parent change in resonance of other parts of the abdomen; the lower part was perhaps rather more bulging than normal, but the granulating surface of the wound made at the first operation looked healthy. He had now (December 13th) developed another symptom—vomiting—which was regarded as very important. As the attempt made to reach the collection of pus which was supposed to be present in the splenic region had not been successful, and it was evident that he could not live long unless he did obtain relief, I made an incision in the left linea semilunaris and carefully explored the abdomen from the wound. The spleen was adherent to the diaphragm, but no abnormal swelling of any kind could be felt in the upper part of the abdomen, either by myself or Mr. Abbott, who ably assisted me; but in the lower abdomen a distended coil of small bowel could be felt, which gave the impression that it was possibly obstructed in consequence of partial fixation to the median wound. Mr. Abbott passed his finger from the wound in the linea semilunaris to the upper part of the old median wound, and cut down on it. When the peritoneum was reached there was a gush of gas and offensive purulent material mixed with some blood. This came from the pelvis, and the abscess cavity extended across towards the right iliac fossa, in the situation of the first purulent collection. This was washed out and drainage provided for. The wound in the linea semilunaris was closed and that in the side redressed, the drainage tube not being replaced.

The day following this, December 14th, he was better, for the vomiting had ceased and the temperature fallen, but he still looked very ill, and had a rapid, weak pulse. There was much discharge from the wound. At 4.30 A.M. of the 15th he pulled out the glass drainage tube, being only partially conscious of his action, and restless. He afterwards gradually sank and died at 7.30, four weeks after admission.

Dr. Mackenzie, who made the *post-mortem* examination, reported as follows: The intestines were distended and were adherent to one another and to the abdominal wall in front. The adhesions, however, could be easily broken down. In making the central incision the intestine was slightly injured in two places, but there was no evidence that any perforation had existed during life. In the splenic region a collection of pus was found, amounting to about 10 ounces. This was contained in a pocket of the peritoneum, bounded by the diaphragm above, the spleen to the left, the stomach below and to the right. This pocket was completely separated by adhesions from the general peritoneal cavity. The spleen was flattened, and was closely adherent to the diaphragm posteriorly. It was of a slaty-black colour. The peritoneal cavity had not been opened by the incision which had been made in the splenic region. On placing the finger in the wound, one came on the spleen in one direction, while above there was only the peritoneum separating the finger from the abscess cavity. The liver was very firmly adherent all over. Careful examination failed to discover a cause for the peritonitis. The vermiform appendix looked suspicious externally, but when opened up there was no sign of perforation or of ulceration. The intestinal tract was examined from end to end without discovering anything abnormal. The liver and kidneys were normal. The pericardium contained about 6 ounces of serum. The heart was normal. The right lung was adherent nearly all over, and there were a few slight adhesions at the left apex. There was no effusion or inflammation in either pleura. The lungs were normal.

In the previous history there were complaints of vague abdominal pains and occasional *malaise* with headache, not sufficient to make the patient give up work as a waiter, but it is noteworthy that he mentioned a date on which this change in his health commenced. It is not uncommon to get a history like this in cases of appendicular disease.

When admitted, the patient was seriously ill, and suffering acutely from paroxysmal pain in the abdomen. The diagnosis of peritonitis was made without much difficulty, the face, the attitude of the man, the thoracic respiration, and the hard, tender, fixed abdomen pointed to this, especially when the high temperature, rapid pulse, and dry mouth were taken into consideration. Although the severity of the pain, muscular rigidity, and temperature would have argued the presence of a commencing purulent peritonitis, the extension of the dulness to the left of the middle line and its outline showed, in our opinion, the presence of a considerable collection of pus, whilst its extension more to the right suggested its possible origin in the region of the appendix. We came, therefore, to the conclusion that the case was one of acute septic peritonitis, and that an immediate operation would give the patient the best chance of recovery.

The absence of vomiting was regarded as favourable to the success of operation, for he was less exhausted than he would have been, whilst he could take food and stimulants as might be required.

