REPORTS TO THE SCIENTIFIC GRANTS COMMITTEE OF THE BRITISH MEDICAL ASSOCIATION.

REPORT ON THE CHOLERA-BACILLUS.

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I HAVE also injected a syringeful of a pure cultivation of these organisms in nutrient jelly into each of four mice. On one occasion, for two of the mice, a cultivation nine days old was employed, and both mice died in about six hours. In about an hour, they seemed sleepy and less lively than usual, sitting crouched up in a corner, and breathing rapidly. For at least an hour before death, however, they lay on their sides breathing very slowly, and apparently with great difficulty; in fact, rather gasping than breathing.

On another occasion, the other two mice were injected with a cultivation three weeks old. One of these remained unaffected, the other died in thirty-six hours. On *post mortem* examination, the blood was dark and fluid, and the intestines contained very liquid faeces. Cultivations were made from the blood of the heart, and from the contents of the small intestine. In both instances, large numbers of cholera-bacilli developed. The result in the first two cases was, I think, clearly due to a chemical poison; that in the last, to growth of the organisms in the blood. It is interesting, with regard to the last case, that the organisms had found their way into the intestine, and grown there in large numbers. I have not yet examined the wall of the intestine microscopically.

It is held by many that the virus of cholera produces a chemical poison which is absorbed from the intestine into the blood, and gives rise to the symptoms of the disease. This is a very probable view. Dr. Vincent Richards (*Indian Medical Gazette*, April 1884) found that the administration of large quantities of the contents of the intestines of cholera-cases to pigs was, in some instances, followed by rapid death of the animal, apparently from a chemical poison. He mentions five experiments, in three of which the result was negative (in only two, however, was choleraic material from man employed); in the other two, the result was positive, one animal dying in 2 hours, 50 minutes, and the other in 1 hour, 38 minutes. From these experiments, he draws various sweeping conclusions, but there is a complete absence of control-experiments, and, as I have just mentioned, the result in three instances was quite negative. Hence no conclusion can be come to as to whether or not it was the cholera-virus which produced the poison that killed the two animals. Before I knew that the experiments were so incomplete, having only seen a notice of them in one of the English medical papers, I performed the following two experiments. My idea was that, if the poison in Dr. Richards' experiments were produced by the virus of cholera, and if the cholera-bacilli were that virus, the same results ought to be obtained by the administration of a fluid in which cholera-bacilli had grown, as by the administration of cholera-stools. Therefore, having, through the kindness of Mr. Horsley, obtained a young pig, I on two occasions made it swallow a large quantity of meat-infusion, containing peptone, in which cholera-bacilli were actively growing. On the first occasion, I used three and a half ounces of a cultivation five days old, in meat-infusion containing 1 per cent. of peptone; a week later, I used about twelve ounces of a cultivation three days old, in meat-infusion containing 4 per cent. of peptone. In neither case were any symptoms produced. Having by that time made myself acquainted with Dr. Richards' paper, I saw how incomplete his experiments were, and I did not, therefore, continue the investigation; for it was quite clear that, by working with these cultivations in the first instance, I was beginning at the wrong end, as the investigations must first be thoroughly carried out with cholera-evacuations and other materials for control, before one had any basis to go upon; and this I could not do. Nevertheless, I have thought it right to mention the facts, though I do not think that any conclusions can be drawn from them.

Nicati and Rietsch (*Comptes Rendus*, vol. xcix, pp. 928-9) found that,

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by filtering fluids in which cholera-bacilli had been growing, and then injecting the filtered liquid into the veins of animals, serious symptoms were produced. In a first series of experiments, they found that the results were diarrhoea, vomiting, general depression, and recovery in an hour. In a second series, there were respiratory trouble, vomiting, paralysis of legs, and death. In a dog, there was found, after death, extensive ecchymosis in the duodenum; the bladder was empty; the cortical part of the kidney was much injected; the blood was dark, no clots, etc. They state that this result will not be obtained unless the cultivations be at least eight days old; recent cultivations are quite inactive; subcutaneous injection of the material produced no result. The age of my cultivations may be a possible source of fallacy in the experiments on the pig mentioned above; for, in the case of the two mice previously referred to, in which the cultivations were nine days old, death obviously resulted from a chemical poison.

