond being emaciated, presented no definite symptoms of typhoid, and physical examination of the lungs and other organs failed to detect any lesion. Later, the temperature pursued an irregular course, and examination of the lungs showed, in scattered areas, breathing which approached tubularity and fine subcrepitant râles. The child died later with all the symptoms of acute miliary tuberculosis. On admission, the Widal's reaction was positive in dilution (1-50) in three-quarters of an hour, and in (1-100) in two hours. No post-mortem examination was allowed, which would probably have shown healed typhoid intestinal lesions. But for the Widal's reaction there would probably have been doubt as to the existence of typhoid, even although the father was suffering from this disease.

Case III.—Nurse J. M'A., while on duty in the typhoid fever pavilion, took ill with a feeling of languor and headache. Her temperature was 99°Fah. She had several old tubercular scars in the submaxillary and cervical regions of her neck, and examination of her urine showed pretty marked albuminuria and tube casts. There was no evidence of any mischief in her lungs, and repeated examinations during the first fortnight thereafter failed to detect anything beyond a few bronchitic râles. On the 6th day her blood for the first time gave a positive Widal's reaction in dilution (1-50) in half-an-hour, and in (1-100) in one and a quarter hours. The stage of steep curves became interrupted by a recrudescence of temperature, which became somewhat irregular, and patient eventually died with all the symptoms of acute tuberculosis.

In **retrospective diagnosis** of the disease it is one of the best aids we have. I might here quote three cases as illustrative of this point :—

Case I.—An old woman (Mrs R.) who lived alone had had an indefinite slight illness lasting for about ten days, after which she was up and about again, but had to take to bed again for another week. She got up again and kept about trying to attend to her house duties, but was forced to give up and take to bed. Some relatives came through and stayed with her until she was convalescent. Later some of the friends, after going home, sickened with what proved to be typhoid, and the Medical Officer of Health, suspecting the old woman as the source of infection, had her removed to hospital. On admission she was considerably emaciated, her temperature was normal, her spleen was not palpable, but her leucocyte count showed a leucopenia of 3500. Her blood gave an active Widal's reaction, clumping the bacillus typhosus in a dilution of (1-300).

Case II.—A. M., aged 8 years, was admitted along with two other members of the family who were suffering from typhoid. She had been ill six weeks previously, complaining of headache and giddiness, but had no other symptoms,

TABLE VII.

Table showing cases in which several bacilli were tested with patients' blood.

Name.	Age.	Day of Illness.	B. Typhosus (1-50).	Maximum dilution in which positive result obtained with B. Typhosus.	B. Coli (1-50).	B. Gaërtner (1-50).	Paratyphoid A (1-50).	Paratyphoid B (1-50).	Remarks.
R. M'K.	5	14	Partial reaction in 1 hour	......	Partial reaction in 1 hour	No clumping	Slight clumping	Slight clumping	Mild—Delayed Widal
		19	Do.	......	Do. nearly complete	Do.	......	... ..	
		24	Complete	(1-100)	Very slight clumping	......	......	......	
G. R.	1¼	7	Very little clumping	......	Considerable clumping but not complete	Very slight clumping	......	......	Moderately severe—Delayed Widal
		14	More marked but not complete	......	Do.	......	......	......	
		18	Do.	......	Do.	.. ...	......	......	
		21	Complete	(1-100)	Less marked than prev.	......	......	......	
M. C.	23	14	Practically no clumping	......	......	......	......	... ...	Severe
		25	+	(1-50) in one hour	......	......	......	......	
S. M'F.	19	12	Slight clumping	......	Slight clumping	......	......	......	Severe—Fatal
		20	+	(1-50) in one hour	Do.	......	......	......	
J. R.	55	7	No clumping	......	No clumping	......	......	......	Severe—Fatal
		13	Do.	......	Do.	......	......	......	
B. R.	20	8	Slight clumping	......	Partial reaction	......	......	......	Severe—Fatal—Hæmorrhage
		14	Do.	......	Do.	......	......	......	
		20	Do.	......	Do.	......	......	......	
A. C.	30	16	No clumping	......	Very slight	No clumping	Very slight	+	Complete in ½ hour
		24	Do.	......	Do.	......	......	+	Complete in 1 hour in (1-200) and
		31	Do.	......	......	......	......	+	in (1-300) in 2 hours
F. M'N.	24	10	Do.	......	Partial reaction	+ in 1½ hours	......	Very slight	Not clump in higher dilution than (1-50)
		15	Do.	......	Do.	+	......	Do.	Complete in (1-100) in 1½ hours
Mrs W.	30	27	+	(1-1000) in 2 hours	......	......	Slight clumping	Slight clumping	
J. R.			+	(1-1000) in 1¾ hours	Slight clumping	......	......	......	
H. B.	33	16	+	(1-500) in 1 hour	......	......	......	......	Tubercular Peritonitis
Mrs M.	18	16	......	......	......	......	......	......	
		24	......	......	......	......	......	......	Mild case
J. S.	12	22	+	(1-300) in 2 hours	......	......	......	Very slight clumping	Moderately severe
J. G.	37	13	+	(1-100) in 1½ hours	......	......	......	......	Moderately severe
Mrs C.	17	22	+	(1-200) in two hours	......	......	......	......	Influenza—Previous typhoid
J. P.	24	12	+	(1-50)	......	......	......	......	Influenza
M. F.	12	15	......	......	......	......	......	......	Influenza
A. G.	50	12	......	......	......	......	......	......	Abortive case
A. M'L.	3½	14	+	(1-100)	Slight clumping	......	......	......	Very severe case
R. B.	30	?	+	(1-250)	Do.	......	Slight clumping	Slight clumping	Pneumonia
J. L.	29	7	......	......	......	......	......	......	Severe—Fatal
T. B.	48	8?	+	(1-50)	......	......	......	......	Mild—Delayed Widal
M. M'C.	9	24	+	(1-100)	......	......	......	......	Scarlatina Anginosa
H. M'C.	8	14	......	... ..	Very slight clumping	......	......	......	Gastro-enteritis
M. D	5	14	......	......	Do.	......	......	......	Acute miliary tuberculosis
T. B.	4	16	......	......	......	......	......	......	Tubercular Peritonitis
D. S.	16	21	......	......	Very slight clumping	......	......	......	Mild case
J. W.	16	16	+	(1-100)	......	......	......	......	Protracted and severe
J. M'C.	9	14	+	(1-50)	......	......	......	......	Severe—Fatal
Mrs W.	23	10	+	(1-500)	......	......	......	......	

and was in bed for only two days. On admission, beyond a leucopenia of 4687·5 she had no indication of having had typhoid, but her blood gave a positive Widal's reaction. The diazo reaction was not present, but bacilluria developed on the second day after admission.

Case III.—M. M., aged 2 years, was admitted with a brother and three sisters who were suffering from typhoid fever. She had been going about suffering from an occasional diarrhœal flux, for six weeks previous to admission. On admission, there were no symptoms of typhoid, but the Widal's reaction was positive.

My own experience, therefore, leads me to the opinion that the Widal's reaction is of great value in diagnosis, provided proper attention be given to the technique, and neither too low a dilution be employed, nor too long a time limit allowed. It must be borne in mind, that owing to its occasional delay in appearing, and its habit of intermitting, if a negative result be obtained at first, repeated examinations must subsequently be made. We must also bear in mind the possibility of retention of typhoid agglutinins in the blood from a previous attack of the disease. Bearing these all in mind, we can rely upon it, and it enables us to recognise mild and atypical cases, which would probably otherwise escape detection. It is, as we have seen, a valuable aid in retrospective diagnosis. Some underrate its value, because it does not usually appear until the end of the first or beginning of the second week after splenic enlargement is detectable and the roseolæ have appeared, but there is this to be said for it, that when present, it is distinctive, and is present in a much greater proportion of cases than either the eruption or the enlargement of the spleen. Moreover, it is present, and in as great intensity, in the mild and atypical and otherwise unrecognisable cases as in the severe, which considerably enhances its value in diagnosis. Moreover, it indirectly leads us to the diagnosis of the closely allied but bacteriologically different disease, paratyphoid fever. In those cases which clinically seem to be typhoid, and in which the reaction with bacillus typhosus is awanting, it behoves us to test the blood with some of the paratyphoid organisms, and if a well-marked reaction be obtained in a high dilution with one member of the group to the exclusion of the others, then it is probable that this bacillus is the causal factor in the disease. I had two such cases under my own care, one clumping the bacillus enteritidis (Gaërtner), and the other paratyphoid B. (See appendix).

Typhoidal bacilluria.—Bacteriuria is the term applied to the condition of the urine in which bacilli are found. This condition was first pointed out by Sir William Roberts in 1881, but attracted little attention at the time. Later, in 1896, Krogius called attention to it, but the credit of first describing a case of cystitis with this condition of the urine due to the bacillus typhosus is due to Melchior. Regarding its frequency in typhoid, there is more or less unanimity of opinion among observers. Thus, Horton-Smith observed it in 28 per cent. of cases, Richardson of Boston in 22·5 per cent. Muir says it occurs in about 25 per cent., Curchmann in 25 to 30 per cent., and Osler says it is present in one-third of the cases. My own observations place its presence at a higher percentage, for I noted it in 36 out of 98 cases in which it was looked for, or 36·7 per cent.

The bacilli may be present in enormous numbers, causing a diffuse turbidity, and if a glass containing such urine be held up to to the light and gently shaken, a peculiar shimmer is noticeable, resembling that produced by a bouillon culture, which is turbid. Such a shimmer at once distinguishes a turbidity due to bacilli from that caused by mucus, phosphates, or urates in suspension, the explanation being that the bacilli are able to catch and reflect the light in a manner in which the latter cannot. This peculiar or " bacilluric " shimmer has been commented upon at some length by Horton-Smith in his Goulstonian Lectures. If urines from typhoid fever patients be examined systematically for the bacilli, it will be found that in the positive urines turbidity is the rule ; those cases with clear urine, in which bacilli are only detected by culture examination, being the exception. Thus, Horton-Smith, in fourteen cases examined for this purpose, found turbidity in twelve, only two being noted as clear. The appearance of the urine containing the bacilli varies considerably, however, according to my observations, this depending almost exclusively on the day of illness. In the few cases in which it occurs during the height of the fever, the concentrated urine is high in colour, and the shimmer is not so distinct as in those where the urine is pale, occurring later in the disease.

Date of appearance.—Curchmann says that the bacilli do not usually appear in the urine before the 15th day, while Horton-Smith says it is rare to find the bacilluric shimmer before the third week, although he has observed it in one case on the 13th day, and was of the opinion that it had been present earlier. My results are, however, slightly at variance with the statements of these two observers, as the table shows. In no fewer than 4 did I observe it on the seventh day of the disease, in 1 on the ninth, in 1 on the tenth, and in 2 on the twelfth ; 9 showed it during the third week, 3 during the fourth week, 8 during the fifth week, 6 during the sixth week, 1 in the seventh week, and 1 in the eighth week. As the table shows in the remarks on the condition of the urine, the colour varied. In the four cases in which it was present on the seventh day, the urine was dark amber in colour, and had a slight or marked deposit of mucus,

while the supernatant fluid showed the characteristic shimmer. From my observations on the condition, we have three types of urine exhibiting it :—

I.—Urine dark amber in colour, with or without mucus.

II.—Pale urine showing only the bacilluric shimmer.

III.—Pale urine with deposit of pus, and exhibiting the shimmer in the supernatant fluid.

In one of my cases, that noted on the 12th day, there was in addition, a trace of blood. Microscopically, the urine shows bacilli exhibiting motility, some-times very active, at others sluggish, this latter condition being usually associated (as I have noted) with the long filamentous forms. Pus cells are frequently noted. There seems to be a consensus of opinion among the few writers on this subject as to the frequency of associated pyuria. From my own observations, I conclude that it is difficult to draw a hard and fast line between simple bacilluria and cystitis. In Horton-Smith's series 50 per cent. showed pyuria, while in my own 16 showed it, or 44·4 per cent. The degree of pyuria varies markedly from an occasional pus cell detectable microscopically in some cases, to a marked deposit of pus. In the latter cases, probably a true typhoidal cystitis exists. Horton-Smith's theory as to the pathology of the condition is the one that has gained most support. He believes that the bacilluria is due to the infection of the urine by a stray bacillus excreted by the kidney from the blood, and its multiplication in the bladder urine. If retention occurs, or if the bladder wall be damaged, then a true cystitis results. The reaction of the urine in typhoidal bacilluria is generally acid, the bacillus typhosus not having the power to decompose urea. In my own cases, 28 were markedly acid, 6 faintly so, and 2 were neutral.

We must recollect, however, that bacteriuria may be due to other organisms than the bacillus typhosus. I observed the characteristic turbidity and shimmer, with pale urine, in two children during the first afebrile week of scarlet fever. The naked eye appearance of the urine was practically that of typhoidal bacilluria, but micro-scopical examination, followed by cultures, showed the organism in both cases to be the streptococcus pyogenes. Again, in two female cases, a child and an adult, who were suffering from typhoid fever, bacilluria was noted, but examination of the organism, by culture methods, showed it in both cases to be the bacillus coli. This is the organism to be specially guarded against before concluding that a case of bacilluria in typhoid is due to the bacillus typhosus, and that for two reasons—(1) the bacillus coli can easily penetrate the damaged intestinal wall ; and (2), the chances of contamination by this organism in the female are considerable. We must, therefore, take precautions to guard against contamination, if reliable results are to be obtained. The method which I adopted was as follows :—In the case of the male, I cleansed the glans and prepuce with (1-20) carbolic lotion, and passed a sterilized catheter, running the urine into two sterilized ward urine

specimen glasses. I kept the second tube for examination, the first usually being discarded. With the female cases, I made the charge nurse use the same precautions as I adopted, but in addition made her carefully sponge the skin for several inches around the genitalia, before passing the catheter. Having obtained the specimens, I inoculated agar tubes with one or two loopfuls of the urine, and allowed the remainder to stand in the urine glass, the mouth of which was carefully closed with a plug of cotton wool. In those cases with no turbidity, if any sediment formed, I later made cultures from it, in addition. If growth appeared on the agar, I submitted it to the usual tests for the identification of the bacillus (*q.v.* later).

Value of bacilluria in diagnosis.—Although it is only within the past few years that attention has been paid to this subject, those who have instituted enquiry into the condition of the urine have found it an important diagnostic aid. The chief objections to it are its late development, usually after the other signs have made their appearance, and the small percentage—occurring in about one-third of the cases. It must be remembered, however, as my statistics show, that it may on some occasions appear early in the disease, the 7th day, before roseolæ or splenic enlargement have been detected. Again, it occurs with almost equal frequency in the mild and in the severe cases, and in the atypical cases, and it is thus of importance in that it is chiefly in the last type of the disease that bacilluria and other bacteriological aids are required for clinical discriminative purposes. As a restrospective diagnostic agent, it is the only one which we have, in addition to the Widal test (except during convalescence when the differential leucocyte count may aid us). It is known to persist in many cases long after the patient is convalescent and has returned to his home, and thus the recognition of the condition is important also from a public health view point, as a patient with such a condition is a serious menace to his neighbours. I might here quote two interesting cases from my series, which illustrate this latter point, and also the value of bacilluria in retrospective diagnosis. I admitted to hospital, patients from two separate outbreaks of typhoid in miners' rows, and in both cases the infection was traced to a child. The child in each instance had had a slight ailment, but had only been in bed for a day or two, after which it got up and about. These children, although convalescent, were removed with the others from the house to hospital, and in both cases, the urine showed bacilluria, in one on the day of admission, and in the other two days later.