Most classifications of the causes of septic peritonitis give cold as one, or perhaps speak of "idiopathic peritonitis," in other words, the origin of the disease as in this case was not explained by the *post-mortem* examination, although it was carried out by a careful expert.

Septic peritonitis is caused, as we know, by the escape into the peritoneal cavity of the bacterium *coli commune*, which is present in all parts of the intestinal tract, and in cases similar to this, but which have proved fatal at an earlier stage, this bacillus has been found passing through the wall of the appendix, without the aid of any ulcerative process. Dr. Hawkins has illustrated this very clearly. It is very probable that the disease started in this manner, but impro-

bable that microscopic examination, so long after the invasion of the peritoneum, would have proved it. To the naked eye, the appearance of the appendix was normal when opened up.

It is generally recognised that an injury of the intestinal canal in any part of its course may, by lowering its vitality, or by some disturbance of the local circulation, so alter the normal resistance that the bacterium *coli commune* can get out by passing through the wall of the bowel. This bacterium is found throughout the intestinal tract and always in the appendix. It is probable that the jar of the fall which the patient experienced the day before the onset of symptoms was primarily responsible for their unusual activity, having acted on the appendix in the way indicated.

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THE TECHNIQUE OF "SERUM DIAGNOSIS," WITH SPECIAL REFERENCE TO TYPHOID FEVER.*

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It is unnecessary here to enter upon general considerations on the phenomena upon which this method is based, this I have done elsewhere.¹ Neither is it desirable to consider the various diseases in which serum diagnosis is applicable.² I venture to say, however, that there is probably not a single disease in which this method is likely to yield more useful results in this country than typhoid fever.

Having followed closely the development of various doctrines concerning immunity, and more specially the instructive controversy which has been kept up for the last few years between Metchnikoff and Pfeiffer, a controversy in which Max Gruber joined at a later period, I was quite prepared for the announcement made by Widal about the middle of last year, and having myself made many experiments with the typhoid bacillus, I was able to repeat Widal's experiments, even before a complete account of his work appeared in the French papers on July 29th.³

Having tried the various methods which seemed likely to yield good results, I selected the one that had been used in my laboratory ever since (and which I was able to demonstrate to my class of bacteriology in the first half of July). The results obtained with this method by Dr. Sidebotham and myself have been carefully tested in over fifty cases by independent observation of patients kept under close supervision by Dr. Marsden at the Monsall Fever Hospital, and have proved to be remarkably accurate. For these reasons I consider myself justified in discussing critically the various ways in which serum diagnosis may be applied.

The serum of an immunised animal or that of a patient affected with a specific fever may be used for the purpose of diagnosing whether a bacillus is the bacillus causing that fever, or on the contrary the specific bacillus may be used for the purpose of finding out whether the fever has been produced by the microbe in question.

In both cases the technique may be the same; it is important, however, to keep in mind that for practical purposes the diagnosis of a fever by the action of the serum on a known bacillus is far more useful and, as a matter of fact, a far more reliable method than the diagnosis of the bacillus by means of the serum of an immunised animal. It is the happy idea of reversing all the experiments which had been made up to then which led Widal to the valuable application which he introduced at the beginning of last summer. He must also be credited with the very important notion that the action on which the test is based is not one possessed only by the blood of animals or persons who have become more or less completely immunised, but also by the serum of individuals who have been too recently infected to give any evidence of what is generally known as immunity. These individuals are undoubtedly undergoing

* This is part of an address delivered before the Manchester Pathological Society on The Bacteriological Diagnosis of Typhoid Fever.

processes which will end in more or less complete immunity, but they are as yet on the wrong side of the fever, which may or may not kill them. The reaction under those circumstances becomes less one of immunity than one of infection.

At the beginning of 1896 four kinds of methods had been used to demonstrate the action which the blood or blood serum of immunised animals has on the corresponding microbes.

