endemiological conditions. It is proposed to deal more fully with the endemiology and epidemiology of the disease on a later occasion.

12. We think that the evidence in favour of the etiological importance of the fine small bacillus is stronger than any that has yet been adduced for any other pretended "yellow fever germ." At the same time there is a much further work to be done ere its final establishment can be claimed. The acquisition of a new intestinal bacterium would explain the immunity of the "acclimatised."

NOTES AND REFERENCES.

¹ The completion of the interim report, of which this is an abstract, was interrupted by the onset of attacks of yellow fever in both of us. The loss of my much-lamented colleague renders it advisable to submit this shortened report only for the time being.—H.E.D. ² We find these constantly enlarged and much injected, though whether this is specific we are not able to say. ³ *Report on Etiology and Prevention of Yellow Fever*, 1890. ⁴ We have found this sometimes useful in examining the blood of ague patients.

THE MARGIN OF ERROR IN BACTERIOLOGICAL DIAGNOSIS.

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BACTERIOLOGICAL methods of diagnosis have become so generally adopted that the question of the reliability of such methods becomes one of the highest importance. After passing through a period of neglect and mistrust, bacteriology is becoming fashionable, and the danger at the present time is lest undue importance be attached to its procedures to the detriment of sound clinical observation. The diseases with which I purpose dealing in the present paper are enteric fever, diphtheria, general blood infections, and tuberculosis.

ENTERIC FEVER.

The discovery of the paralysis of motion and the agglutination of typhoid bacilli by the blood of typhoid patients has done much to facilitate the diagnosis of enteric fever. It is not generally recognised, however, that all cases do not give this reaction, or that the agglutinating property may not present itself until late in the disease, or that it may be present at one period of the disease and absent at another. Widal himself was one of the first to record a case of enteric fever in which the reaction was absent throughout, and Horton-Smith, in the Goulstonian Lectures of 1900, estimates that it is absent in about 3 per cent. of all cases. In the last 200 cases which I have examined I find 7 which at one time or other failed to give a positive reaction in half an hour with a dilution of 1 in 20. The brief outline of such examinations is as follows:

- CASE 1.—8th day. No reaction.
18th day. Positive.
30th day. Positive.
- CASE 2.—16th, 17th, 26th day. No reaction with dilution 1 in 10.
22nd day. Tested by medical officer of health. Negative 1 in 5.
31st day. Relapse.
48th day. Positive.
52nd day. Tested by medical officer of health. Positive.
- CASE 3.—16th, 24th, 31st days. Negative.
41st and 44 days. Tested by medical officer of health. Negative, doubtful, 1-20. July 20th, 1899. Some clumping in 8 min., but much movement of free bacilli, even after 2½ hours. (Blood in vaccine tube.) July 23rd. 1-20. Loose clumps formed but considerable motility in ¾ hour.
About 52nd day. Relapse.
53rd day. Positive.
This case terminated fatally, and the diagnosis of enteric was confirmed by *post-mortem* examination.
- CASE 4.—7th, 8th, and 9th days. Negative.
11th day. Positive.
- CASE 5.—About 13th day. Negative.
17th day. Negative.
21st day. Positive.
- CASE 6.—21st day. Negative.
26th day. Examined by Professor Kent. Negative.
33rd day. Professor Kent. Positive.
35th day. Examined by medical officer of health. Positive.
- CASE 7.—About the 13th day. Examined by medical officer of health. Negative.
16th day. Negative.
18th day. Negative.

This patient died on the 23rd day, and the diagnosis of enteric was confirmed at *post-mortem* examination.

In all cases the day of the disease can only be approximately correct, and possibly in Cases 1 and 5 the examinations were made in the early days of the attack before the agglutinating substance was elaborated, for it was not until the end of the first week that the reaction was obtained.

In some instances there was imperfect clumping, but this was always slight or disappeared rapidly, so that in every case the report was negative. Such slight alterations are often seen in testing the blood of patients other than those suffering from enteric fever, and consequently are of no diagnostic value.

I have dwelt at length upon these cases in order to accentuate the fact that where the clinical signs and symptoms are well marked, the absence of the agglutinative reaction does not necessarily negative a diagnosis of enteric fever.