On seeing the bacilluric shimmer, before concluding that the condition under examination is typhoid, we must remember that such a diagnosis can only be founded on specific bacilluria, *i.e.*, due to the bacillus typhosus, and we must submit the urine to careful cultural and morphological tests to establish the identity of the bacillus in question. One point which must not be overlooked, and to which too little attention has been paid, is that, like the Widal reaction, only in a more marked degree, it has a liability to intermit, being present for several days in succession,

then disappearing to return again. Time and again I have observed this, so that if a negative result is obtained at the first inspection of the urine, the latter should be daily examined before declaring the condition to be absent.

TABLE VIII.

Table showing cases with bacilluria and date of its appearance.

Name.	Days of illness on which Bacilluria occurred.	Condition of Urine.	Remarks.
Mrs W.	27 to 29	Clear, acid, no deposit	Fatal case
T. M.	17	Pale, turbid, shimmer, pus	Do.
J. R.	21	Dark amber, acid, turbid, pus cells	Severe case
J. S.	34	Pale urine	Mild
A. M.	27 and 30	Do.　　　pus deposit	Do.
J. R.	21	Do.	Do.
Mrs R.	41 to 71	Pale, neutral, pus cells	Severe
W. H.	24	Dark amber, pus cells	Moderately severe
M. M.	6th week	Pale, shimmer	Retrospective diagnosis
J. M'M.	6th week	Do.　　　pus deposit	Mild case
T. W.	44	Do.	Mild case
R. B.	3rd (?) week	Dark amber, shimmer	Ambulatory case
B. C.	21 and 41	Pale, shimmer	Mild case
G. R.	36	Do. slight pus	Do.
A. R.	9	Dark amber—turbid—Some blood—pus	Moderately severe
Mrs T.	43	Pale, shimmer	Do.
Mrs B.	18, 45, and 56	Pale, turbid, pus cells	Severe case
J. C.	14 and 19	Pale	Mild
H. M'V.	32	Pale, slight pus	Do.
M. M'C.	51	Do.	Do.
S. H.	12 and 43	(1) Dark amber, (2) pale	Severe and protracted case.
J. R.	29 and 43	Light amber, pus	Severe
R. B.	7 and 11	(1) Dark amber, turbid, pus, (2) pale	Severe
M. M'V.	7 and 21	(1) Dark amber, (2) pale	Moderately severe
J. W.	10 and 27	Pale, no turbidity	Mild
M. M'N.	18 and 20	Amber, mucus-like deposit	Mild
T. T.	29	Pale, pus	Mild
D. M'K.	32	Pale, slight pus	Severe case
Mrs S.	12 to 18	Light amber, turbid	Moderately severe
J. R.	7	Dark amber, mucus	Fatal
L. D.	28	Pale, turbid, pus	Mild
D. S.	16, then 29 to 31, and on 56	Pale, turbid, no deposit	Severe case
J. H.	19, 25, 31	Pale, turbid, pus	Moderately severe
B. R.	7	Dark amber, considerable mucus	Fatal on 9th day
J. W.	14	Dark amber, mucus present	Moderately severe
J. B.	27	Pale urine, turbid, no deposit	Mild case

Photographs showing bacilluria.—The glass on the extreme left shows the typical shimmer; that next, mucus; the third, mucus in suspension, and deposit of urates; the one on the right, urates in suspension.
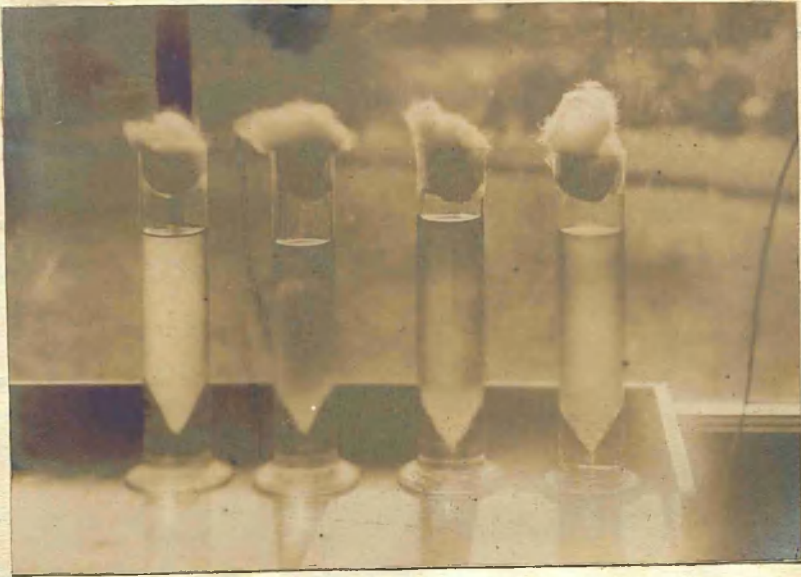
Bacteræmia is the term applied to denote the presence of bacteria in the circulating blood, and is a condition associated with a number of acute infections, although it is not always possible or easy to demonstrate the specific organism by the bacteriological examination of the blood. It is only within the past five or six years that success has attended attempts to isolate the bacillus typhosus from the blood. The earlier attempts ended in failure, and some of those who had repeated failures went so far as to deny the existence of the bacillus in this medium. Subsequent methods of examination have proved the fallacy of such a statement, and have demonstrated beyond doubt that typhoid is a septicæmia. Among those who, adopting the older methods, of directly drawing off a few drops of blood and inoculating media directly therewith, failed in their search for the bacillus, were Gaffky himself, Chantemesse, and Widal, while Fraënkel and Silvistrini

were only successful in a few cases. The reasons for these failures were two (1) they employed too little blood, only withdrawing a few drops; and (2) the employment of the blood undiluted permitted the destruction of the bacilli by the bactericidal action of the former, this property being probably more potent in stagnant than in the circulating medium. With the adoption, however, of the dilution method, originally introduced by Castellani in 1899, better results were obtained. This authority himself obtained positive results in twelve out of fourteen cases, and Courmont and Lesieur were successful in 33 out of 37 cases. Among others who have reported successful results are Richardson, Curchmann, and Neufeld. By diluting the blood immediately after its withdrawal, with a large quantity of bouillon, the bactericidal property of the former is greatly weakened, and the agglutinins are considerably diluted.

Technique.—The method of procedure which I adopted was a modification of that advocated by Castellani. As it is of the greatest importance to prevent contamination of either media or instruments absolute asepsis is essential. I cleansed the skin over the whole arm with soap and water, followed by turpentine and then methylated spirits, as in the preparation for an aseptic operation. Then a (1-20) carbolic dressing was laid on for an hour or two, and immediately before starting, the skin was again bathed with (1 to 20) carbolic, which was finally removed by a sterilized swab. Having thoroughly sterilized a Parke Davis & Co. serum syringe of 10 c.c. capacity, I selected a prominent superficial vein near the bend of the elbow or middle of the forearm, and inserted the needle into it in an upward direction, with one gentle push. This is a procedure which is easily carried out in adults, and it is easy to ascertain whether one has penetrated the vein or not, as the needle, after penetrating the more resistant structures, can be felt to suddenly slip into the vein. In children the veins are not so prominent, and the procedure is attended with more difficulty. If, however, pressure be made for a second or two above the elbow before puncturing, the vein becomes more prominent. This, however, is not advisable unless absolutely necessary, for the reason mentioned, that the bactericidal property of the blood thus temporarily arrested is greater than when in circulation. The piston having been pulled out, the syringe readily and quickly fills with blood, after which the needle is withdrawn, and the blood is divided among three flasks, each containing 100 c.c. of sterlized bouillon. The puncture in the skin can be covered with collodion. The three flasks are thoroughly shaken up to intimately mix the blood and bouillon, after which they are placed in the incubator at 37oC. Most authorities advocate even greater dilution of the blood, than I adopted. If examined at the end of twelve hours, in many cases, it will be found that the blood has settled to the bottom of the flask, and the supernatant fluid shows a diffuse turbidity. On the other hand the turbidity may not develop until 18 or 36 hours afterwards. I have on several occasions observed that the supernatant fluid was quite clear at the end of 18 hours, and if one or two loopfuls were removed and stroked on agar,

no growth developed, but if then the whole flask were thoroughly shaken and placed again in the incubator for another twelve hours, and a few loopfuls removed and placed on agar, growth appeared. The explanation of this I cannot positively give, but I thought that while the bactericidal property of the blood had been destroyed by the bouillon, the agglutinins had not been sufficiently diluted to prevent the few bacilli being clumped at the beginning and falling to the bottom.

As regards the frequency with which positive results can be obtained, most authorities who, so far, have investigated the matter are agreed more or less. Castellani obtained positive results in 85 per cent. of cases examined, Courmont in 89 per cent., while other observers place the percentage at 75. My own results come pretty near to these. In 42 cases examined for the bacillus, I obtained a positive result in 33 or 78·7 per cent. Of the positive cases it is noteworthy, that the majority were severe or moderately severe cases, while of those in which a negative result was obtained, two were fatal. A growth was obtained from the blood of one of the latter, which proved to be staphylococcus albus. As my precautions against contamination were very carefully carried out, I was inclined to regard this as an example of what Da Costa has called attention to, viz., that in the later stages of the disease, pyogenic bacteria are sometimes found. This was a protracted case. The growth on agar, obtained from one of the cases, proved on subsequent examination not to be the bacillus typhosus, but to be identical with paratyphoid B. The remaining negative cases were all mild, one of them being admitted, and his blood examined in relapse. One which showed no growth, gave also a negative serum reaction with bacillus typhosus, but clumped bacillus Gaërtner in a dilution of (1-100). The following table shows some of the points in connection with these results.

TABLE IX.

Table showing results of examination of blood for bacillus.

Name.	Age.	Day of Illness.	Result.	Remarks.	Name.	Age.	Day of Illness.	Result.	Remarks.
M. B.	19	10	+	Severe	J. M'G.	12	13	+	Moderate
Badavisk (Pole)	20	?	+	Severe case	S. M.	16	5	+	Mild
J. Smit (Pole)	24	?	+	Severe case	D. M'K.	13	8	+	Very severe
M. S.	16	8	+	Fulminant, fatal	J. S.	13	12	+	Moderately severe
A. R.	13½	7	+	Moderately severe	M. M'V.	9	4	+	Moderately severe
J. R.	16	4	+	Abortive	J. A.	6	7	+	Very severe
H. B.	33	15	+	Staphylococcus	P. M'L.	9	10	+	Moderate
T. M.	9	12	+	Severe, fatal	A. M'J.	12	8	+	Mild
S. H.	30	11	+	Severe, protracted	J. F.	24	12	+	Moderate
M. C	23	13	+	Delayed Widal, very severe	J. L.	29	6	—	Pneumonia
					G. S.	18	10	—	Mild
A. S.	10	10	+	Severe	J. R. (Pole)	25	15	—	Mild
J. S.	21	9	+	Moderate	F. M'N.	20	10	—	Paratyphoid, mild
S. M'F.	19	8	+	Severe, fatal	J. S.	12	22	—	Mild
J. M'C.	9	11	+	Severe, protracted	J. G.	37	30	—	Examined during relapse
H. B.	8	9	+	Mild					
B. R.	20	5	+	Fatal	J. T.	14	20	—	Mild
A. C.	30	10	+	Fatal, paratyphoid	J. M. (Pole)	28	?	+	Moderately severe
M. M.	10	12	+	Mild	J. C.	18	10	+	Mild
M. K.	7	8	+	Moderately severe	M. R.	17	6	+	Severe
J. R., Senr.	55	7	+	Fatal	W. N.	11	8	+	Very severe
J. R., Junr.	23	11	+	Severe	T. G.	8	16	—	Mild

NOTE : + means positive result ; — means negative result.

Recognition of bacillus.—It is not sufficient to conclude that, because we have obtained a growth on solid media from the blood of a person suffering from an affection which, in its clinical aspects, resembles typhoid, the bacillus in question is the bacillus typhosus. Such a growth may be due to bacillus coli, or a member of the paratyphoid group of organisms, or there may be more than one micro-organism present, as occurs in a mixed infection. We must, therefore, submit the bacillus so isolated to certain morphological and cultural tests, in order to establish its identity beyond doubt. Among the principal tests, the following are the most important, and are those which I employed, except the last mentioned (Pfeiffer's), which cannot be applied unless under circumstances attended with difficulty :— (1) Motility ; (2) Agar stroke ; (3) Litmus-lactose-media ; (4) Dextrose gelatine-shake cultures ; (5) Litmus milk ; (6) Medium I. Proskauer and Capaldi ; (7) Medium II. do. ; (8) Indol test ; (9) Agglutination test ; (10) Pfeiffer's test.

The following table shows the results so obtained :—

TABLE X.

Name of Patient.	Agar Slope.	Litmus Lactose.	Dextrose Gelatine (shake)	Litmus Milk.	Proskauer and Capaldi.		Indol Test.	Bacillus tested against Blood from known Typhoid Patient	Stock Culture of B. Typhosus tested against Blood from known Typhoid Patient.	Stock Culture of B. Typhosus tested against Patient's Blood.	
					Medium I.	Medium II.					
M. C.	Bluish grey	...	...	Acidity—no curdling	...	Growth and Acid	...	Blood from Mrs W. (1-300) +	Mrs W. (1-1000) +	(1-100) +	
M. B.	,,	...	...	,,	...	,,	...	T. M. (1-200) +	T. M. (1-200) +	(1-200) +	
Badavisk (Pole)	,,	...	...	,,	...	,,	...	M. R. (1-500) +	M. R. (1-400) +	(1-500) +	
J. Smit (Pole)	,,	...	...	,,	...	,,	...	M. T. (1-200) +	M. T. (1-200) +	(1-500) +	
M. S.	,,	...	...	,,	...	,,	...	C. M. (1-100) +	C. M. (1-100) +	(1-20) —	
A. R.	,,	...	...	,,	...	,,	...	A. A. (1-200) +	A. A. (1-300) +	(1-200) +	
Janet R.	,,	...	...	,,	...	,,	...	J. S. (1-100) +	J. S. (1-200) +	(1-100) +	
H. B.	,,	...	...	,,	...	,,	...	J. S. (1-200) +	J. S. (1-200) +	(1-200) +	
T. M.	,,	...	...	,,	...	,,	...	Janet R. (1-200) +	Janet R. (1-200) +	(1-200) +	
S. H.	,,	...	...	,,	...	,,	...	A. M. (1-50) +	A. M. (1-50) +	(1-300) +	
A. S.	,,	...	...	,,	...	,,	...	J. B. (1-100) +	J. B. (1-100) +	(1-100) +	
J. S.	,,	...	...	,,	...	,,	...	M. H. (1-500) +	M. H. (1-400) +	(1-200) +	
S. M'F.	,,	...	...	,,	...	,,	...	J. B. (1-100) +	J. B. (1-100) +	(1-50) +	
J. M'C.	,,	...	...	,,	...	,,	...	M. H. (1-300) +	M. H. (1-400) +	(1-100) +	
B. R.	Separate colonies	...	...	,,	...	,,	...	W. H. (1-100) +	W. H. (1-100) +	(1-20) —	
M. M.	Bluish grey	...	...	,,	...	,,	...	W. H. (1-100) +	W. H. (1-100) +	(1-100) +	
M. K.	,,	...	...	,,	...	,,	...	A. R. (1-50) +	A. R. (1-100) +	(1-500) +	
J. R. (Senior)	Separate colonies	...	...	,,	...	,,	...	D. M. (1-50) +	D. M. (1-50) +	(1-20) —	
J. R. (Junior)	Bluish grey	...	...	,,	...	,,	...	A. R. (1-100) +	A. R. (1-100) +	(1-100) +	
J. M'G.	,,	...	...	,,	...	,,	...	W. H. (1-50) +	W. H. (1-100) +	(1-1000) +	
S. M.	,,	...	...	,,	...	,,	...	T. M. (1-100) +	T. M. (1-2co) +	(1-500) +	
D. M'K.	,,	...	...	,,	...	,,	...	D. M. (1-50) +	D. M. (1-50) +	(1-50) +	
John S.	,,	...	...	,,	...	,,	...	M. H. (1-300) +	M. H. (1-400) +	(1-100) +	
M. M'V.	,,	...	...	,,	...	,,	...	M. H. (1-200) +	M. H. (1-400) +	(1-300) +	
J. A.	,,	...	...	,,	...	,,	...	J. M'G. (1-800) +	J. M'G. (1-1000) +	(1-200) +	
P. M'L.	,,	...	...	,,	...	,,	...	J. B. (1-200) +	J. B. (1-100) +	(1-50) +	
J. F.	,,	...	...	,,	...	,,	...	J. M'G. (1-600) +	J. M'G. (1-1000) +	(1-50) +	
J. M. (Pole)	,,	...	...	,,	...	,,	...	J. B. (1-100) +	J. B. (1-100) +	(1-100) +	
J. C.	,,	...	...	,,	...	,,	...	J. M'G. (1-800) +	J. M'G. (1-1000) +	(1-200) +	
M. R.	,,	...	...	,,	...	,,	...	John R. (1-1000) +	John R. (1-1000) +	(1-100) +	
W. N.	,,	...	...	,,	...	,,	...	Janet R. (1-50) +	Janet R. (1-200) +	(1-500) +	
A. C.	White and more opaque	...	Gas	Acid then alkaline—no curdling	Slight growth—no acids	,,	Slight	Mrs W. (1-50) + very slight attempt at clumping	Mrs W. (1-1000) +	Bacillus tested against patient's own blood gave + result (1-300) two days after isolation	Stock culture of B. Paratyphoid B tested against blood of A. C. gave + result (1-500)