1. The microbe is cultivated in the serum of an animal immunised against it. By this method Charrin and Roger found in 1889⁴ that the bacillus pyocyaneus forms clumps or flakes, which fall to the bottom of the test tube in the shape of a sediment, the supernatant fluid becoming clear. In the serum of a non-immunised animal the bacilli remain disseminated, giving rise to a uniform turbidity.

2. The serum of an animal immunised against a specific microbe is mixed with the microbe to be tested, and is injected into the peritoneal cavity of a guinea-pig.

By this method R. Pfeiffer⁵ found that motile micro-organisms (bacillus of cholera or typhoid fever) are rapidly immobilised, and that if the serum be potent and the quantity of micro-organisms not too large, the microbes undergo a granular degeneration, and may ultimately disappear by a process of solution, which its discoverer has compared to that of a piece of sugar placed in water. Other microbes than the specific ones do not undergo the same degeneration.

A loopful = 2 milligrammes of a 20-hours' culture on agar of the bacillus to be tested, made into an emulsion with bouillon, is mixed with 0.1 to 0.2 c.c.m. of the serum of an animal strongly immunised against the specific bacillus, say of typhoid fever. The total amount of fluid thus obtained is made up to 1 c.c.m. This is injected into the peritoneal cavity of a guinea-pig, weighing 300 grammes; 15 minutes, 30 minutes, one hour after the injection a few drops of the peritoneal exudation are removed and examined under the microscope. If the bacillus be a genuine typhoid bacillus it will be found at the end of an hour to have undergone the degeneration described above. This is what is known as Pfeiffer's phenomenon. In his first experiments, instead of mixing the bacilli with immunised serum, and injecting the mixture into a non-immunised animal, Pfeiffer injected the bacillus into the peritoneal cavity of a highly immunised animal. The bacilli, which are not of the same species as the one which has been used to immunise the animal, do not undergo the degeneration above described to any marked extent.

3. The microbe to be tested is mixed with the blood serum of an animal strongly immunised against the specific micro-organism which is looked for. A hanging drop preparation is made with the mixture and examined under the microscope.

This method was used by Metchnikoff⁶ with various modifications to elucidate certain points raised in the controversy between him and Pfeiffer; it has been improved by Bordet⁷. By this method Bordet has observed *in vitro* the phenomena described as occurring only *in vivo* by Pfeiffer, and the agglomeration reaction previously described by Charrin and Roger, Metchnikoff, and others.

A young culture (twenty-four hours old) of the doubtful microbe is mixed with 5 or 7 c.c.m. of bouillon, or of 0.6 per cent. NaCl solution. To 2 drops of this emulsion, 1 drop (or less) of the serum (recently obtained) of an animal immunised against the specific microbe under investigation. A hanging-drop preparation is made with the mixture. (When a complete production of Pfeiffer's phenomenon is wanted, a small quantity of the fresh serum of an ordinary animal is added to the mixture.) If the microbe tested be the specific one, say the vibrio of cholera, it is rapidly immobilised, then it runs into clumps, and, when fresh serum has been added, the vibrios are seen to undergo granular degeneration. Other vibrios than the one against which the serum has been immunised do not in the same degree undergo these changes. Bordet considers this reaction quite as specific as Pfeiffer's reaction.

4. The microbe to be tested is mixed with the more or less diluted serum of an animal immunised against the special microbe under investigation. The mixture is placed in a test tube, and allowed to stand for some time. A positive reaction is indicated by the formation of a precipitate composed of clumped bacilli, and by the supernatant fluid becoming clear. A negative reaction is shown by the turbidity of the fluid remaining general and no precipitation being formed.

This is the method specially introduced by Max Gruber, and Durham.⁸ These observers also used a microscopical method much resembling Bordet's and they insist specially on the importance of a certain degree of dilution, as Pfeiffer had done also in connection with his own method.