In the series of examinations under review I have not met with any instance of repeated positive reactions given by the blood of patients suffering from diseases other than enteric fever. Such cases, however, although extremely rare, have been recorded. From time to time I have met with partial clumping, partial arrest of movement, reactions which one could only class as "doubtful." In an earlier series of examinations when the technique was less perfect, and the dilution as low as 1 in 10 mistakes were not uncommon.

DIPHTHERIA.

In no disease does the medical practitioner mistrust his powers of clinical diagnosis more than in diphtheria. This is well instanced by the fact that out of 131 consecutive swabbings examined by me in the last two years only 42 (32 per cent.) showed typical Klebs-Loeffler bacilli. The majority of these cases came, however, from the Royal Infirmary or General Hospital, and at such institutions, where the means of research are at hand, swabbings are more readily taken. From a series of cases coming under my own observation, and on which I took notes, I am of opinion that about 10 per cent. of true cases of diphtheria would escape detection if the diagnosis were made without bacteriological examination. On the other hand, there is a small percentage of cases presenting clinically all the signs of diphtheria from which the Klebs-Loeffler bacillus cannot be cultivated. I have dealt with such cases in a previous paper.

In a case exhibiting well-marked symptoms of diphtheria, failure to find the specific bacillus in a given culture should not lead to a modification of the diagnosis, for the bacteriological finding is open to many fallacies. Thus the swab may have been imperfectly inoculated, from the surface rather than the under edge of the membrane, or the culture tube may have failed to receive an infected portion of the swab, or the peculiar variety of bacillus present may fail to grow on the medium provided or under the circumstances in which it is placed.

Nor can we implicitly rely on a positive finding, for in doubtful cases it is extremely difficult by microscopical examination alone to identify a given bacillus, and this is especially the case when we are dealing with the so-called short varieties. The bacteriologist can simply state that in his opinion such-and-such a bacillus resembles one of the many varieties of diphtheria bacillus.

The following two cases illustrate, however, the value of bacteriological examinations in this disease.

CASE I.—An infant, under the care of Dr. Rogers, in the Children's Hospital, suddenly developed double otorrhœa. Microscopical examination of the discharge showed a few cocci and many typical long Klebs-Loeffler bacilli. This led to an examination of the nose and throat, and a hitherto unsuspected nasal diphtheria was discovered.

CASE II.—A child, aged 3 years, fell, cutting the lower lip. A superficial ulcer covered by a thin grey membrane formed, and at Dr. James Swain's request a culture was made from this, and diphtheria bacilli found. This was on March 10th, 1890, and the bacilli were still present on March 17th. The child had no symptoms of diphtheria throughout, and the ulcer healed rapidly. On March 21st a younger sister, aged 18 months, was notified as suffering from diphtheria, which terminated fatally on the 26th.

We may summarise the matter thus:

The finding of the Klebs-Loeffler bacillus is of value in cases presenting doubtful clinical symptoms, but is of less importance when symptoms of disease are absent, or when the exact nature of the organism is doubtful.

Failure to find the specific bacillus is only of value when confirmed by repeated examinations.

BACTERIOLOGICAL EXAMINATION OF THE BLOOD.

In cases of general blood infection a bacteriological examination is often of the greatest value both for purposes of diagnosis and prognosis. The blood (not less than 2 c.cm.)

should be drawn from a vein by means of a sterile syringe. It is then spread over the surface of agar or other medium and incubated. If rigid aseptic precautions are observed the margin of error is very small.

Of 19 cases examined by me organisms were present in the blood in 5. We may exclude from these 5 one case in which the blood was taken in capillary vaccine tubes with every probability of contamination. The 4 remaining cases were briefly as follows:

1. *Puerperal Sepsis*, which terminated fatally; the organism present was the staphylococcus pyogenes albus.
2. *Ulcerative Endocarditis*.—Streptococci were found in the blood on three different occasions. The case terminated fatally.
3. *Ulcerative Endocarditis*.—The staphylococcus albus was found in the blood. The patient died.
4. *Pneumonia*.—The pneumococcus was present in the blood. The case terminated fatally.