I may add, however, that for convenience, and as a saving in time, I resorted to the serum agglutination test first, and thus was often able to say that the bacillus was that of typhoid within 36 hours from the time of admission of the patient. I tested the bacillus against the blood of a genuine case of typhoid in the wards, and one which agglutinated the stock bacillus typhosus in dilutions of (1-300) and (1-500). This is by far the most rapid method of arriving at an approximate idea of the identity of the bacillus under consideration, and certainly of all the tests, it is by far the best (except Pfeiffer's) and most reliable. As some of the cultural tests can be imitated very closely by members of the paratyphoid group, and even by the bacillus coli, they become individually of comparatively little value, and are only guides taken in conjunction with others. Moreover, they require some time for their complete development.

Value in diagnosis.—From the foregoing we see that we have in the blood examination and culture, a valuable aid in the discrimination of typhoid, and one which is certain and available in the early days of the disease before either the Widal reaction can be obtained or before the development of the cardinal symptom complex. Hence its great value where practicable. Unfortunately, its application is practically limited to hospital practice, and this is its only drawback. Its value as a sure diagnostic agent cannot be exaggerated, as it enables us to distinguish between typhoid proper and paratyphoid due to organisms other than the bacillus typhosus, and leads us to a correct diagnosis in obscure, atypical, or aberrant forms, so frequently seen in children, or in early cases before the development of the Widal's reaction, or later where the latter is delayed or wanting, and it facilitates diagnosis in cases of mixed infection in typhoid. From the examination of the table, it will be seen that I obtained a positive result in 7 cases in the first week—in one on the 4th day, in two on the 5th, in one on the 6th, and in three on the 7th day of illness. In no fewer than 8 cases, was I able to isolate the bacillus before the development of the Widal reaction.

The bacillus may be isolated from other sources during the illness. They are invariably present in the fæces during the first week, but the great difficulty in their isolation lies in separating them from the bacillus coli which in this affection are greatly increased beyond the usual numbers. Several media have been introduced to assist in their separation. After repeated trials with different media, including Elsner's and MacConkey's, attended with indifferent results, I gave it up, finding that I could islolate them with less difficulty from other sources. The spleen also contains them in varying nnmbers during the attack, and many clinicians advocate splenic puncture as a means of isolating the bacillus for purposes of diagnosis. As the bacilli are often grouped in small colonies in this organ, a single puncture may fail to find them. The chief objection to this procedure however, and the one which deterred me from pursuing it, is that it is not unattended with danger to the patient. Lumbar puncture has also been resorted to by some. I cannot, however, speak from experience of any of the latter methods, as I entirely discarded them, the first by reason of the great difficulty attending the separation of other closely allied bacilli and the unreliable results which I obtained, and the latter two, on account of the attendant risk to the patient.

Resume.—In the preceding pages, I have called attention to the different means at our disposal for the proper identification of the affection due to the bacillus typhosus, and have attempted to show the close relationship which exists clinically between it and affections due to other organisms, leading to confusion in diagnosis, and I have ~~attempted~~ *endeavoured* to show the relative worth of each of these aids, as based upon my own experience from personal application of them. Before proceeding to deal with differential diagnosis, and to give illustrative cases from my own series, I would like to briefly summarize the chief points treated in the previous pages.

In a disease so diverse in its manifestations, and so variable in its course, at one time pursuing a course characterized by the presence of all the cardinal symptoms, and almost answering a text-book description, at another, running a short, mild course with paucity of signs, or running a protracted course, or it may be pursuing a rapidly fatal course in a few days, with no symptoms except high fever, and those pointing to a profound intoxication—difficulties in diagnosis must of necessity arise, especially if we have no knowledge of the immediate circumstances attending the development of the illness. No one symptom is pathognomonic of the disease, the most distinctive of all the clinical data being the roseolous eruption. Even with the existence of that symptom complex so often mentioned by authors as distinctive of the disease (typical temperature curve, enlarged spleen, roseolæ, diarrhœa), in the light of our present knowledge, all we can say without bacteriological aid is, that we are dealing with an acute infectious process, due to the invasion of the body by some organism of the typhoid, coli, or intermediate group of organisms. To place the different data at our disposal for diagnosis in the order of their importance, I would say that the ideal method of diagnosing typhoid fever proper would be the rapid and certain demonstration of the bacillus typhosus during the disease. So far as our methods have yet gone, this has not been possible in every case, but a good percentage of positive results can readily be obtained. The isolation from the blood, with the technique which I practised, is comparatively easy and void of danger, but is practicable only in hospital. Splenic and lumbar puncture are fraught with danger, and are not to be recommended. Isolation from the stools is a procedure which is as yet attended with too great difficulties in the separation of the bacillus from bacillus coli. To cultivate the bacillus from the rose spots is fairly easy, but is scarcely necessary for diagnosis when that eruption is characteristically developed. My experience with cultures from the blood leads me to recommend the practice of it in doubtful cases. The percentage of positive results is very encouraging, and I have no doubt will yet be higher, especially if the procedure be carried out in all cases early, before the end of the period of defervescence when the bactericidal property of the blood has destroyed all the bacilli in the circulation. This method is of inestimable value in all early cases, especially the atypical, *i.e.*, the fulminant and abortive types with rapid onset, and gives a positive result before the development of the Widal reaction. It also enables us to discriminate mixed infections, and is the only certain method of recognising the paratyphoid cases. In

carrying out this procedure, I would be inclined to advocate even greater dilution than I employed, in order to make sure of the dilution of the agglutinins and lysogenic power of the blood.

Next in importance and accuracy to the above, is the serum-agglutination reaction, which if properly carried out, with a good and sensitive stock culture, incubated in bouillon for 12 hours previous to use, and with attention to details as regards dilution and time limit, gives valuable results. If done in a haphazard and careless fashion, using either too low a dilution or allowing too long a time limit, the results are unreliable and misleading. Many authorities using a dilution (1-20) allow one hour for a complete reaction, while others insist on a dilution of (1-50) with this time limit. The consensus of opinion, however, is that with the former an occasional serum may clump which is not typhoid, while with the latter an isolated case may be missed, the serum at the time of examination not having agglutinating powers so strong. In either case the margin of error is not a large one. Care, however, must be taken to simultaneously use a control, and also to make certain that before a reaction is returned as positive, complete cessation of motility of the unclumped bacilli has occurred. A positive reaction can be looked for in from 95 to 97 per cent. of cases. By the application of this test we are enabled to recognise atypical forms, to separate typhoid from paratyphoid cases, and to detect cases recovering from the disease, when no other evidence is present. In fact, for retrospective diagnosis it is the only certain agent we have, unless in those rare cases of late suppurative conditions (cholecystitis, osteomyelitis) recorded in the literature, where the bacillus may be obtained from the lesion in pure culture. We are also enabled by this means to distinguish typhoid from conditions simulating it at some period of their course, such as influenza, tubercle, typhus, suppurative conditions, malaria, etc.

Another important factor in diagnosis which is partly clinical, and in part bacteriological, is the specific bacilluria. I say partly clinical, because the characteristic shimmer can be recognised by the naked eye at the bedside, but bacteriological aid must be invoked to enable us to say that the bacilluria is specific and not due to organisms other than the bacillus typhosus. Care must be taken, however, if the test is to be of any value, that no accidental contamination of the urine occurs. It is not of such value as the serum-agglutination reaction, occurring as it does in only about one-third of the cases, but like the latter it is to be observed alike in severe and in mild atypical cases, and is often of value in retrospective diagnosis. In the majority of cases, however, it occurs late in the disease.

Of the clinical guides, the two most important are the specific roseolous eruption and the changes in the leucocytes. The eruption, when present, is distinctive, and can rarely be imitated by that of any other disease. It is true that cases have been reported of acute miliary tuberculosis, and secondary syphilis, in which a roseolous rash has been observed similar in appearance to that of typhoid. If, however, the date of appearance of the exanthem, its situation and its character be noted carefully,

and observations made as to whether or not it appeared in successive crops, I am of opinion that little doubt would be left regarding its true nature. I have mentioned a case of tubercular peritonitis with such a rash. Its value as a diagnostic agent is considerably impaired by the fact that it only occurs in a certain (not large) percentage of cases. It is frequently absent also, in those cases which give most trouble in diagnosis, the mild and abortive. Its non-appearance until the 7th day at the earliest causes it to be of no value in the early days of the first week, except in children, in whom it appears frequently on the 5th day. It is also present in paratyphoid fever. The scarlatiniform rash, appearing in the early days of the disease, might give rise to some trouble, but a leucocyte count would probably settle the matter.

Of great value in discriminating typhoid from most of the acute infections which resemble it, is the leucocyte enumeration, both absolute and differential. The total absence of leucocytosis in the first week, followed by a leucopenia later, serves to distinguish between this fever and typhus, septic infections, cerebro-spinal meningitis, tubercular affections with secondary pyogenic invasion, and several others, but does not differentiate it from malaria, influenza, measles, tubercular peritonitis, and acute miliary tuberculosis. On the other hand, the presence of complications, inflammatory or suppurative, may cause a leucocytosis, and such complications must be sought for before coming to a definite conclusion. It must be borne in mind, however, as previously mentioned, that a few cases, in the absence of any complication, never show a leucopenia. Valuable aid is also obtained from the differential count. In most acute infectious diseases there is an increase in the polymorphonuclears, but in typhoid these are progressively diminished during the illness. This, however, frequently occurs in influenza, and is present also in malaria, tubercular peritonitis and acute miliary tuberculosis. We have, however, one distinguishing feature in the behaviour of the large hyaline forms. These, which include the larger lymphocytes, large mononuclear forms, and transitionals, undergo a marked increase with the progress of the disease, a condition which has not been observed in any other affection except malaria (Rogers). The small lymphocytes are slightly increased, especially in children. From my own observations, I would say, that in no other affection do we meet with this group of changes in the leucocytes. It must be remembered, however, that these alterations are not marked during the first week of illness. In fact, in many cases, there is little or no departure from the normal rates, so that it is chiefly in the second and subsequent weeks, that it comes to be of diagnostic value. In the presence of an inflammatory or suppurative complication, however, the polymorphonuclears may be increased or raised to the normal percentage, so that in such cases, careful clinical search should be made for existing complications. As a retrospective diagnostic agent, it is some-times of service, for in many cases the altered ratio above mentioned persists for a few weeks after convalescence.

Of much less diagnostic value than the preceding is the diazo reaction of Ehrlich. It is present, and usually during the last days of the first week, in most cases of typhoid, but is perhaps a better negative than a positive test, on account of its comparatively frequent occurrence in other affections, and particularly in those that are most liable to be mistaken

for typhoid. Among these may be mentioned, acute miliary tuberculosis, typhus, measles, malaria, acute pneumonia. These facts considered, we see that it is only with relative infrequency that it has any decisive significance.

Enlargement of the spleen is another valuable guide, especially if it be perceived by palpation or percussion about the end of the first week, and is observed to be slightly or markedly progressive with the further course of the disease. Although present in some of the acute infections, in none of them does it persist so long. It must be remembered that it does not occur in all cases, being prevented in some by such complications as hæmorrhage, or profuse diarrhœa, or by antecedent disease of the organ. In some cases, owing to abdominal distension, it cannot be definitely palpated, and if the enlargement is only slight, it cannot be accurately mapped out by percussion.

Among the clinical guides to which great importance was formerly attached, to no one was more value attributed than to the course of the temperature. When following the typical course, the condition is unmistakable, but as experience shows, this does not occur in a large percentage of cases, and especially in children, in whom the disease is apt to be of short duration and of less intensity. The greatest difficulty is experienced in the fulminant, the abortive, the very mild, and in those in whom the fever pursues a more or less irregular course, and especially if rigors occur without evident cause. Under such circumstances, the temperature offers no guide whatever, and a diagnosis can only be arrived at if some of the other cardinal symptoms are present.

The character and rate of the pulse are often of inestimable value in discriminating typhoid from other closely resembling conditions. In no disease do relative infrequency and dicrotism occur so often as in typhoid, and especially is this the case with young, healthy patients, and with children over twelve years of age. In younger children and in infancy, these conditions of pulse are rarely found, but they may occur in people advanced in years. If the patient has been ill from some antecedent disease, these characters are not to be found. In influenza, however, they may both be present. In basilar meningitis, it is true, slowing occurs, but is more marked, and often accompanied by irregularity, but rarely by dicrotism. Though each is only of slight value, when both are simultaneously present, one would be suspicious of typhoid, and if another clinical sign were present, the diagnosis would probably be placed beyond doubt.

The condition of the stools does not bear the diagnostic significance formerly attached to them, for observation has shown that constipation is equally common with diarrhœa. When diarrhœa does occur, with peasoupy stools, the question of typhoid might be raised, but other symptoms must needs be present to make a diagnosis certain, for in such conditions as pyæmia, malignant endocarditis, and scarlet fever and diphtheria where there is hyperplasia of the intestinal lymphoid tissue, similar stools are frequently voided. Again, in infancy, the stools in typhoid may be greenish yellow, or of the appearance of café-au-lait.

Meteorism does not always occur in typhoid, and it occurs with such frequency in most conditions involving the intestinal tract, that in the discrimination of typhoid little value is to be attached to it.

Intestinal hæmorrhage and perforation are of more value when present, but fortunately they are of rare occurrence, being present in only a small percentage of cases. As a rule, they are somewhat late in development, but in ambulatory cases they may be the first indication of the disease.

Other signs which, though of less value, may be mentioned, as they may occur in atypical cases and give something of a clue to diagnosis.—Among these, are bronchitis, milaria crystallina, impairment of hearing, and epistaxis. Their chief value lies in their relative frequency in typhoid as compared with other diseases, and taken in conjunction with one or more clinical signs, are often of considerable aid.

The mode of onset and the prodromata may often not only create a suspicion of the existence of typhoid, but during an epidemic may warrant a diagnosis of such, and lead to early isolation of the case, not an unimportant point both from the view point of treatment and of public health.