The bacillus to be tested is grown for twelve to twenty-four hours on agar. A loopful of the culture (= about 3 mg.) is made into an emulsion by thorough mixture with 0.5 c.c.m. of bouillon; 5 or 10 mg. of the serum of an animal strongly immunised against the special microbe under investigation are mixed with enough bouillon to get an amount of fluid equal to 0.5 c.c.m. The emulsion of the microbe to be tested and the diluted specific serum are mixed. The mixture is kept in a narrow

specimen tube measuring three-eighths of an inch in diameter. Thirty minutes or sixty minutes after, if the bacillus is of the same kind as the one which has been used to produce the specific serum, and if the serum be potent enough, the microbes will form a sediment at the bottom of the tube, and the supernatant fluid will be clear, or nearly so. The sediment is composed of clumped bacilli. If, on the contrary, the microbe belongs to a totally different species from the one against which the serum has been immunised, the contents of the tube will remain uniformly clear.

In his work Widal adopted several of the methods just described, with slight modifications. Pfeiffer's method, very important from a theoretical point of view, was evidently not applicable, but the three others were suitable. He used specially two methods, which may be described as the quick and the slow.

1. *Quick Method.*—To 10 drops of a 24 or 48 hours old, neutral bouillon culture of the typhoid bacillus, 1 drop of the blood serum to be tested is added. The serum and the culture (which should be uniformly cloudy) are mixed together in the sterilised trough of the hematimetre. A drop of this mixture is taken and placed on a slide, covered, and examined at once under the microscope. A positive reaction, showing that the serum comes from a case of typhoid fever, is indicated by the bacilli becoming motionless and running together to form clumps, which are of various sizes. Sometimes the bacilli are not immobilised at once, and the agglomeration takes place slowly. In such cases the reaction may not be distinct for a quarter, half, or even several hours.

2. *The Slow Method.*—This is the one used by Widal in his first experiments. It resembles much that followed in Charrin and Roger's experiments, from which it differs by the serum being diluted instead of being used undiluted. One part of the serum to be tested is added to 10 or 15 parts of bouillon. This mixture is inoculated with a typical bacillus typhosus. The tube is incubated at a temperature of 37° C. Twenty-four hours after the culture is examined. If the reaction is positive, a more or less abundant sediment, composed of clumps, will be found at the bottom of the test tube and the supernatant fluid will be more or less clear. In a negative case the fluid would be uniformly turbid.

After mentioning Widal's method it may be well to describe the one used by Grünbaum.⁹ The chief modifications introduced by this observer are (1) the use of a U-shaped tube to separate blood serum by centrifugalisation; (2) the dilution of the blood serum by means of a graduated pipette, the blood being diluted sixteen times; (3) the preparation of a hanging drop for examination under a high power of the microscope (oil immersion); (4) a time limit of 30 minutes for the observation of the phenomenon. Although the reaction can be very well seen by using the method described by Grünbaum, which resemble closely that originated by Bordet, I am quite convinced from personal experiments carried out in my laboratory more than two months before the publication of Grünbaum's first paper that many of the precautions he suggests are superfluous, and by introducing complications may interfere with the efficacy of the test. I speak here, not of investigations in which one wants to experiment on the properties of the various elements of the blood, but of those which have for their object a clear and unambiguous diagnosis of typhoid cases and a rapid estimation of the potency of the serum of such cases.

I must now refer to my own experiments. My first care was to obtain a typical culture of the typhoid bacillus. Among those I had isolated from typhoid spleens during the last four years I selected one separated two years ago, highly pathogenic at the time, and which ever since had invariably given all the reactions which are now associated with the Eberth's bacillus.

1. On slightly acid potato gelatine, growth slow, scanty, colonies transparent and small.

2. On slightly acid potato, growth quite transparent, colourless glaze-like.

3. In glucose peptone gelatine, no production of gas.

4. On litmus (or phenolphthalein), slightly alkaline lactose-peptone-agar, or gelatine, no production of acid reaction.

5. In milk, no coagulation.

6. In peptone bouillon or water, no production of indol.

7. In presence of minute traces— $\frac{1}{100}$, $\frac{1}{1000}$, $\frac{1}{10000}$ —of serum of an animal immunised against typhoid fever, immobilisation and agglomeration well marked by any of the methods mentioned above.