The result of my experiments on animals is, then, the following. In two instances, guinea-pigs died undoubtedly as the result of the growth of the cholera-bacilli in their intestines; they certainly did not die of septicæmia. I have, in Figure 6, given a drawing of bodies which were found in the large intestines of these animals, along with other bacteria, straight and curved. The woodcut shows them thicker than natural. I think it most probable that these bodies are the cholera-bacilli, which were found, on cultivation, to be present in enormous numbers, because there were no other markedly curved organisms present, and because they seemed to show all gradations between small slightly curved rods, and the large coiled bodies shown in the drawing. It is, however, only right to say that the gentleman who made the drawings for me thought that these bodies were minute cæntozoa, but this view did not seem to me probable. The microscopic appearance is, however, of no consequence; the essential fact being that, on cultivation, I found that almost all the colonies which developed on the plates, were colonies of cholera-bacilli, showing that they were present in the intestine in enormous numbers. I should also state that I have made cultivations from the intestinal contents, and from the dejecta, of healthy guinea-pigs, and have never found cholera-bacilli. Why the other animals escaped after the injection, I cannot explain, but somewhat similar facts have been obtained by other observers. As remarked in regard to case No. 17, the fluid was seen to pass upwards into the stomach, as well as downwards into the duodenum; and it is quite possible that this acid material, passing immediately afterwards from the stomach into the duodenum, killed the bacilli which had not entered the stomach. As regards mice, in two instances death occurred in a few hours after subcutaneous injection of a cultivation, as the result, apparently, of absorption of a chemical poison from the material injected; and, in one instance, the cholera-bacilli grew in the blood of the animal, passed into the intestine, and killed the animal.

Conclusions: Diagnostic Value.—If, now, we consider carefully the meaning of the foregoing facts, it will be evident that the discovery of the cholera-bacillus is a most valuable addition to our knowledge, quite apart from the conclusions which may be come to as regards its causal connection with Asiatic cholera. For, in the first place, it seems to be constantly present in Asiatic cholera. I do not mean to assert that the cases I have examined are sufficient to prove this, but they are, nevertheless, very striking, for I had not selected the cases in any way. I did not say, "This seems a typical case of the disease, I will examine it," or "This does not seem a good case, I will not have material from it;" I was glad to take all the material offered me, without reference to whether it came from a typical case or not, the only stipulation being that it should come from a recent case. Therefore the foregoing cases, though few in number, afford very strong confirmatory evidence of the statement that these organisms are always present in Asiatic cholera. This is a fact which is, I think, hardly disputed. In the second place, this organism has never yet been found anywhere else than in Asiatic cholera. I have mentioned a large amount of evidence in support of this statement, and, for my own part, I am now thoroughly convinced that it is correct. As I have pointed out, various organisms with somewhat similar morphological characters have lately been described, but accurate examination has shown that these are different from the cholera-bacillus, and can be readily distinguished from it. Hence the converse of these propositions necessarily follows, namely, that, if the cholera-bacillus be found in dejecta, these dejecta must have come from a patient suffering from Asiatic cholera; in other words, the presence of this bacillus may be used as a means of diagnosing Asiatic cholera. The only fact¹ which could be brought forward against this view is that

¹ I do not here take into account the statements made by Dr. Klein in *Las week's JOURNAL*, for these require confirmation before they can be accepted. The experiments are unfinished and uncontrolled, and have, therefore, been too hastily published.