Differential diagnosis—Having in the preceding pages pointed out the chief aids, clinical, hæmatological, and bacteriological, in the discrimination of typhoid, and the value to be attached to each, it remains for me to consider briefly some of the most important affections which are liable to be mistaken for it. Some of these conditions only bear a resemblance to typhoid during some stage of the disease, while others closely resemble it throughout the entire course. Among these, few give so much trouble in differential diagnosis as tuberculosis im some of its forms.

Acute miliary tuberculosis occurring in the so-called typhoidal form without local manifestations is an affection which, more frequently than all others, causes difficulty in diagnosis. Cases of this affection are frequently mistaken for typhoid, and many cases of typhoid are diagnosed as acute miliary tuberculosis, until the recovery of the patient suggests the correct nature of the ailment. The chief obstacle to diagnosis lies in the fact that both affections may exist for a time, without any evident local manifestations, while the general disturbance due to toxæmia may be as pronounced in the one as in the other. Engel regarded " both dyscrasiæ as a single albuminous dyscrasia." In the typhoidal form, splenic enlargement, meteorism, diarrhœa, roseolous rash, and intestinal hæmorrhage may completely simulate the picture of typhoid fever (Curchmann). Occasionally the disease sets in abruptly, but in most cases the onset, as in typhoid, is more or less insidious. The appearance of the patient may be a guide. In tuberculosis there is frequently cyanosis and difficulty in breathing, but in typhoid, if the bronchitis is extreme, the same conditions may be present. The course of the fever may assist, if the typical curve of typhoid be present. In acute miliary tuberculosis, the fever, as a rule, is scarcely so high as in typhoid, but is very irregular, and may show the inverse type. Irregularity, however, occurs frequently in typhoid,

especially in children, and in both conditions we may have the disease pursuing an afebrile course. The pulse rate in tuberculosis is usually increased proportionately to the temperature, and does not show the relative bradycardia so prominent in typhoid, which, however, is lacking in that disease in children. The spleen may be enlarged in both conditions, though more frequently in typhoid. Enlargement of this organ, however, beginning at the end of the first week, and progressing throughout the second and third weeks, is in favour of typhoid. A papular eruption, simulating in appearance that of typhoid, has been met with in acute miliary tuberculosis, but observation as to whether it appeared in successive crops would assist in the distinction. Meteorism and diarrhœa, with peasoupy stools, may occur alike in acute miliary tuberculosis and in typhoid, and even intestinal hæmorrhage may occur in the former. As regards the condition of the lungs, normal percussion resonance, dry snoring or sibilant râles may be detected in both conditions, and only later, a fresh irruption of tubercles in the lung, in miliary tuberculosis, leading to impairment of resonance in parts, and to prolongation of respiration, with a few subcrepitant râles may clear up the confusion which previously existed. The diazo reaction is present in a considerable proportion of cases of miliarytu berculosis, and so is of little value in the differential diagnosis. The more recent methods of examination, however, are really the only ones which enable a diagnosis to be made with certainty. Leucopenia is the rule in uncomplicated typhoid, while a slight leucocytosis, a normal count, or slight leucopenia may be present in miliary tubercle. The differential count is, however, of more value. The polymorphonuclear cells may show a slight increase, be normal, or even exhibit a slight diminution, while there may be a slight increase in the small lymphocytes, but we do not get a progressive increase in the larger hyaline forms, which more frequently than otherwise are not affected. The serum agglutination reaction usually clinches the diagnosis. With a dilution of (1-50) and a time limit of one hour, the blood of acute miliary tuberculosis never gives a positive reaction. Specific bacilluria and the examination of the blood for the bacillus of Eberth are other distinguishing tests. Those cases are of special interest, and cause greater confusion, where both conditions co-exist. Among my own series four children were admitted notified typhoid, but were found to be suffering from acute miliary tuberculosis. In two of these, but for the Widal's reaction being negative (1-20), one hour, there would have been difficulty in the diagnosis, particularly as they presented no local signs, and came from a typhoid infected district; of the other two, one later showed dissemination of tubercles in the lung, and the other in the cerebro-spinal system.

Of even greater clinical interest were two cases in which both diseases were present, or rather in both acute tuberculosis developed during convalescence from typhoid. One of these, a little girl, was admitted with her father, who had a genuine attack of typhoid. The child had been ailing with indefinite symptoms for four weeks prior to admission. Her appearance did not suggest typhoid, and

she had a leucocyte count of 10,000, the different elements bearing a normal ratio to each other. Careful examination failed to reveal any local lesion, except a few sibilant râles in her lungs. Her blood gave a positive Widal's reaction. A week later she developed several rigors, and examination of the lungs thereafter showed evidence of tubercular dissemination, and the child died ten days later. No post-mortem examination was allowed. That the child had had typhoid was beyond doubt, and she was probably the source of her father's infection. The other case was that of a nurse who contracted typhoid and died five weeks later from acute tuberculosis. Her blood gave a positive Widal's reaction on the eighth day.

Tubercular meningitis may be mistaken for typhoid in most cases where the convulsive phenomena are preceded by a prodromal stage characterized by nervous-ness, lassitude, a feeling of weakness and febrile disturbance lasting one or two weeks. Confusion may also arise if a case of tubercular meningitis is not seen until the stage of paralysis is reached with the development of the "typhoid" state. It must be remembered also that typhoid in children may be ushered in with convulsions, intractable headache, and photophobia. In adults occasionally the nervous symptoms are so pronounced as to cause some difficulty. We have several clinical guides to aid us. The roseolar eruption is never present in meningitis, while enlargement of the spleen is neither so frequent, so early, nor so marked as in typhoid. Constipation and retraction of the abdomen are the rule. The pulse may be slow in the latter period of the irritative stage, but shows usually in addition marked irregularity. Later in the disease, while the temperature is falling, the pulse increases in frequency. Vomiting is more marked in meningitis. The existence of an old tubercular focus or caseating glands, while it may strengthen the diagnosis of tubercle, would not preclude the existence of co-incident typhoid infection. In meningitis there may be a normal leucocyte count or slight leucocytosis, but leucopenia is not so frequent or so marked as in typhoid. The polymorphonuclears or lymphocytes may be slightly increased or diminished, but the large hyaline forms are never increased. The Widal's reaction is never positive in a dilution of (1-50) in tubercle. Examination of the blood and urine for bacilli are important aids.

Tubercular peritonitis.—Cases of this affection with insidious onset, abdominal pain and tenderness, tympanites, diarrhœa, and continuous fever are liable to be mistaken, for a time at least, for typhoid, and if, after waiting, the cardinal symptoms of typhoid fail to develop, the difficulty of diagnosis becomes greater. A family history of tubercle or the existence of a tubercular focus elsewhere, while strengthening the diagnosis of tubercle, would not necessarily preclude co-existing typhoid. The spleen may be slightly enlarged, though enlargement is less common than in typhoid. Diarrhœa and peasoupy stools may also occur. In the majority of cases, however, we have to depend upon other than purely clinical methods for diagnosis. The leucocytes may show a slight leucopenia, a normal count, or a slight degree of leucocytosis. The polymorphonuclears may be normal or diminished,

though they are more often slightly increased. If the lymphatic glands are involved to any extent, the lymphocytes may be increased, but the larger hyaline forms are not affected. The diazo reaction is often present, but the Widal's reaction is always negative in dilutions of (1-50) and upwards. Examination of the urine and the blood for bacilli render further assistance.

Latent tubercle.—Cases occasionally occur of this type, which for a time at least offer a considerable difficulty in diagnosis. In these cases, some of which puzzled even Murchison, there are tubercular deposits in parts of the body which repeated physical examinations fail to locate. The patient loses strength and begins to emaciate, and has more or less elevation of temperature, with or without nocturnal exacerbations. These cases are apt to be confounded with atypical typhoid, in which, it may be, none of the so-called cardinal symptoms are present. The pulse, however, is increased in rate relative to the temperature, and does not usually show dicrotism, but as previously explained, these two signs are more or less limited to cases of young, healthy males, and are not to be looked for in children, who form the greater number of the atypical cases. The further progress of the case, of course, settles the diagnosis, but this means delay, and if an early diagnosis is demanded, bacteriological and hæmatological methods must be resorted to. The diazo reaction may be positive. While a leucopenia is often present, and a reduction in the polymorphonuclears, there is never a progressive increase in the larger hyaline forms. The Widal reaction is negative in dilutions of (1-50) and upwards. Cultures from the blood and urine assist in the diagnosis.

Acute cerebro-spinal meningitis.—That pronounced cerebro-spinal meningitic symptoms may occur in the earlier days of typhoid fever, and may so thoroughly dominate the clinical picture that great difficulty in diagnosis may arise, must be remembered. The bulk of such cases occur in the class known as meningo-typhoid. There may be severe headache, photophobia, vertigo, hyperæsthesia, twitchings or convulsions. In such cases the real nature of the disease may only be appreciated when roseolæ or splenic enlargement develop, but in those pursuing a more fulminant course, death may occur before the end of the first week. The chief guides towards the diagnosis are the Widal's reaction, the leucocyte count, and the bacteriology of the blood. In all cases of cerebro-spinal meningitis in which the blood has been examined, a marked leucocytosis with increase in the polymorphoneuclears has been noted. The Widal's reaction is always negative. Lumbar puncture and culture examination of the blood will reveal the bacillus of epidemic cerebro-spinal meningitis.

In septic lepto-meningitis there is always a leucocytosis, and careful examination may show that there is an exacerbation of an old suppurating focus as in the middle ear.

Typhus fever. As the history of the two affections shows us, great difficulty may be encountered in differentiating between them during the early days of the

fever, and before the appearance of the distinctive rash, especially if there is no accurate history of exposure to the infection of one or the other. The physiognomy in the two diseases is different. In typhus the face is red and turgid, the conjunctivæ injected, the pupils contracted, and the whole face has a somewhat wild expression, differing from the dull, stupid expression of typhoid, with dilated pupils. The fever course in typhus shows abruptness in onset, and after running a shorter course terminates by crisis, but in the abortive forms of typhoid the same occurs, and in the fulminant type the onset is equally abrupt. The pulse may guide us, for in typhus it is increased correspondingly to the temperature, and does not show the relative bradycardia and dicrotism so frequently noted in typhoid. The rash when present is distinctive in each, appearing, however, earlier in typhus and later becoming petechial, but in children in typhoid the rash may appear as early, and in the hæmorrhagic cases may likewise become petechial. While diarrhœa and intestinal hæmorrhage are practically never present in typhus, they are, as previously mentioned, often absent in typhoid. The enlargement of the spleen is not so frequent in typhus, and when it does occur it is demonstrable earlier, and often disappears during the second week. The diazo reaction is frequently present. The leucocytes, however, are of considerable importance in discriminating between them. In typhus, according to some observers who have noted a few cases, and to Love, who has perhaps more than any other studied the changes in the elements of the blood in this affection, there is a leucocytosis with increase of the polymorphonuclears. This agrees with my own observation in three cases though I was unable to note a distinct increase before the end of the first week. Love, however, observed it from the beginning. The serum agglutination reaction is of course only of value after the end of the first week. Bacilluria, if present, may be a guide, but the most valuable of all, since positive results may be obtained as early as the middle of the first week, is the demonstration of the bacillus typhosus in the blood. In the event of a negative result being obtained, a subsequent examination would be necessary before deciding.

Pneumonia.—This affection may cause some confusion in diagnosis, either in the so-called pneumo-typhoid group, which begin with pronounced pulmonary symptoms, or in those cases of typhoid in which pneumonia develops in the course of the illness, and before the patient comes under our observation. Difficulty also arises in those cases of atypical pneumonia, particularly central pneumonia, in which there is some degree of delirium, and often no rusty sputum expectorated, and there is a complete absence of physical signs. No definite diagnosis may be arrived at for some days, by clinical examination alone, until the development of some distant tubular breathing or a little pleurisy. Such a case came under my own care, notified typhoid. The spleen is occasionally enlarged in pneumonia. The diazo reaction is often present. Diagnosis may, however, not be arrived at until a leucocyte count be made, the Widal reaction tried, or the blood examined and submitted

to culture tests. In pneumonia, unless in the very malignant cases, there is a leucocytosis with increase of the polymorphonuclears. The Widal's reaction is never positive in a dilution of (1-50). The diplococcus of Fraënkal may be cultivated from the blood.

Septicæmia and Pyæmia —Occasionally cases are met with, which, for a time at least, offer considerable difficulty in diagnosis. One form which is specially prone to present difficulty is *Cryptogenetic septicæmia or septico-pyæmia*, so called because that no primary focus of suppuration is evident during life. Those cases of this affection which occur without rigors are most liable to be mistaken for typhoid. It must, however, be remembered that, although rigors occur, still confusion may arise, as some cases of typhoid are complicated by severe rigors, frequently repeated, and with no demonstrable cause for such. Such a case is reported by Bolton. In the absence of rigors in this condition, the temperature may be of the continued remittent type. The pulse, however, is usually increased proportionately to the temperature. The spleen is frequently enlarged, and diarrhœa, sometimes with peasoupy stools, may be present. The diazo reaction may be present. Sometimes the development of an icteric tinge in the skin aids in the diagnosis, but sometimes typhoid also is complicated by icterus. As a rule, the diagnosis is only definitely settled by the leucocyte count, the Widal reaction, and the examination of the blood for bacilli. Leucocytosis is always present, and there is an increase in the polymorphonuclears. The Widal's reaction is negative. Bacilluria may occur, but examination of the culture shows the existence only of pyogenic cocci ; while cultures made from the circulating blood usually show streptococci and staphylococci. One such case came under my own observation, where no diagnosis was arrived at until shortly before death, and in which post-mortem examination established the diagnosis. Application of the foregoing tests, repeatedly applied, negatived the existence of typhoid during life.

Malignant endocarditis is another condition which is apt to create some confusion in diagnosis. In the typhoid type, so called from its similarity to that disease, the symptoms are less prominent than in the other forms, and the disease runs a more protracted course. The fever may be intermittent, or may not show such irregularity, as in the other forms. The tongue is dry and parched, and low muttering delirium is present. Diarrhœa is frequently present, and splenic enlargement occurs in a number of cases, while even parotitis has been observed. The cardiac symptoms are so slight as to cause them to be often overlooked. Later, however, the development of infarctions in some of the viscera, or of petechiæ, seals the diagnosis. Before such take place, and in the absence of the development of roseolæ, the diagnosis is extremely difficult, and can only be arrived at by making a leucocyte count, or applying the Widal test, or examining the blood for bacteria. Three cases of this affection came under my care notified typhoid, and in only one could the correct diagnosis be arrived at on clinical observation alone.

Occasionally an insidious simple endocarditis causes trouble, for a few days at least.

Puerperal septicæmia.—This form of septicæmia may occasionally cause some anxiety as to the diagnosis. If severe, and following a typhoid-like course, in the absence of a definite history, some difficulty might be experienced. On the other hand, the two conditions may co-exist. A leucocytosis is always present, with an increase in the polymorphonuclears, while the Widal's reaction is always negative. With the existence of a septic discharge, or an icteric tint of the skin, the diagnosis is more easy.

Acute osteomyelitis, in children especially, might, on the development of the "typhoid" state, cause considerable difficulty, if only seen then for the first time. Thorough examination for localized tenderness and swelling should be made, and with a previous history of a slight injury, such would justify the diagnosis. Later, the development of infarcts would place the diagnosis beyond doubt. A marked leucocytosis is always present, with increase in the polymorphonuclears, and the Widal's reaction is negative.