8. The bacillus was very motile in neutral bouillon cultures.

9. At least ten cilia could be demonstrated in well-stained specimens.

10. The bacillus did not stain by Gram's method.

The next step was to test the action of the blood of various

individuals on that bacillus. The following types of cases were selected:

1. Normal individuals of various ages, having never had typhoid fever or having recovered from it for a great number of years (over twenty in one case).

2. Patients affected with various febrile diseases, certainly not enteric fever, and who never had had typhoid fever.

3. Patients affected with enteric fever, in whose cases the clinical features left absolutely no doubt as to the diagnosis. The patients were of various ages, in different stages of the fever, more or less severely affected, and suffering from various complications.

With material thus obtained the test was applied in various ways suggested by the known methods already described, and it was found that by any of these methods it was possible to obtain the reaction in cases of typhoid fever.

The blood was used, quite fresh and entire, dried and entire, coagulated, separated by centrifugalisation, and in every case the reaction could be obtained more or less clearly in cases of the fever.

The blood was used in various dilutions from $\frac{1}{2}$ to $\frac{1}{100}$, and it was found that the dilution $\frac{1}{10}$ was the most suitable. In quite exceptional cases it seemed that the proportion $\frac{1}{2}$ gave better results than the $\frac{1}{10}$. In several instances in which the reaction appeared slowly, a proportion of serum equal to $\frac{1}{20}$ or $\frac{1}{30}$ seemed insufficient to bring about a clear reaction within two hours. The bacillus was grown on various media, such as ordinary nutrient agar, gelatine and bouillon, or carefully neutralised peptone bouillon. Young and old cultures were used. The cultures in neutral bouillon were invariably found to be the best when not more than twenty-four hours old.

It was soon apparent, however, that all the methods were not equally good; thus:

1. The test-tube method recommended by Durham and Gruber failed to give clear results much more often than the microscopical method introduced by Bordet. When the serum was weak the precipitation was incomplete. When very small quantities of half-dried blood, such as are often obtained from weak anæmic patients, and specially from young children, arrived at the laboratory, it was difficult to obtain enough clear serum to make up the mixture to a sufficient bulk. Then occasionally the blood of people not affected with typhoid fever produced a partial precipitation. For those reasons I soon discarded the method.

2. The hanging-drop method introduced by Bordet and used by most observers gave very good results, but in measuring the fluid with pipettes and mixing the emulsion of bacilli and the serum in small capsules, or even on slides, I soon noticed that extraordinary care had to be taken to avoid errors. Graduated pipettes were unsuitable when eight or ten observations had to be conducted within a short time, unless one had as many pipettes to dispose of, for it was not only necessary to wash the pipettes thoroughly, but also to boil them in water to destroy all traces of the substances causing agglomeration. The same thing had to be done with the troughs, slides, and cover glasses used. At first I replaced graduated pipettes by ordinary capillary pipettes, which were destroyed after each observation, the dilutions being made by counting the number of drops, the same pipette being used for counting drops of diluted serum and of the emulsion of the bacillus; but this implied much waste of time and also of material; and, when one has only a small quantity of serum, it is not always easy to get a small drop out of it, as the serum has a tendency to adhere to the point of the pipette. Exact measurement of the dilution becomes difficult under those conditions.

3. I finally adopted a method the objects of which are:

(1) To permit the measurement of extremely small quantities of blood.

(2) To simplify the apparatus required so as to diminish chances of contamination.

(3) To make it easy to destroy rapidly by heat all traces of serum which may remain attached to the measuring instrument.

(4) To obtain conditions under which spurious clumping is not likely to occur.

All the apparatus required consists of:

(a) A sterilised lancet-shaped needle.