Of the 14 cases in which no general blood infection could be demonstrated 2 died, and the subsequent history of some few others I have been unable to trace. Amongst these 14 were cases of puerperal fever, pernicious anæmia, ulcerative endocarditis, cerebro-spinal meningitis, and enteric fever.

The noteworthy point is that all the cases showing general blood infection terminated fatally, illustrating the fact that from the point of view of prognosis this method of bacteriological research is of the highest importance.

In the case of blood examinations failure to detect micro-organisms cannot be accepted as proof of their absence, for the quantity of material examined is relatively small. The chances of error with a positive result are, however, small, and depend solely on the care and attention bestowed upon the sterilisation of the syringe and skin.

TUBERCULOSIS.

In 200 consecutive specimens of sputa examined bacteriologically, tubercle bacilli were detected in 50 per cent.

Whilst the finding of the bacillus may settle the question of diagnosis, failure cannot be taken as evidence of the absence of tuberculous infection. In early stages of phthisis and in the acute disseminated variety, tubercle bacilli may not be present in the expectoration, there being as yet no breaking down in the lung. Success in finding the bacillus is the reward of patience and perseverance, and depends upon several factors: (1) the nature of the sputum chosen; (2) the number of cover slips prepared; (3) the time and care spent in examining the films. Students often fail because they prepare too few specimens, and examine these too superficially. Agitation of the sputa with carbolic acid and subsequent sedimentation is useful in as far as it gets rid of the stringy mucus, but I do not find that I get better results by this method than by examining in the fresh state. In a case presenting the ordinary clinical features of phthisis, I should require a large number of negative reports to convince me of its non-tuberculous nature. One such case in a diabetic patient I have under my care at the present time.

For many and obvious reasons it is impossible to gauge the severity of the disease by the number of bacilli in a given specimen; but, on the other hand, if the patient's sputum be systematically examined at definite periods during the illness, the progress towards recovery will be seen to be marked by a steady diminution of the tubercle bacilli. These, however, remain long after the excess of other micro-organisms has abated. This in my experience is the case especially with patients undergoing the so-called Nordrach treatment.

In the examination of serous fluids, pus, or sections of tissues the margin of error is very great if reliance be placed on negative results. A positive result is, of course, conclusive, but this can seldom be arrived at without inoculation experiments. Even if inoculation be resorted to, the possibility of error is not eliminated, for the quantity of centrifuged material inoculated into a guinea-pig is very small.

In actual practice the only bacillus which is likely to be mistaken for the tubercle bacillus is the smegma bacillus, and this has recently been shown to have a wider distribution than was formerly thought. For this reason the examination of urine for tubercle organisms is useless unless the water be drawn off with aseptic precautions, and unless the films be (subsequent to decolorisation with acid) allowed to soak in alcohol for at least thirty minutes.

SOURCES OF ERROR IN METHODS EMPLOYED.

Error in bacteriological diagnosis is frequently due to the fact that cultures only are taken and no films prepared. For example, an abscess is incised and some of the pus inoculated on culture tubes; no growth results, and the pus is regarded as having been sterile, whilst in reality it has been caused by an organism which does not grow on ordinary media, or which only grows under anaërobic conditions. Whenever possible, therefore, films should be prepared and stab cultures made in glucose media. From neglect of these precautions I have more than once failed to elucidate the cause of lesions which were probably due to such organisms as the *B. tuberculosis* and *B. capsulatus aërogenes*. Some organisms, too, such as the diplococcus of Fraenkel, are far easier to recognise in fresh films than in cultures.

It has not been my purpose in the foregoing remarks in any way to disparage bacteriological methods of diagnosis, which I believe to be invaluable. It is necessary, however, to receive all bacteriological findings with caution, and to regard them merely as useful adjuncts to clinical observations.

THE PROTECTION OF THE OBSERVERS IN CASES OF INFECTIOUS SORE THROAT.

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I BELIEVE that nothing is so difficult as to induce a surgeon to take habitual precautions for the safety of his own health, and the much-lamented death of Dr. Lewis, a young and promising surgeon, affords an instance which adds weight to this conviction. It is now more than a year ago since he succumbed to an attack of malignant scarlet fever, contracted while examining the throat of an infectious patient; and yet I do not think that any of his many friends—and I include myself—have since that time practised any special precaution.

Celluloid or talc screen for infectious cases.