Appendicitis.—Occasionally this condition is mistaken for typhoid. I admitted one such, which was diagnosed as a case of the latter condition. The pain complained of may be general all over the abdomen, while there may be more tenderness over M'Burney's region than one finds over an inflamed Peyer's patch in the ileo-cæcal region. Vomiting may not be present, or only very slight, and diarrhœa may even be present. The spleen is not usually enlarged, though as in all acute affections it may be sometimes so, but is never progressive as in typhoid. The temperature curve may show no marked features. The pulse is increased proportionately to the temperature. Careful examination may later reveal slight swelling over the appendicular region, but as pathology has shown us, typhoid lesions of the appendix are not altogether unknown. There is always a leucocytosis. The serum agglutination reaction with bacillus typhosus is negative, unless in the typhoidal appendicitis. Cultures from the blood render assistance.

Influenza and pseudo-influenza.—There is no doubt that many of the mild and abortive cases of typhoid have been relegated to the category of influenza since this latter disease became prevalent. The two chief forms of this affection which bear a close resemblance clinically to typhoid are (*a*) the gastro-intestinal form, and (*b*) the protracted "febrile" form. In the former variety we have vomiting, abdominal pains, diarrhœa, and splenic enlargement in a proportion of cases. Several cases of this type were admitted under my care with a diagnosis of typhoid. Relative bradycardia is quite common. In its short course it bears a resemblance to the abortive forms of typhoid. The leucocyte count is usually about normal, or a leucopenia may be present, unless there are co-existing complications. The differential count does not show a marked progressive increase of the larger hyaline forms. The Widal's reaction is negative. Bacilluria and

blood culture may aid the diagnosis. (*b*) In the protracted " febrile " form, beyond malaise and a temperature curve showing remissions, we have no symptoms, and so it cannot be wondered that it may be regarded as one of the atypical forms of typhoid.

Malaria and typhoid are frequently confused with each other, especially if the latter develops in a person in a malarial district. Besides, typhoid and malaria may co-exist in the same patient. With remittent or continued fever, malaria may be mistaken for typhoid, and fulminant typhoid may be confused with pernicious malaria. Ambulatory cases of typhoid, if intermittency of temperature exists, may closely resemble malaria, especially if chills are present. In both conditions the spleen is markedly enlarged. As regards the leucocyte count, both affections show a leucopenia, and both show a diminution in the polymorphonuclears. In malaria the larger hyaline forms are much increased as in typhoid, but the lymphocytes are not affected, at least to any extent. The Widal's reaction is negative, while bacilluria is not present either. Examination of the blood will reveal the malarial parasite.

Gastro-enteritis.—Some cases of acute gastro-enteritis are apt to be confounded with typhoid fever, especially in children, and when from dietary indiscretion, the condition becomes protracted. Diarrhœa is profuse, and the stools in some cases may be peasoupy, while the spleen is in a proportion of cases, enlarged. In the absence of roseolæ, diagnosis may only be arrived at by the leucocyte count, which usually shows a leucocytosis, or by the application of the Widal test. The polymorphonuclears may be increased, or occasionally diminished ; while the lymphocytes, especially in children, are increased, but the larger hyaline forms are not affected.

Secondary syphilis, in which the roseolæ appear with pyrexia and splenic enlargement may, in the absence of a distinct history, or in the absence of other signs, cause some difficulty. There is usually a leucocytosis, and the Widal's reaction is, of course negative.

Paratyphoid or paracolon fever is an affection which simulates typhoid fever in every clinical detail, but is due not to the invasion of the body by the bacillus typhosus, but by one of the paratyphoid group of organisms, intermediate between the bacillus coli and bacillus typhosus. The chief known members of this group are the bacillus enteritidis (Gaërtner), bacillus psittacosis, and the hog cholera bacillus, the last-named not being pathogenic to man. There are others, forming two broad groups, called respectively paratyphoid A and B, both of which are capable of producing a disease in man, closely resembling true typhoid, though differing in their behaviour in culture media. The two specimens which I had were obtained for me from Kral by the Medical Officer of Health.

To sum up briefly, paratyphoid fever resembles typhoid in every clinical detail. The mode of onset is similar, as is also the temperature curve, and splenic enlargement, roseolæ, diarrhœa, and intestinal hæmorrhage may all be present. Relapses

TABLE XI.

Disease.	Bronchitis.	Intestinal Hæmorrhage.	Eruption.	Diarrhœa.	Spleen.	Pulse.		Temperature.	Leucocytes.		Serum Reaction.	Diazo Reaction.	Bacilluria.	Bacteræmia.
						Dicrotism.	Relative Bradycardia		Total.	Differential.				
Typhoid	Present	May occur	Roseolæ	Frequent Stools Peasoupy	Enlarged Progressive	Present	Present except in children	Ascent usual in step-like fashion—fastigium remittent, then steep curves. May be abrupt and fall by crisis in atypical cases	Leucopenia	Polynuclears diminished Lymphocytes increased Large Hyaline increased	Positive with B. Typhosus	Present	Due to B. Typhosus	Bacillus Typhosus
Paratyphoid	Present	May occur	Roseolæ	Frequent Stools Peasoupy	Enlarged Progressive	Present	Present except in children	Do.	Leucopenia	Do.	Positive with B. Paratyphoid	Present	Due to B. Paratyphoid	B. Paratyphoid
Acute Miliary Tuberculosis	May be present	......	Pseudo-r seolæ may develop	May occur	May be enlarged	.. ...	......	Irregular usually	Leucopenia	Polynuclears may be diminished or increased Large Hyaline unaffected	Negative with dilution (1-50)	Often present	......	Tubercle Bacilli
Tubercular Peritonitis	...	...	......	May occur	......	......	......	More or less of hectic type occasionally afebrile	Leucopenia	Do.	Do.	Often present	......	......
Tubercular Meningitis	...	......	......	Constipation	......	......	May be very slow and irregular—later rapid	Irregular	Leucopenia	Do.	Do.	May be present	......	......
Latent Tubercle	May be present	......	......	May occur	......	......	......	Ascent may be protracted—Evening rise but temperature as a rule not high	Leucopenia	Do.	Do.	May be present	......	......
Acute Cerebro-Spinal Meningitis	...	......	Petechiæ Pseudo-roseolæ may develop	......	May be slightly enlarged	......	......	Abrupt onset	Leucocytosis	Polymorphonuclears increased	Do.	...	......	Diplococcus
Typhus	Present	......	Distinctive subcuticular mottling Petechiæ	......	May be enlarged	......	......	Abrupt rise—Fall by crisis or modified crisis	Leucocytosis	Do.	Do.	Present	......	......
Influenza	Present	......	......	May occur	May be enlarged	Present	Present	Rise usually abrupt. Defervescence by crisis or rapid lysis	Leucopenia	Polynuclears diminished. Large Hyaline not affected usually	Do.	May be present	......	Bacillus Influenza
Cryptogenetic Septicæmia or Septico-pyæmia	...	......	May have scarlatiniform rash	May occur and Stools may be Peasoupy	May be enlarged		......	Irregular and with rigors	Leucocytosis	Polynuclears increased	Do.	...	Due to pyogenic cocci	Streptococci Staphylococci
Malignant Endocarditis	...	Only if embolism of branch of mesenteric artery	Icterus and Petechiæ	May occur Stools may be Peasoupy	May be enlarged	......	......	Irregular and with rigors	Leucocytosis	Polynuclears increased	Do.	...	Due to pyogenic cocci	Streptococci Diplococci
Malaria	...	......	......	......	Enlarged	......	......	Remittent or Intermittent	Leucopenia	Polynuclears diminished Large Hyaline increased Small Lymphocytes unaffected	Do.	...	......	Malarial Parasite
Gastro-Enteritis		May be slight at onset	......	Diarrhœa Stools may be Peasoupy	May be slightly enlarged	......	......	Abrupt rise usually	Leucocytosis	Polynuclears and sometimes small lymphocytes increased	Do.	...	......	......
Acute Osteomyelitis (children)	...	.. ...	......	......	May be slightly enlarged	......	......	Do.	Leucocytosis	Polynuclears increased	Do.	...	......	If Pyæmia Streptococci Staphylococci
Pneumonia (atypical)	May be present	......	......	......	May be slightly enlarged	Dicrotic	......	Do.	Leucocytosis	Do.	Do.	May be present	......	Diplococcus

also may occur. The diazo reaction is present, and the leucocytes in the two conditions are identical in their behaviour. Complications such as occur during the course of typhoid, are also prone to develop. Speaking generally, however, from the cases which have been recorded, this affection is rather less severe, and intestinal hæmorrhage and perforation are less frequent. In those which have terminated fatally, and a post-mortem examination been conducted, the anatomical lesions denoted less intensity than in true typhoid, there being very little ulceration, and even the endothelial proliferation in the lymphoid tissue of the intestine, has been awanting in many. As there is no difference in the symptomatology of the two affections, but only a difference in the infecting agent, the recognition of this disease can only be arrived at, by bacteriological and allied methods. The diagnosis rests on the following points :—

(1) A negative Widal's reaction with bacillus typhosus, after repeated tests in a case clinically typhoid, might arouse suspicion of the existence of paratyphoid.

(2) A positive reaction with one of the paratyphoid bacilli in dilutions of (1-50) and (1-100) and over, if no agglutination were obtained with other bacilli.

(3) Isolation from the urine of a bacillus, which in cultural properties resembles one of the paratyphoid group.

(4) Isolation from the blood of a bacillus with properties as above.

(5) Positive reaction with this bacillus so isolated, when tested against patient's own serum.

Two cases of this condition came under my own care, both having been notified as typhoid fever. In one, all these conditions were fulfilled, and the diagnosis placed beyond doubt, but in the other, no bacillus was isolated from the blood, and the diagnosis was based on a positive reaction with one of the paratyphoid organisms, a negative result being obtained with the others and with bacillus typhosus (see appendix).

Probably many of those cases which have been reported, in which the clinical signs of typhoid were present, but which gave a negative serum reaction, were examples of paratyphoid. It is a good plan, therefore, and one which I adopted, in the event of obtaining a negative reaction with bacillus typhosus, to test the patient's serum with all the strains of paratyphoid bacilli which we may have at our disposal.

The following table shows the chief points to be considered in arriving at a diagnosis in those cases which are liable to be mistaken for typhoid :—

Before concluding, I will briefly sketch a few cases, which were under my personal observation, and which are illustrative of many of the points commented upon in the preceding pages. Some of these are examples of atypical forms of typhoid, while others are "negative" cases, being admitted with a diagnosis of this condition, which was subsequently revised as the result of the application of the methods of diagnosis which I have dealt with in this paper.

Case I.—Protracted typhoid fever, with absence of splenic enlargement, roseolæ, and diarrhœa. Irregular temperature curve showing remissions and intermissions. Diazo reaction absent. Widal's reaction delayed until 18th day.

W. S., aged 37, was admitted to the Royal Infirmary, on August 18th, 1902, complaining of loss of appetite and weakness, of eleven days' duration. He had had no pain or sickness, no shivering or cough, and only had headache on one occasion. On admission, he appeared to have lost considerably in flesh. His face was pinched, his pupils dilated, and his expression dull and stupid. There was a distinct malar flush. His decubitus was dorsal. The lips were dry and crusted, and the tongue dry, brown in the centre, but white towards either edge. The knee jerks were deficient. To physical examination, his lungs and heart presented nothing abnormal. There was slight abdominal distension and tympanicity, but no pain or tenderness was complained of to palpation. No roseolæ were present. Bowels were constipated. Pulse was 112 per minute, regular and dicrotic. Temperature on admission was 104°F. The leucocytes numbered 6,250. The diazo reaction was negative, and continued so throughout the whole illness. The Widal's reaction was negative on the 13th and 16th days of illness, but was positive on the 18th day. Spleen was neither palpable nor enlarged to percussion. On the 28th day of illness, without a previous movement of the bowels, he had a large intestinal hæmorrhage, with a fall in the temperature from 103.2°F. to 98.8°F., and with all the signs of collapse. He had several slight hæmorrhages on the day following, and another large one on the 34th day of illness, two days after the temperature had been normal. His temperature kept at high limits and of the continued type for seven days after admission, then a collapse-like fall occurred, after which it again rose to its previous record, and continued thereafter in an irregular fashion, showing both remissions and intermissions until the 32nd day. After this, the temperature remained within normal limits until the 70th day, when it rose again and continued in a remittent fashion for 17 days more.

NOTE.—This was a severe and protracted case, characterized by a remarkable paucity of symptoms. In fact, the only diagnostic clinical sign present was the intestinal hæmorrhage. Constipation was present throughout, and the spleen was never demonstrably enlarged, even to percussion. The pulse showed dicrotism, but never relative bradycardia. No roseolæ ever appeared, and the diazo reaction never was positive, being on one occasion returned as doubtful. There was a leucopenia, with diminution in the polymorphonuclears, and increase in the larger hyaline forms.

Unfortunately, the blood was not examined for the bacillus typhosus. Until the development of the positive Widal's reaction, typhoid was only suspected by a process of exclusion. Two large bedsores, with absorption therefrom, probably accounted for the later elevation in temperature on the 70th day.

Case II.—Severe typhoid, with delirium and very slight enlargement of the spleen. Widal's reaction delayed until the 25th day of illness.

M.C., aged 23, was admitted to the Middle Ward Hospital on the 14th day of illness, having been complaining of repeated shiverings, slight cough, headache, abdominal pain, and diarrhœa (four to five motions daily). On admission she was delirious, and continued so for two days thereafter. Temperature was 104·6°F., and pulse was 106 and dicrotic. The facies was suggestive of typhoid, and tongue was dry and brown in the middle, but coated with white fur on either side. There was no abdominal distention, but diarrhœa was present, and the stools were peasoupy. The spleen was slightly enlarged to percussion, but on palpation, only a feeling of increased resistance in the left hypochondrium could be detected. Several roseolæ were present. Bronchitic râles were audible all over both lungs. Leucopenia was present, and later became more pronounced. The diazo reaction was present, but the Widal test gave a negative result. On the seventeenth day her spleen was palpable in the right lateral position. Roseolæ came out in successive crops, but the Widal's reaction was not positive until the 25th day of illness.

Day of Illness.	Leucocytes.	Polymorphonucleurs.	Lymphocytes.	Large Hyaline.	Eosinophylls.
15	4062	53·9	30	14·7	1·2
22	2812	51·6	31·2	18·2	—

Case III.—Fulminant case of typhoid, with pronounced cerebral symptoms and fatal on the ninth day, before Widal's reaction was present. Bacillus typhosus isolated from blood—Spleen not enlarged—Slight leucocytosis.

Mary S. aged 13, was admitted to the Middle Ward Hospital on the 8th day of her illness, her brother and sister (both mild cases) having been admitted during the previous week. On admission she was wildly delirious, her pulse was rapid, and her temperature 105·2°F. No roseolae were present, and enlargement of the spleen could not be detected. There was no diarrhœa. Bronchitic râles were audible over both lungs. The diazo reaction was present, but the Widal test gave a negative result. The bacillus typhosus was isolated from the blood. Death occurred on the day following her admission.

Day of Illness.	Leucocytes.	Polymorphonuclears.	Small Lymph.	Large Hyaline.	Eosin.
8	12,600	65·9	20·4	13·6	—

NOTE.—The surrounding conditions and the immediate circumstances attending her illness were responsible for the early recognition of this case. On admission there were no distinctive symptoms of typhoid, the blood count even showing a leucocytosis, though the differential enumeration was suggestive. The only positive

sign was the isolation from her blood of a bacillus, which culturally resembled typhoid, and was clumped by the blood of a typhoid patient in the ward.

Case IV.—Severe case admitted on fifth and fatal on twentieth day of illness. Hyperpyrexia —slight enlargement of spleen, which later became reduced from profuse diarrhœa and hæmorrhages. Bacillus isolated, on fifth day from blood, on seventh day from urine. Death before development of positive Widal's reaction.