(b) The small pipette in which the blood has been collected,

and of such diameter that after it has been broken across the platinum loop, which is used for measuring the serum, can easily be introduced into it if necessary.

(c) A platinum loop measuring about 1 mm. in diameter, and holding about 2 mg. of fluid.

Each loop has a definite capacity which can be easily estimated by direct weighing. A glass slip is placed on one of the pans of a delicate chemical balance. This is exactly counterpoised. A drop of fluid is then taken with the loop and deposited on the slip, this is immediately weighed by means of the rider before evaporation has had time to cause a sensible diminution of weight. Then four more drops are rapidly added in such a way that they do not touch each other, and the rider being moved so as to counter-balance a weight five times greater than that of the first drop, the beam should remain horizontal, and so on.

(d) Slide and cover glass, absolutely clean; if they have been used before for the test they should be boiled in water.

(e) A tube of culture of the typhoid bacillus in neutral bouillon (twenty-four hours old at most). This tube should be free from clumps, and the bacillus should be actively motile.

When the typhoid bacillus is reinoculated in neutral bouillon daily for weeks or months, there comes a time when, all of a sudden, all the cultures will clump spontaneously, or on the addition of any serum; this is not due to a failure in the growing power, cultures in alkaline bouillon show the same property. In fact the importance of the reaction of the mixture of serum and culture is of great importance. Dr. Sidelbotham will shortly give the results of a number of experiments bearing on this point. The same thing may be observed in cultures grown repeatedly on agar. If, however, cultures on agar, gelatine, or solidified blood serum are made at longer intervals, and the bouillon tubes are inoculated daily from these cultures on solid media, the difficulty caused by this spontaneous clumping can be got rid of, at least for a time. It is well to keep up the virulence of the typhoid bacillus by the usual method of reinoculation.

The procedure is as follows: With the sterilised loop 9 drops of the evenly turbid bouillon culture are taken and deposited separately on the clean slide or cover glass.

The platinum loop is again sterilised, and, when cool, one drop of the blood is taken, and deposited also separately on the cover glass or slide.

The 10 drops are then mixed thoroughly and rapidly together.

If the mixture has been made on the cover glass the cover is placed on the slide moist face downwards, and gently pressed so as to obtain an even film. If the mixture has been made on the slide, it is simply covered with a clean cover. In either case the preparation consists of a thin film of culture mixed with the serum investigated and a certain number of red blood corpuscles, separating the slide from the cover-glass so that a capillary space of pretty uniform thickness is obtained.

It will be noticed that instead of separating entirely the blood corpuscles from the serum, I try on the contrary to retain a part of them in the preparation. They do not interfere in the least with the reaction, and they have the advantage of acting as supports for the cover glass, and of causing the film in all preparations to be nearly of uniform thickness. Under these conditions the bacilli are free to move about; and when the preparations are kept in a moist chamber they can be observed from day to day for more than a week.

A. *When the blood tested is that of a non-typhoid patient*, the bacilli remain diffused all through the preparation; they move freely about, and even when kept for days they hardly ever show any tendency to form good clumps. This absence of characteristic clumping is observed even when the proportion of blood is one-fifth or even one-half. An imperfect clumping without loss of motility has been observed in a few cases after twenty-four hours, but the appearance of the preparation in such cases is quite different from what is observed in cases of typhoid fever.

The motion of the bacilli is quite characteristic; they move at different rates, some, especially the very short ones, darting across the field, and disappearing in a few moments; others pursue a zigzag course. Some of the long ones are less active, and progress by an undulating motion; some are almost motionless. The actively motile bacilli, by striking against blood corpuscles, keep them in constant motion. The power of some of the bacilli is such that they often drag or push the corpuscles through a portion of the microscopical field. The bacilli have generally seemed to me to be most active after they have been in contact with the blood for a short time. After a few hours they generally become less motile, but not altogether motionless, and the progressive motion is seldom lost before several days have elapsed.

When clumps are formed they are generally very small,

ery few, and composed of bacilli which are quite motile still and are very often seen to separate themselves again. Owing to the activity of the bacilli these small imperfect clumps are seen to alter in shape. As this phenomenon is seldom observed, and as, when it occurs, it does not take place till after several hours have elapsed, it is not (under the conditions explained above) a serious source of difficulty.

When bacilli are kept for days under observation, they multiply, and many of them become very long.

In making these observations it is not necessary to use very high microscopical powers, unless one wishes to study the minuter changes taking place in the bacillus, in which case the best immersion lenses are necessary. The bacilli can very clearly be seen with a magnification of 200 to 300 diameters, and the formation of clumps can be easily recognised with a magnification of 50 or less. In fact, it is quite possible to see with the naked eye a marked change in a drop of a mixture in which the agglomeration phenomenon is taking place.

B. *When the blood tested is that of a typhoid patient* in a suitable stage of the fever (that is, after the third or fourth day from the beginning, and better still after the seventh or eighth day), the phenomena observed differ according to whether the serum is potent or not.

When the serum is potent changes take place so quickly, that, however rapidly the mixture is covered and placed under the microscope, many of the bacilli will already have become nearly motionless, and several clumps will have formed before the preparation can be seen. The greater part of the bacilli, however, will still be actively motile, in fact, they seem very often to be in a state of extraordinary activity, as if they were under the influence of stimulation. Soon however, that is in from two to five minutes, they gradually lose their power of translation, they seem paralysed, and exhibit nothing more than an oscillatory motion, which after a time becomes feeble, and cannot be distinguished from Brownian movement. At the same time clumps are forming rapidly. In from five to thirty minutes hardly any free bacilli remain between the clumps, which may be of various sizes. The presence of the corpuscles does not affect this phenomenon of agglomeration. The corpuscles behave like perfectly indifferent bodies. The bacilli are not attracted by them; they do not seem either to be clearly repelled, but it is worth noticing that clumps very seldom enclose a corpuscle or form against them.

All bacilli do not behave exactly in the same way; some of the very small bacilli, almost coccus-like, very often retain their motion for a longer time than the others. In some parts of the preparation the bacilli remain swarming, whilst in other parts they are already completely agglomerated. I thought at first that this was the result of imperfect mixture, but the perfectly even distribution of the red blood corpuscles (when these are retained) showed that this was not the case. Within a few minutes, however, all these differences may disappear, and the preparation present a uniform appearance.

When the serum has a feeble agglomerating power the changes described above take place much more slowly and less completely. The motility of the bacilli is generally considerably reduced (after being first increased), but it may never be entirely abolished in a $\frac{1}{10}$ dilution.

The clumps form gradually; they are in most cases sufficiently numerous at the end of half an hour to make the diagnosis possible, but in some cases one may have to wait one and even two hours before the preparation takes a very characteristic appearance. These cases are few.

Both in the case of the complete and of the incomplete reactions just described, the agglomeration remains clearly distinct for days after the preparation has been made. In some cases the bacilli remain motionless, but in most cases many bacilli regain their activity.

There is also marked evidence of growth. The bacilli forming the clumps may reach a great length, but the filaments thus formed remained clumped together. In very few cases the bacilli become granular and indistinct; this has usually been observed when the reaction has been intense.

Before concluding, I must add that when the question of applying this test to diagnosis, and the method of collecting the blood had to be considered, I thought it necessary, in order to remove chances of contamination, to recommend (1) that the skin from which the blood was obtained be sterilised; (2) that a needle which had not possibly come in contact

with any other blood, and been thoroughly sterilised, be used; (3) that nothing but blood collected in sterilised hermetically sealed pipettes be sent to the laboratory. Further experience has convinced me that all these precautions are useful.