Bridget R., aged 20, was admitted to the Middle Ward Hospital on the fifth day of her illness, having been suffering from shivering, abdominal pain, headache, and vomiting. On admission, her facies was suggestive of typhoid and her hearing was greatly impaired. Temperature was 104°F., and pulse was rapid and dicrotic. Tongue was dry and furred. Bronchitic râles were audible all over both lungs. The spleen was not palpable, but the upper border to percussion was in the seventh interspace. Diarrhœa was present, and motions were peasoupy. Two spots were noted on the abdomen on the ninth day, and on the succeeding days fresh ones appeared. Intestinal hæmorrhages occurred on the fourteenth, fifteenth, seventeenth, and eighteenth days, there being in all, fifteen and necessitating saline transfusion. Death occurred on the twentieth day. The leucocytes showed a normal count on the sixth day (7500), but thereafter, leucopenia was manifest. The bacillus typhosus was isolated from the blood on the fifth day and from the urine on the seventh. Repeated tests for the Widal's reaction always gave a negative result, in a dilution of (1-20).

Case V.—Case of typhoid, fatal on fifteenth day—Profound toxæmia—scanty eruption—very slight splenic enlargement—delayed Widal's reaction.

Simon M'F. (Pole), aged 19, was admitted on the twelfth day of illness. As he could not speak English, no definite history of the onset of his illness could be obtained. On admission he presented a picture of the "typhoid" state, with low muttering delirium, carphology, and incontinence of urine. The tongue was red, dry, and fissured. Considerable abdominal distension was present. The spleen was not palpable, but enlarged to percussion. A few roseolæ were present. Bronchitis was very marked. Temperature was 104°F., and pulse rate 106, the pulse showing dicrotism. A leucopenia of 3125 was present. The diazo reaction was positive, but the Widal test was negative. The bacillus typhosus was isolated from the blood. He died on the fifteenth day of his illness, with a picture of the most profound toxæmia. A few more roseolæ appeared, but the spleen was never palpable. Constipation existed. The blood was again tested for the Widal reaction on the day o his death, but again gave a negative result.

Case VI.—Mild case of typhoid with scarlatiniform eruption. No roseolæ present. Leucocytosis during second week of illness.

H. T., aged 30, was admitted on the 12th day of illness, his early symptoms having been headache, abdominal pain, pain in the back of his neck, and shivering.

On admission, there was slight abdominal distension, but no roseolæ were present. There was, however, a well-marked scarlatiniform rash present on the thorax and flanks. The spleen was palpable. Pulse was dicrotic. No bronchitis existed. The spleen continued to enlarge, and on the eighteenth day its lower border could be felt 1½" below the lower costal margin. Later, miliaria crystallina appeared, and during the third week he developed phlebitis of the left femoral vein. Both the Widal's reaction and the diazo were positive.

Day of Illness.	Leucocytes.	Polymorph.	Small Lympho.	Large Hyaline.	Eosin.	Mast. Cells.
15	11,875	79·5	13·5	6·4	·3	·3
29	8438	64·8	25·8	9·3	—	—
48	4062	54·2	34·2	10·8	·6	—

The leucocyte count taken on the fifteenth day showed a leucocytosis, while the differential count approached closely to the normal.

Case VII.—Abortive case in child. Defervescence by crisis on 12th day.

A. M'L. aged 3½, was admitted on the 10th day of illness, his early symptoms having been headache, sickness, and abdominal pain. On admission, his facies was quite suggestive of typhoid, while the tongue was moist and fairly clean. There was considerable abdominal distension, and three roseolæ was evident. The lower border of the spleen could be felt 1½" below the costal margin during quiet respiration. A few bronchitic râles were audible. Temperature was 102·8°F., and pulse was compressible but not dicrotic. Both Widal's reaction and the diazo were positive. Leucopenia (4375) was also present. A few fresh spots continued to appear on the three days following his admission. There was no diarrhœa. The temperature dropped to normal in critical fashion on the twelfth day, and convalescence was rapidly established thereafter.

Case VIII.—Mild and of short duration. No roseolæ or diarrhœa. Very marked leucopenia.

J. Boyle, aged 17, was admitted on the 8th day of his illness, having been suffering from backache, shivering, and vomiting. On admission, his facies was fairly suggestive of typhoid, and his hearing was greatly impaired. There was no abdominal distension or diarrhœa, and no roseolæ were present. The lower border of the spleen was felt ½" below the costal margin during tranquil respiration, and at the end of deep inspiration, 1½". There was no bronchitis. No spots appeared at any time during the illness. On the 10th day, the lower border of the spleen was palpable 1½" below the costal margin during quiet respiration. Both Widal's reaction and the diazo were positive. Typhoidal bacilluria was noted on the 27th day of illness, the urine being very pale and with no deposit. Leucocytes, 938.

Case IX.—Typhoid fever in an infant fifteen months old. Irregular temperature. Delayed Widal reaction.

G. R., æt. 15 months, was admitted from a house endemic on the sixth day of his illness. He had been suckled at the breast until his mother's removal to hospital, she having previously contracted typhoid. His early symptoms were sickness, vomiting, and diarrhœa. On admission he seemed pretty ill, diarrhœa being profuse, and with greenish yellow, foul-smelling motions. No roseolæ were noted, and none appeared during his residence in hospital. His abdomen was considerably distended, and his spleen was palpable. Pulse was small and rapid, and bronchitic râles were audible in both lungs. He was very drowsy at times, and at others very restless and fretful. The diarrhœa continued until five days after his temperature had reached normal, which it did on the 22nd day of illness. There was a leucopenia. The Widal reaction was delayed until the 21st day of illness (see table).

Day of Illness.	Leucocytes.	Polymorphonuclear.	Small Lymphocytes.	Large Hyaline.	Eosinophyll.
8	6875	77·1	18	4·7	—
15	5970	72·2	19	8·7	—
22	5326	69·4	20·1	10·2	·2

Case X.—Retrospective diagnosis of typhoid by Widal's reaction and changes in leucocytes.

Mrs R., aged 60, was admitted to the Middle Ward Hospital. She lived by herself, and had had an illness which only confined her to bed for one day, though she was troubled with abdominal pains and diarrhœa and a feeling of being easily tired, for ten days. She felt a little better thereafter, but was again seized with a somewhat similar illness, which caused her to spend the greater part of each day in bed, though she did not entirely give up. She was, however, finally prostrated, and a daughter was sent for, who nursed her until she was able to be up. Before she had so far recovered, however, some friends went to see her, and stayed for several days. Some of those, after returning home, sickened and developed undoubted typhoid fever. The illness was traced to the old woman, and the Medical Officer of Health had her removed to hospital. On admission she was much emaciated, as if she had just come through a serious illness. She had slight abdominal distention, but no diarrhœa, and no spots were visible. The spleen was not enlarged. Her temperature was normal, and her pulse rate 64. The diazo reaction was not present, but the Widal reaction was positive in a dilution of (1-100) in less than an hour, and in (1-300) in two hours.

Leucocytes.	Polymorph.	Small Lymph.	Large Hyaline.	Eosin.
5600	60·4	27·4	10·4	1·6

NOTE.—But for the fact of her having had visitors who contracted the infection this case would have escaped detection, and some doubt might even then have been thrown on the diagnosis of past typhoid in the old woman, but for the well-marked Widal reaction, which was to some extent corroborated by the absolute and differential leucocyte counts.

Case XI.—Retrospective diagnosis of a mild and apparently atypical case of typhoid, which was the source of infection in a house endemic, and thereafter of a local outbreak.

A. Mullen, aged 8, was admitted to hospital along with two other members of the household, who were suffering from typhoid.   She had been ill six week previously, complaining of headache and giddiness, but no abdominal pain or diarrhœa, and had only been confined to bed for two days. On admission, her temperature was normal. There was no abdominal distension, tenderness, diarrhœa, roseolæ, or demonstrable splenic enlargement.   The diazo reaction was not present, but a positive Widal's reaction was obtained with a dilution of (1-100) in an hour.   Leucopenia (4688) was present.   Typhoidal bacilluria was present on the second day after admission, and was again present a week later.

Case XII.—Retrospective diagnosis of typhoid in a child of two years of age, the subject of an unrecognised typhoidal attack, and the probable source of infection in a local outbreak of the disease.

Mag. Moore, aged 2 years, was admitted to hospital with a brother and three sisters, who were suffering from typhoid.   She herself had been going about suffering from diarrhœa for six weeks prior to admission.   On admission, she presented no symptoms of the disease, except diarrhœa, with greenish yellow stools, but she was somewhat emaciated.   The Widal's reaction was positive, and the leucocyte count was 6800.

Note.—This case was regarded at home as an example of summer diarrhœa until the other members of the house sickened in turn.   Of the four others admitted, two were mild cases, one was moderately severe, but the fourth, a girl of 16, died from toxæmia and intestinal hæmorrhage.   The well-marked positive Widal's reaction and the leucocyte count left no doubt but that this patient was the source of infection in this house at least.

Case XIII.—Influenza notified typhoid, Widal negative; later typhoid from nosocomial infection, Widal positive.

Two brothers, C. B. and D. B., aged respectively 14 and 16 years, were admitted to hospital notified typhoid fever.   Both cases were regarded, after examination, as examples of influenza, one of them, D. B., having the gastro-intestinal type.   The leucocyte counts in the two cases were respectively 9365 and 8750.   In both cases, as absolutely negative, Widal's reaction was obtained.   As the father (who was the only other occupant of the house) had met with an accident, it was decided to keep the lads in hospital.   On the 17th day after admission, C. B. complained of a tired feeling, backache, and disinclination for food.   He was put to bed, and his temperature registered 99°F.   His temperature, thereafter, began to rise in step-like fashion, and on the eighth day several roseolæ appeared, and his spleen could

be palpated. The latter organ continued to enlarge; and on the tenth day, for the first time since admission, his blood gave a positive Widal reaction in a dilution of 1-20) in an hour. On the fourteenth day the reaction was more marked, being complete in a dilution of (1-100) in an hour. Leucocytes numbered 6500.

NOTE.—That this case was not a relapse of typhoid was quite clear, for his temperature at first did not reach normal until two days after admission, and he had not a single clinical or other symptom of typhoid. The Widal reaction was tested on three occasions during his first illness, and was pronounced negative in all.

Case XIV.—Typhoid from nosocomial infection. Death from acute tuberculosis.

Nurse J. M'A., aged 22, who had been on duty in the typhoid pavilion, complained of headache, a sick feeling, disinclination for food, and slight shivering. She had never been really a healthy girl, and she presented old tubercular scars in the submaxillary and cervical regions. She was pallid, and further examination revealed ædema of the feet and ankles. Her urine contained a "cloud" of albumen, and numerous granular and hyaline casts were noted microscopically. She was put to bed and given a slight calomel purge, the treatment recommended by some in the early stage of typhoid. She had a slight cough, but beyond an occasional sibilant râle, nothing could be detected in either lung, on physical examination. Her temperature rose in step-like fashion, and on the 8th day a few roseolæ appeared, while on the 9th day her spleen was palpable. She had diarrhœa following upon the administration of the calomel, and the stools were peasoupy. She manifested slight delirium at night, but showed no sweating, her skin remaining hot and dry. On the third day her leucocytes numbered 7500, the differential count being practically normal, and on the thirteenth day, the number was reduced to 5600, with a diminution in the polymorphonuclears and an increase in the large hyaline forms. Her blood, tested daily from the third day, gave a positive Widal reaction on the sixth day in a dilution of (1-20) in an hour, but on the thirteenth day the reaction was more pronounced, being positive in a dilution of (1-200) in one and a half hours. The temperature curve was almost typical, the remissions during the fastigium being very slight, but the stage of steep curves, after it had been in progress for five days, was interrupted, the temperature from thence onward pursuing an irregularly remittent course. Her condition became worse, her cough more troublesome, and night sweating set in. Examination of her lungs showed impaired resonance at the left apex, with tubular breathing, and a few subcrepitant râles. Her sputum was examined, but no tubercle bacilli were found. The mischief in the lung extended, and later dulness, with tubular breathing and subcrepitant râles appeared in the right lung towards the lower angle of the scapula. Examination of her sputum at this stage revealed the presence of tubercle bacilli. Later she complained of sudden abdominal pain, which continued for several days, but examination failed to detect any friction or any local tenderness or swelling. She became unconscious and died in the fifth week of her illness.

Case XV.—Typhoid in a child followed by acute miliary tuberculosis.

S. D., aged 3, was admitted to hospital along with her father, who was undoubtedly suffering from typhoid. The child had been ill for a month prior to admission, and was said to have had pneumonia. Sickness, vomiting, and diarrhœa were present on admission, and continued at intervals until death, five days later. The child was markedly rackitic, the ribs showing beading, and the chest was of the pigeon type, while the head on percussion gave the pseudohydrocephalic note of rickets. The stools were greenish yellow and foul-smelling. The abdomen was distended and tympanitic, but no roseolæ were observed. The spleen was slightly enlarged. Auscultation of the lungs showed in many places, fine subcrepitant râles, and with tubularity of breathing, though no definite dulness to percussion could be elicited. An impetiginous eruption was present on the scalp. The diazo reaction was present. A leucocytosis of 18,000 was noted. The Widal's reaction was positive in a dilution of (1-50) in three quarters of an hour. The temperature was very irregular, showing both remissions and intermissions, finally touching 106°F. immediately before death. Meningeal symptoms developed on the day before death occurred. That this child had had typhoid seemed to be placed beyond doubt by the well-marked Widal reaction, and by the father's story that the child had improved somewhat after the first illness. No post-mortem, unfortunately, was allowed, or evidence of healed typhoid lesions in the bowel might have been obtained.

Case XVI.—Fatal case of typhoid admitted late in the disease. Positive agglutination reaction in the lacteal fluid.

Mrs W., aged 30, was admitted on the 26th day of her illness, having suffered from headache, pains over the body generally, and in abdomen, diarrhœa, and repeated shiverings. On admission she was much emaciated and the prostration was extreme. Up till her removal to hospital, she had been suckling her child. Her tongue was dry, brown, and fissured. There was no abdominal distension, but diarrhœa with peasoupy stools was present. Only one roseola was noted. Her spleen was enlarged, the lower border being felt one inch below the costal margin. Her pulse was rapid and thready, and bronchitic râles were audible all over both lungs, but later hypostatic congestion developed, and she succumbed on the 31st day of the disease. Bacilluria was present from the 27th to the 30th day inclusive, but was not present on the day of her death. A leucopenia was present.

Leucocytes.	Polymorph.	Small Lymph.	Large Hyaline.	Eos.	Mast.
3438	67·8	20·2	10·7	·6	·6

The Widal's reaction was positive, the agglutinating properties being evidenced both by the blood and by the lacteal fluid expressed from her breast, though, as the following table shows, more marked with the former:—

Fluid.	Dilution (1-50).	Dilution (1-100).	Dilution (1-1000).
Blood	Complete in 20 minutes	Complete in $\frac{3}{4}$ hour	Complete in 2 hours
Lacteal Fluid	Complete in 1 hour	Partial reaction	......

Case XVII.—Ambulatory, severe and fatal case, with profuse diarrhœa and intestinal hæmorrhage, but with no splenic enlargement. Roseolæ capped with small vesicles.

Henry B., aged 33, had been ailing for a fortnight before admission to hospital, but, as he thought he was suffering from influenza, would not consent to have medical advice, until intestinal hæmorrhage developed. On admission, his condition looked serious, his tongue being dry, brown, and fissured, and his pulse rapid and thready. Several roseolæ were present, some of which were capped with a small vesicle. The spleen could not be palpated, and no enlargement was demonstrable to percussion. Diarrhœa with peasoupy motions, as many as ten per day, occurred, until death took place three days after his admission. Several large hæmorrhages also occurred. Leucocytes, 7812. Widal reaction was positive. Blood was abstracted from a vein and cultures made, but these showed only staphylococcus albus.