I will not refer here to the results obtained by Dr. Sidebotham and myself with this method, since it has been applied to the diagnosis of cases occurring in ordinary practice. I may say, however, that they confirm entirely the results obtained in a series of over fifty hospital cases. In applications of this kind the technique must be such that scientific investigations will not suffer from accidental circumstances which would vitiate the results. I have already explained the way in which I have attempted to remove these difficulties.

The administrative part of the work presents difficulties of another nature, but which have to be overcome before the scientific methods can be applied at all in public health work. Dr. Niven has very successfully removed these administrative difficulties in the case of diphtheria, so that now, practically, all possible notified cases of diphtheria are examined bacteriologically. By following the same methods in the case of typhoid fever since the beginning of this year, a similar measure of success has already been nearly obtained in connection with typhoid fever. With the object of assisting others who might wish to carry out elsewhere the same kind of work, I have arranged with Dr. Niven to give shortly a report on the administrative working of the method in Manchester.

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¹For fuller accounts of other points, not referred to here, see S. Delépine, *Medical Chronicle*, October, 1896; *Lancet*, December 5th, 1896; Delépine and Sidebotham, *Lancet*, December 12th, 1896. ²With regard to diseases prevalent in this country, the one which has, so far, given me results as good as typhoid fever is glanders; Professor MacFadyen some time since announced a similar result in the *Journal of Comparative Pathology*. ³F. Vidal, first communication to the Société Médicale des Hôpitaux de Paris, Séance du 26 Juin, 1896, *Semaine Médicale*, July 1st, 8th, 29th, etc.; *Presse Médicale*, July 29th, 1896; *Lancet*, November 14th, 1896. ⁴*Comptes Rendus et Mémoires de la Société de Biologie*, November 23rd, 1889, p. 667. ⁵R. Pfeiffer, *Zeitschrift für Hygiene*, 1894, xviii, p. 1, *ibid.*, 1895, xix, p. 87; R. Pfeiffer and Kolle, 1896, xxxi, p. 203. ⁶E. Metchnikoff, *Annales de l'Institut Pasteur*, 1894, pp. 714-16; 1895, p. 433, etc. ⁷J. Bordet, *ibid.*, 1895, p. 462, 1896, p. 191, etc. ⁸Durham, *Journal of Pathology and Bacteriology*, July, 1896, p. 13; Gruber and Durham, *Münch. med. Woch.*, March 31st, 1896. ⁹A. S. Grünbaum, *Lancet*, September 10th, 1896. Although this paper was published over two months after Vidal's results were generally known, Dr. Grünbaum was already working with Gruber during the month of March.

A CASE OF TYPHOID FEVER TREATED WITH ANTITYPHOID SERUM: RECOVERY.

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A NURSE, aged 29, of somewhat delicate constitution, who had lately been engaged in nursing a case of typhoid fever, complained of feeling ill and unable to do her work on February 10th, 1897. She said that she had been feeling poorly and tired with some headache for a week or ten days. Her tongue was slightly furred. The temperature in the morning was 101° F., but rose at night to 104° F.; she had a slight sore throat. She was sent to bed, and, as the bowels had not acted for two days, an aperient was given.

Temperature Table.

Date.	Morning.	Evening.	Date.	Morning.	Evening.
Feb. 10	101.2	100.2	Feb. 22*	98.2	100.8
" 11	99.6	100.2	" 23	68.2	99.6
" 12	100.0	101.4	" 24	97.2	98.2
" 13	101.8	102.2	" 25	97.4	98.6
" 14	102.0	102.0	" 26	97.6	99.6
" 15*	98.4	100.2	" 27	99.8	99.2
" 16	100.6	101.8	" 28	98.2	97.0
" 17*	100.0	102.4	Mar. 1	97.2	99.6
" 18*	99.0	101.2	" 2	98.0	98.6
" 19	89.4	98.0	" 3	97.0	97.2
" 20*	98.4	101.0	" 4	97.0	97.2
" 21	98.2	100.8			

* 10 c.cm serum.

On February 11th she felt a little better, but still had headache, and the tongue was dry.