Leucocytes.	Polymorph.	Small Lymph.	Large Hyaline.	Eosin.
7812	76·9	13·1	9·6	—

The absence of enlargement of the spleen in this case was probably to be attributed to the profuse diarrhœa and intestinal hæmorrhage. The last was probably also responsible for the absence of leucopenia (there being a slight post-hæmorrhagic leucocytosis, which raised the leucocytes in number.)

Case XVIII.—Case of influenza notified typhoid. Positive Widal reaction due to previous attack of typhoid.

Jeanie P., aged 24, was admitted to hospital on the eighth day of her illness, having suffered from general weakness, pains all over the body, sickness, and a "feeling of cold all over the body." She had been confined to bed from the first day. She declared that she had suffered from typhoid fever six years previously, being at that time unconscious for some days. On admission, there was no splenic enlargement and no roseolæ. Her temperature fell to normal on the tenth day.

Leucocytes.	Polymorph.	Small Lymph.	Large Hyaline.	Eosin.	Mast.
6000	35·3	58·1	5·4	—	·5

The Widal reaction was complete in less than an hour in a dilution of (1-50).

NOTE.—This patient presented no symptoms of typhoid, the only suggestion of the latter being the positive serum agglutination reaction. As this shows only typhoid infection, the probable explanation of its presence lay in the previous attack of typhoid, her blood probably still having some of the agglutinins, whether or not some stray bacilli were lurking in some corner as the gall bladder. This case is of importance as illustrating the necessity for careful enquiry regarding a previous attack, when applying the Widal's reaction.

Case XIX.—Case of typhus notified typhoid. Positive Widal reaction from previous attack of typhoid.

Nurse M. B., our district nurse, was taken ill with severe headache and shivering but she continued to discharge her duties for two days more, until the headache becoming intense and backache becoming unbearable, she took to bed. She had

been in attendance on a family, three members of whom had been ill. The first member who died was thought by the medical man in attendance to have had tubercular meningitis. The second member was thought to have influenza, and on the third sickening, typhoid was diagnosed, and the cases notified as such.

Condition on 5th day of illness. Headache was still intense, and slight epistaxis was present, but there was no tennitus aurium. Her face was swollen and red, and her pupils slightly dilated, but there was no distinct suffusion of the eyes. She was listless, and kept up conversation with the greatest difficulty. Her memory was much confused as to the dates of her symptoms and patients visited. The tongue was coated with a yellow fur, but presented no tremor. The skin was hot and dry. She had a slight cough, but beyond a slight pharyngeal hyperæmia and an occasional bronchitic râle, there was nothing abnormal in the respiratory system. There was slight abdominal distension, but the spleen was neither palpable nor enlarged to percussion. Bowels were constipated. The typical rash of typhus was present on the chest, abdomen, and back. On the 6th day the rash was present, in addition, on the arms and legs, and to a slight degree on the face. She became slightly delirious at night, thereafter, and during the day complained of everything in the room appearing to be dark in colour. The temperature reached normal on the fifteenth day by a modified crisis. The spleen was never enlarged throughout the illness. Diazo reaction was present. Blood was taken on the eighth day, and sent to the bacteriologist of the Public Health Department, Glasgow, who reported a positive result with a dilution of (1-50) in one hour.

Day.	Leucocytes.	Polymorph.	Lmall Lympho.	Large Hyaline.	Eosin.
4	5940	75·2	11·3	3·2	·3
7	7500	85·5	10·5	3·9	—
14	8500	84·9	9·8	5·3	—

NOTE.—There was not the slightest doubt but that this patient suffered from typhus fever and not typhoid as notified. There was a slight leucopenia on the fourth day, and by the seventh the leucocyte count was normal, while on the fourteenth day there was a slight leucocytosis. The differential count never suggested typhoid. She informed me that four years previously, while engaged in district nursing in Edinburgh, she contracted typhoid fever, and was treated in hospital for it.

Case XX.—Case of influenza of gastro=intestinal type, notified typhoid. Large splenic enlargement from malaria.

A. G., aged 50, was admitted on the 11th day of illness, his previous symptoms having been headache, pains all over the body, shivering, abdominal pain and diarrhœa. On admission, there was no abdominal distension, and no spots were visible, and none appeared during his residence in hospital. The

diarrhœa disappeared two days after admission, the stools however never having been peasoupy. Pulse was slow and compressible. Temperature reached normal. on the twelfth day. The lower border of his spleen was felt one inch below the lower costal margin at the end of inspiration. On the eleventh day the leucocyte count was 9375, and on the thirteenth 7500. The Widal's reaction, tested on two occasions, was negative in a dilution of (1-20), there being no attempt at clumping. He had been twelve years in the army, the greater part of which was spent in India, where he contracted malaria. That this was the cause of the splenic enlargement was undoubted, for, had it been due to the acute condition for which he was admitted, it would have shown partial or complete subsidence with the fall in temperature. His temperature was normal on the day after admission, but there was no diminution in the splenic enlargement when he left hospital twenty-one days later.

Case XXI.—Case of malignant endocarditis notified typhoid.

R. W., aged 18, was admitted to hospital on the twelfth day of his illness, having been complaining of shivering, headache, sickness, and vomiting. He had continued at his work, however, until six days before admission. On admission, his tongue was heavily furred but moist. Numerous subcutaneous hæmorrhages, were present, and there was a marked degree of icterus, most distinct, however, in the conjunctivæ. No roseolæ were present. There was no abdominal distension, but the spleen was definitely enlarged and palpable. Diarrhœa was present, and the stools were peasoupy. Temperature was 103·6°F. and pulse was 106. Vomiting occurred several times after admission. The cardiac impulse was heaving, and was carried downwards and outwards as from hypertrophy, and a rough systolic mitral murmur was audible. On the morning following his admission, he suddenly became unconscious, and was seized with convulsive movements of both arms and legs, followed later by complete paralysis. His knee jerks were exaggerated and ankle clonus was present. At first there was conjugate deviation of the head and eyes to the left, but this gave way to oscillatory movements of both eyeballs. His breathing became stertorous and irregular, and death took place four hours later. Leucocytes 11,875. The Widal reaction was absolutely negative, there being no attempt at clumping in a dilution of (1-20) at the end of an hour.

NOTE.—On admission, the question of hæmorrhagic typhoid was raised, but the leucocytosis and negative Widal reaction negatived this diagnosis. His medical adviser had attended him previously on several occasions for attacks of subacute rheumatism, and was aware of the existence of cardiac hypertrophy, with a mitral lesion. There was no hæmorrhage from the bowel or kidney, as both of these viscera acted after admission. The diagnosis of malignant endocarditis seemed the most probable, and the fatal issue was probably due to a basal embolism.

Case XXII.—Case of malignant endocarditis notified typhoid.

M. H., aged 23, was admitted in the second week of her illness, having been suffering from shivering, headache, and diarrhœa. On admission, her temperature was 104°F., and her pulse 120. She had diarrhœa, and her stools were peasoupy. There was slight abdominal distension, but the spleen was not palpable, and no roseolæ were present. Widal's reaction was absolutely negative. Leucocytes numbered 34,500. There was slight increase of the area of cardiac dulness, and the apex beat was carried downwards and to the left, and auscultation revealed a loud blowing systolic murmur of mitral origin. On the second day after admission patient developed hemiplegia followed in a few days by hæmaturia and gangrene from embolism of the right femoral artery.

Case XXIII.—Case of pneumonia, followed by malignant endocarditis of typhoid type, and simulating typhoid fever.

A. Sillars, aged 40, complained of shivering, headache, and cough, taking to bed on the same day. On the following day, when I saw him, his temperature was 104°F., his pulse 104, and his respirations 30. He had slight cough, and his sputum was tenacious and rusty looking. Physical examination of his chest, revealed consolidation over the lower aspect of the right lung. This spread until finally the whole lung was involved. The crisis occurred on the ninth day, and, thereafter, he felt better, and signs of resolution set in, in the lung. After a week of complete apyrexia, his temperature rose to 103°F., but his pulse rate kept at 86. He had no complaint beyond slight pain in the abdomen before going to stool, though diarrhoea was present, and the stools were peasoupy in appearance and consistency. His temperature continued elevated, and of the remittent type, ranging between 101·8° and 102·8°F. with pulse rate varying from 84 to 96. The diarrhœa still continued, the motions being peasoupy, and numbering from six to eight per day. His abdomen became distended, but there was no tenderness, and the spleen was not enlarged even to percussion. Miliaria appeared, but there were no roseolæ. There was considerable impairment of hearing. His tongue at this stage was dry and brown in the centre, but red at the tip and edge. His cough was somewhat troublesome, and his sputum was now mucopurulent and frothy. Examination of his lungs revealed a dull tympanitic note over the right lung in front, which gave way lower down to distinct dulness merging into the hepatic dulness. Behind, the right lung showed dulness in areas, more particularly at the angle of the scapula. In front, the respiratory murmur showed relative weakness, but with a tubular quality, but no râles were audible except just above the hepatic region, where a few of the subcrepitant type could be detected. Behind, the respiratory murmur was somewhat weakened, but tubular, and abundant râles were audible, carrying a suggestion of the consonating type. Both the vocal resonance and fremitus were increased. Examination of the sputum showed no tubercle bacilli, but a few diplococci, many staphylococci and streptococci and a few leptothrix forms were noted. Later, he was seized with rigors, having several in a day, the temperature sometimes reaching as high as 105·4°F. with a pulse rate of 120. He became bathed in profuse perspiration.

His skin assumed an icteric tint, but no petechiæ appeared, and there was no evidence of emboli in any of the viscera. Examination of the heart showed suspicion of an auriculo-systolic murmur, but repeated examinations failed to definitely confirm this. At this stage, he was taken home, and his own medical attendant later informed me that he developed hemiplegia and died.

The question of typhoid was raised on the development of the re-ascent of temperature (although this was somewhat abrupt), the onset of diarrhœa with peasoupy stools, and relative bradycardia. The Widal's reaction, however, was repeatedly negative, and the leucocyte count, taken on two occasions, was 23,750 and 26,875. On the development of the rigors, I was afraid of the existence of an interlobar empyema, but repeated exploration failed to detect such. The spleen was never enlarged. The onset of icterus, the suspicion of a cardiac murmur, the high, irregular temperature with rigors, the diarrhœa with peasoupy stools, the leucocytosis, with increase of the polymorphonuclears, and the later development of hemiplegia, practically confirmed the diagnosis of malignant endocarditis.

Case XXIV.—Case of Cryptogenetic septico=pyæmia in which the question of typhoid was raised :—

J. M'R., aged 46, was admitted to hospital complaining of weakness of six weeks' duration. At the onset, which occurred with shivering, he had some diarrhœa, and vomited once. Taking to bed, beyond a disinclination for food, and weakness, he had no symptoms and no recurrence of the shivering, but thereafter he had a severe rigor, and for three weeks prior to admission he had had on an average one daily. A case of typhoid had been removed to hospital from the vicinity. On admission, he was thin and anæmic. A rigor occurred within a few hours after his admission, during which his temperature rose to 103°F. and his pulse to 120. Thereafter he was bathed in perspiration, and his temperature fell to 98°F. He had slight abdominal distension, but no diarrhœa. No roseolæ were present, and there was no tenderness to palpation over the abdomen. His spleen, however, was palpable. There was no enlargement of the hepatic area of dulness, and nothing abnormal could be detected in the heart or lungs. Beyond a trace of albumen, nothing abnormal was present in the urine. There was a leucocytosis of 25,625, the polymorphonuclears being considerably increased. The Widal's reaction was negative. During the next fortnight there was no change in his condition, except that no rigors occurred, his temperature oscillating between 100°F. and 102°F. Rigors continued at intervals, but nothing more could be noted, except a slight increase in the area of hepatic dulness, and the lower border of the liver became palpable. By the end of the third week after admission, he complained of pain over the hepatic and iliac regions, and generally, all down the right side of the abdomen. Palpation, however, failed to detect any swelling, though there was considerable tenderness. Some œdema was noticed over the hepatic region, and percussion showed that the hepatic dulness measured $6\frac{1}{2}$ inches in the nipple line, and $5\frac{3}{4}$ in the middle

line. He passed a little blood per rectum, apart from any fæcal motion, but rectal digital examination revealed nothing beyond a few congested hæmorrhoids. With the continuation of rigors he sank and died. Repeated examinations gave a negative Widal reaction. There was always a marked degree of leucocytosis. The diazo reaction was never present.

Post-mortem result.—On opening the abdomen, some adhesions were noted over the liver and on the right side of the abdomen, while a large abscess was found in the mesentery. The portal vein contained pus. The liver was enlarged, and on section showed multiple abscesses. There were some old adhesions about the appendix, the lumen of the latter being blocked.

Day of Illness.	Leucocytes.	Polynuclear.	Small Lymph.	Large Hyaline.	Eos.
40	25,625	79·4	16·8	3·7	—
45	16,250	82·7	15·1	2·1	—
48	39,375	83·9	13·9	2·2	—
52	21,560	81·2	15·9	2·8	—

Case XXV.—Case of latent tubercle, simulating typhoid.

J. M'B., aged 16, had complained of shivering, headache, and malaise, for about a fortnight before I was requested to see him. He had kept at his work all that time, however, but finally had to give up on account of increasing weakness. He had no cough or expectoration. I saw him on the 16th day of his illness, and his only complaints were, a feeling of weakness, and disinclination for work. His tongue was furred and tending towards dryness, and there was slight impairment of hearing. There were no roseolæ present, and no abdominal pain, tenderness, or distension. The spleen was not enlarged. Bowels were constipated. His temperature was 102·6° F., with a pulse rate of 86, the pulse being markedly dicrotic. There was no albumen in his urine, and bacilluria was not noted.

Day of Illness.	Leucocytes.	Polymorph.	Small Lymph.	Large Hyaline.	Eosin.	Mast.
16	4062	42·4	34·4	20·9	1·2	·9
34	6875	66·4	24·1	5·8	1·1	2·2

His temperature continued above normal, and with relative bradycardia for ten days, after which it remained at normal. Repeated examinations of the lungs failed to detect any lesion.

Here, the nature of the onset of illness, and the leucopenia with the differential count during the second week, were quite suggestive of typhoid. However, a week later, and before the temperature had reached normal, the polymorphonuclears rose and the differential count approached closely to the normal ratio. Widal's reaction was negative. This patient went for a holiday, and was apparently well, but after returning, his temperature began to rise again, and his cough became more troublesome. Examination of his sputum revealed tubercle bacilli.

Case XXVI.—Case of phthisis, with diarrhœa and peasoupy motions. Typhoid suspected.

Mrs M'V., aged 21, had been confined to bed with a slight cough, abdominal pain and diarrhœa, for a month, when I was asked by her medical attendant to see her, as he was suspicious of typhoid. On examination, she presented a malar flush, was sweating, and had a crop of miliaria crystallina over her abdomen. Her temperature was 103·2° F. She had considerable abdominal distension and general tenderness, and diarrhœa was present, there being on an average four or five peasoupy motions each day. Her spleen was not palpable, and there were no roseolæ. The diazo and Widal reactions were both negative. Examination of her lungs failed to detect any lesion. Her leucocytes numbered 9000, while the differential count showed 81·3 per cent. of polymorphonuclears, 13·1 per cent. of small lymphocytes, 4·6 per cent. of large hyaline cells, and ·7 per cent. of myelocytes. I negatived the suspicion of typhoid, and raised the question of tubercle, especially as there was a marked family history of such. I was asked again to see her, and there was distinct evidence of incipient phthisis at the apex of the left lung. A week later, some of her sputum was sent to me for examination, and I discovered a few tubercle bacilli therein.

Case XXVII.—Case of appendicitis admitted diagnosed as typhoid.

J. G., aged 28, was admitted to the Middle Ward Hospital, notified as suffering from typhoid. He had been complaining of headache, malaise, abdominal pain and diarrhœa for ten days prior to admission. On admission, his temperature was 102·8°F., and pulse was 120. There were no roseolæ, and the spleen was not enlarged. There was considerable abdominal distension, and on palpation, general tenderness all over the abdomen, but in addition an elastic swelling was evident in the right iliac region. Leucocytes numbered 18,000, the polymorphonuclears being present in the proportion of 80·2 per cent. The Widal's reaction (B. typhosus) was negative in a dilution of (1·20). With B. coli there was distinct clumping. (See notes on serum agglutination). The patient was anæsthetized, and the abscess opened, the appendix being found forming part of the cavity wall. The pus from the abscess showed only bacillus coli and staphylococcus albus.

Note.—The absence of the Widal reaction, and of the bacillus typhosus in the pus, showed this not to be a case of typhoidal appendicitis.

Case XXVIII.—Case of empyema, notified as typhoid ; palpable spleen from displacement.

L. B., aged 12, was admitted to hospital on the 16th day of her illness. She had had headache, sickness, vomiting, diarrhœa, and repeated shiverings. On admission, her temperature was 102·8° F., her pulse rate 126, and her respiration rate 38 per minute. There were no roseolæ, but the lower border of her spleen could be felt 1½″ below the costal margin. She was somewhat livid, and presented signs of embarrassment of breathing, while physical examination of her chest showed the left side to be enlarged and immobile, with absolute dulness to percussion, and displacement of the mediastinum to an inch beyond the right sternal margin. The respiratory murmur was deficient, but distantly tubular, and vocal resonance and fremitus were diminished.

Exploration of the pleural cavity revealed pus. Resection of the ribs was performed, and patient recovered. Leucocytes numbered 28,000, giving a percentage of polymorphonuclears of 79·8. The Widal and diazo reactions were negative. The pus, examined, showed only staphylococci and streptococci.

Case XXIX.—Case of scarlatina anginosa, with recrudescence of temperature rising in step-like fashion. Diarrhœa with peasoupy stools—enlargement of spleen—simulating typhoid.

H. M'Cloy, aged 8, was admitted to the scarlet fever pavilion of the Middle Ward Hospital. He had all the cardinal symptoms of scarlet fever, together with an ulcerative patch on his left tonsil. This latter condition extended, and was followed three days later by apthous stomatitis, and a brawny induration of the neck glands. Within a few days, the throat condition improved, and, with a fall in temperature, the swelling of the neck subsided. After three days apyrexia, the temperature began to rise in step-like fashion, reaching 104°F. on the fifth day thereafter. His pulse was 126, and there was considerable general disturbance. The tonsils showed four necrotic patches, diarrhœa with peasoupy stools was present, and there was considerable abdominal distension. The lower border of the spleen was felt 1½″ below the costal margin. The question of typhoid fever was raised at this stage. No roseolæ were present. Leucocyte counts were taken with the following results :—

Day of Illness.	Leucocytes.	Polymorph.	Small Lympho.	Large Hyaline.	Eosin.	Mast.
—	13,125	72·5	21	5·3	·8	·2
—	26,875	79·9	13	3·7	3·2	·2

The Widal test was absolutely negative on three occasions, there being no attempt at clumping, and no impairment of motility. The condition continued thus, with no fresh symptoms for ten days, after which the temperature receded until the normal was reached, and with it, subsidence of the spleen took place. The streptococcus pyogenes was isolated from the throat and tested against the patient's blood, but the latter in a dilution of (1-10) had no effect on it.

Note.—The rise in temperature in step-like fashion, with abdominal distension, diarrhœa and peasoupy stools, and splenic enlargement, suggested, from its close resemblance, a typhoid development. The marked leucocytosis, however, and the repeated negative Widal reactions, negatived this. The condition was probably one of intestinal infection, from the fauces perhaps, with hyperplasia of the lymphoid tissue in the intestine, such as, according to Osler, occasionally occurs in the scarlatina anginosa, and in diphtheria.

Case XXX.—Typhoid complicated with acute ascending myelitis and cystitis.

T. Bowbell (Pole), aged 48, was admitted to the Middle Ward Hospital. No history could be obtained, except that he had received an injury to his back, while at work in the pit. On admission, there was considerable bruising and extravasation of blood over the lumbar region. His facies was suggestive of typhoid, and his tongue was coated with yellowish white fur. There was no abdominal distension and no roseolæ were present. The spleen was enlarged to percussion, the upper border

being on the eighth rib. There was diarrhœa, and stools were peasoupy. The temperature was 102·8°F., and the pulse 90 and compressible. No bronchitis was present. Leucocytes numbered 8000, and showed practically a normal ratio. Widal's reaction was negative in a dilution of (1-20). A culture was obtained from the blood, which subsequent examination showed to be the bacillus typhosus. His temperature continued to show a step-like ascent for three days after admission, after which it pursued the course of a remittent fever. No roseolæ developed, but the spleen continued to enlarge, and was palpable on the fourth day after admission. On the seventh day after admission, he had retention of urine and incontinence of fæces, and on the following day it was observed that he had lost complete power of both legs, although he still retained the power of his arms. Tactile sensation in the legs was gone, but pain could be elicited on firm pressure over the left knee which was swollen, but not reddened, and evidently contained fluid. The knee jerks were completely gone in both legs. On aspiration of the swollen knee joint a small quantity of blood-stained synovial fluid was withdrawn. A few tubes of media were inoculated therefrom, but all proved to be sterile. A few days later, his temperature, which up to this point suggested typhoid, became very irregular, and with this there occurred marked signs of cystitis, necessitating irrigation of the bladder. His condition remained thus for several days, when it was observed that his breathing had become exclusively diaphragmatic, and a day or two later hypostatic congestion of the lungs set in, patient shortly afterwards succumbing. A positive Widal's reaction was obtained for the first time on the sixth day after admission, with a dilution of (1-50) in half an hour, and (1-100) in one and a quarter hours.

NOTE—This patient was admitted from an infected area. As he could only speak Yiddish, no definite history could· be obtained, the only information obtainable, being from a fellow-worker, and related exclusively to his injury. That this was a case of typhoid seemed to me quite clear, as he showed the latter part of the step-like ascent, had relative bradycardia, gave a positive Widal's reaction, and from his blood the bacillus typhosus was isolated. There were also diarrhœa with peasoupy stools, and splenic enlargement. The injury to the lower dorsal and lumbar regions of his spine, was probably an important ætiological factor in the determination of the acute ascending myelitis. This and the cystitis were responsible for the leucocytosis which was evident after the first week. The temperature after the onset of the myelitis and cystitis was suggestive of a septic condition. It is noteworthy that the degree of leucocytosis was not very pronounced, considering the nature of his complications, but this was probably accounted for by the balancing effect of a leucopenia due to the typhoid.

Leucocytes.	Polymorph.	Small Lymph.	Large Hyal.	Eosinophyll.	Myelocytes.
8000	74·6	17·2	6·7	1·4	—
12,187	80	8·9	11	—	
15,625	88·8	4·8	4·8	—	1·3

Case XXXI.—Case of central pneumonia notified typhoid.

J. L., aged 29, was admitted on the sixth day of his illness, having been complaining of shivering and headache. On admission, his facies was not suggestive of typhoid, but his tongue was dry and brown. Temperature was 103·4°F., pulse 102, and respirations 24 per minute. A few sibilant râles were audible in both lungs, posteriorly. Leucocytes numbered 17,500, of which the polymorphonuclears made up 88·6 per cent. The Widal reaction was negative. On the eighth day, tubular breathing was detected over a very small area at the inferior angle of the right scapula, and by the tenth day, his temperature had reached normal by a pseudo-crisis, there being a corresponding reduction in the pulse rate. On this date, examination of the lung showed still, over the area previously mentioned, some tubularity of the respiratory murmur, and a few crepitant râles. He expectorated a little viscid mucoid material, which was not rusty in appearance, and which contained only a few cocci.

Case XXXII.—Mild atypical case of typhoid in a house endemic, admitted on the 7th day of illness. No roseolæ or diarrhœa, and very slight splenic enlargement. Bacillus isolated from the blood on 7th day of illness.

S. M., aged 16, had had headache, shivering, and abdominal pain. On admission she had no abdominal distension, and no roseolæ appeared during her residence in hospital. Her spleen was slightly enlarged, and palpable on the seventh day. Her temperature, which was 102°F. on admission, fell to normal on the tenth day by a non-remitting lysis. The diazo reaction was present. Widal reaction was positive in a dilution of (1-50) on the ninth day. Leucocytes 3750.

Case XXXIII.—Mild case of typhoid from a house endemic. Maximum temperature on second day of illness, gradually declining to normal on fifteenth day. Two roseolæ present on the fourth day. Widal reaction positive on the fifth day, and bacillus typhosus isolated from the blood on 4th day.

J. R., aged 16, had complained of feeling "light-headed," but had had no shivering or abdominal pain. She had no abdominal distension or diarrhœa. On the fourth day two roseolæ were noted, but no others appeared. On the sixth day her spleen was palpable. Typhoidal bacilluria was noted on the twenty-first day. Leucocytes numbered 5625.

Note.—This case might easily have escaped detection, but for the fact that three other members of the household had been previously removed suffering from typhoid.

Case XXXIV.—Case of tubercular peritonitis, notified typhoid. Roseolous eruption simulating that of typhoid.

Mrs M., aged 22, was admitted to hospital notified typhoid fever, having been complaining of headache, vomiting, and diarrhœa for twelve days. On admission she had some abdominal distension and diarrhœa. A number of pinkish and rose-red spots were evident on the abdomen, varying in size from a pin head to a lentil, some of them being capped with a small vesicle. They did not, though

almost, completely fade on pressure, but close examination showed that they were scarcely so well circumscribed as true typhoid roseolæ. Examination of the abdomen showed dulness in both flanks, extending well up towards the middle line, the dulness changing with alteration in the patient's position, and fluctuation could be detected. With a slight rise in temperature, she complained of pain in her left side, and examination revealed friction along the line of insertion of the diaphragm, over the splenic region and over the lower two-thirds of both lungs. Paracentesis abdominis resulted in the withdrawal of 100 ounces of a limpid greenish fluid alkaline in reaction, rich in albumen, and containing sĕrum globulin. Her temperature throughout was of the hectic type. Widal's reaction was negative on several occasions. The leucocyte count, taken on two occasions, resulted as follows :—

Day of Illness.	Leucocytes.	Polymorph.	Small Lymph.	Large Hyal.	Eosin.
14	8750	70·2	16·7	12·3	·5
35	6250	76·2	17	6·6	—

Case XXXV.—Case of paratyphoid fever, due to the bacillus enteritidis (Gaertner).

F. M'N., aged 20, was admitted to hospital, said to be suffering from typhoid fever. She had been complaining of headache, severe abdominal pains, vomiting, and diarrhœa. She was admitted on the 10th day of illness, her temperature being at that time 103°F. It came to normal by lysis on the 15th day. She had considerable abdominal distension, and her stools were peasoupy like. Three roseolæ were noted on the 11th day, two on the 12th, and two on the 13th day of illness. Her spleen was very slightly enlarged, being just palpable below the costal margin. Her leucocyte count showed first a slight leucocytosis, but later a slight degree of leucopenia was present.

Day of Illness.	Leucocytes.	Polymorph.	Small Lymph.	Large Hyal.	Eosin.
11	9062	70·2	19·1	10·7	—
18	6500	56·1	28·2	15·7	—

The polymorphonuclears at the first examination showed no deviation from the normal, but the later count showed a reduction, with increase of the small lymphocytes and larger hyaline cells. The Widal's reaction, tested with bacillus typhosus, was negative on three occasions. Very slight clumping was obtained with bacillus coli, but neither paratyphoid A nor B showed agglutination. The bacillus Gaërtner, however, was clumped in high dilutions (see table). Unfortunately, no bacilluria was present, and examination of the blood gave a negative result, all the culture media inoculated being sterile.

NOTE.—The well-marked serum agglutination reaction with the bacillus Gaërtner, and no agglutination with the other organisms, caused me to regard the former organism as the factor in the production of the disease.

Case XXXVI.—Fatal case of paratyphoid fever. No diarrhœa. Bacillus paratyphoid B isolated from the blood.

A. C., aged 30, was admitted to hospital on the 16th day of his illness, having been complaining of headache, malaise, and loss of appetite. He was

confined to bed for nine days before admission. On admission, his facies suggested typhoid, and his tongue was dry, tending to become brown. Temperature was 104°F., and pulse 90 and dicrotic. There was no diarrhœa or abdominal distension, but a few roseolæ were present. The spleen was not palpable, but enlarged to percussion. He was the subject of a generalized psoriasis. Patient's condition became aggravated, the pulse increased in frequency, and with the development of slight icterus and hypostatic congestion of the lungs, he died in the fifth week of his illness. Constipation continued throughout, and roseolæ kept appearing in successive crops. The spleen was definitely palpable for the first time on the twenty-fourth day of illness. Bacilluria was never present. The Widal's reaction with bacillus typhosus was negative on several occasions, but the blood clumped the paratyphoid B bacillus in fairly high dilution (see table). A bacillus was isolated from the blood on the day after admission, which was clumped by the patient's serum, but not by the serum of two separate cases of typhoid in the ward. At first there was no leucopenia, but later it became manifest, and again gave way on the day before death to slight increase (see table).

Day of Disease.	Leuco.	Poly.	Small.	Large.	Eosin.
18	7800	74·2	19·7	5·8	·2
24	5960	61·9	24·1	13·9	—
32	7000	64·2	22·6	13·1	—

Case XXXVII.—Typhoid—Death from acute osteomyelitis of humerus, Leucopenia. Widal positive.

Mrs P., æt. 29, was admitted on the 12th of her illness. She had been complaining of headache, shivering, diarrhœa, and slight cough. On admission she seemed very ill. Her tongue was dry, brown, and fissured. There was considerable abdominal distension, and diarrhœa was present with peasoupy stools. Several roseolæ were present on the abdomen and back. Spleen was enlarged. The pulse 106, was compressible, but not dicrotic. T. 104°. A considerable degree of bronchitis existed. She was slightly delirious in the night time. Roseolæ kept appearing in crops. On the 18th day of her illness, she complained of extreme pain in the region of the right elbow, and examination of the part showed considerable redness and swelling, with extreme tenderness to pressure over the lower end of the humerus. There seemed to be a slight accumulation of fluid on the joint, but movement could be carried out by herself with pain. It was quite evident that the patient was suffering from acute osteomyelitis of the lower end of the humerus, but permission to adopt operative interference was refused by her husband. She died on the 22nd day of her illness. Her blood gave a positive Widal reaction in dilution of (1-50) in half an hour, and in (1-100) in one and a quarter hours. The leucocyte counts were as follows:—

Day of Illness.	Leucocytes.	Polymorphonuclear.	Small Lymphocytes.	Large Hyaline.	Myelocytes.
16	2188	60·7	24·1	14·2	·2
21	1250	49·8	28	20·4	1·7

There was no doubt but that this patient was suffering from typhoid, as was evidenced by the roseolæ, enlarged spleen, diarrhœa, leucopenia, and active Widal reaction. It is quite probable that the bone lesion may have been due to the bacillus typhosus. Note marked leucopenia on the day before death. The blood was not examined for the bacillus, and no post-mortem was allowed.

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