Dr. Klein states that, by acclimatisation, he is able after a time to cultivate the comma-shaped bacillus found in saliva in the same material as is employed for the cultivation of the cholera-bacillus, and that these cultivations are identical with those of the cholera-bacillus in many respects. I shall refer in detail in the appendix to Dr. Klein's statements with regard to the salivary bacillus. Let us, however, suppose for a moment that they are correct, and let us further suppose that the cultivations obtained by acclimatisation are identical with those of the cholera-bacillus, not merely in many respects, but in all respects: how would that affect the diagnostic value of the cholera-bacillus? It would not interfere with its value as a diagnostic sign at all; for Dr. Klein states that, *in the first instance*, the salivary comma-bacillus will not grow in the alkaline nutrient jelly used for the cultivation of the cholera-bacillus; it must be acclimatised. If, therefore, the comma-shaped bacillus constantly present in Asiatic cholera be the same organism as the salivary bacillus, it must have been "acclimatised," as the result of the choleraic process, for it will grow in the first instance in the alkaline nutrient jelly. But the absence of the cholera-bacillus in diarrhoea from other causes, and under other circumstances, proves that this "acclimatisation" does not occur in other diseases than in Asiatic cholera. Hence, if, *in the first instance*, cultivations of cholera-bacilli be obtained in the alkaline nutrient jelly from dejecta, these dejecta must have come from a case of Asiatic cholera; this conclusion being necessary, as I have just pointed out, whether one holds that the cholera-bacillus is causally related to cholera, or that it is merely the salivary comma-bacillus "acclimatised" by the choleraic process. I feel certain, therefore, that I am not in any way misleading the members of the Association when I state that the presence of the cholera-bacillus in dejecta may be held to be a diagnostic sign of Asiatic cholera.

The importance of this discovery cannot, I think, be overrated; for it is probably only at the commencement of an epidemic that much can be done to arrest the spread of the disease; and if we can with certainty diagnose the first case as true Asiatic cholera, an immense point is gained. In any suspicious case, the patient can be isolated, his dejecta thoroughly disinfected, and all the necessary precautionary measures adopted; while, in the meantime, it is being ascertained whether or not it is a case of true Asiatic cholera. Thirty-six to forty-eight hours would suffice for this purpose; because, in thirty-six hours, the colonies on the glass plates are visible under a low power of the microscope, and their characteristics can be studied. I venture to think that, if Koch's work on cholera lead to nothing more than this, it is an achievement for which he deserves the very highest praise. The great importance of this matter has been insisted on by Dr. Koch, and has been realised by the German Government. During the past few months, over 100 medical men from various parts of Germany, and from other countries, have received instruction from Dr. Koch in the methods of cultivating and distinguishing the cholera-bacillus, and there are now in almost every town in Germany men able at once to ascertain, with regard to any suspicious case, whether or not it is a case of Asiatic cholera. Surely some steps ought to be taken in this country to enable our medical officers of health to acquire like information.

Causal Connection.—But if we look more closely at the facts, it will be evident that there is fair ground for thinking that the cholera-bacillus is, in some way or other, causally connected with the disease. Let us take the two main points which have been discussed in detail in the foregoing paper. In the first place, we have seen that the cholera-bacilli are always present in Asiatic cholera in the early period of the disease. Wherever cases of Asiatic cholera have been thoroughly examined, whether in India, in Egypt, in France, in Italy, or in Spain, these bacilli have been found. Wherever the virus of this disease goes, the bacillus goes; when the virus disappears, the bacillus disappears. The virus has never been found to produce Asiatic cholera without the cholera-bacillus appearing at the same time; the two evidently go hand in hand. In the second place, this bacillus has never yet been found in other diseases, or in places where any connection with Asiatic cholera is out of the question. And yet, if it be only accidentally present in cholera, it follows, from the fact that it is constantly present in that disease, that it ought to be very widely distributed throughout the world; and ought, therefore, to be readily found quite apart from Asiatic cholera. This, however, is not the case, as I have shown at length in this report. And it must be remembered that it is not one investigator alone who has failed to find these organisms apart from Asiatic cholera; but it is, I might almost say hundreds, at any rate not much under two hundred, and probably more, who have been searching for it diligently for months without success. When one considers the immense amount and variety of material which must, therefore, have been carefully examined with negative results,

the statement, that this bacillus is limited to Asiatic cholera, must, I think, be taken as sufficiently proved. The only investigator of note whose results seem, at first sight, to lead to an opposite conclusion is Dr. Klein; but, in the appendix, I shall point out facts in relation to his research which diminish very materially the importance to be attached to it.

Now, let us ask what can be the meaning of these two facts; and, in doing so, we may leave out of consideration for the present the minor points, such as the distribution of the bacilli in the intestinal canal, their relation to the wall of the intestine, etc. Though these may act as additional arguments for or against the view of the causal connection of these bacilli with Asiatic cholera, yet, in the main, have reference rather to the mode of action of the organism, supposing it to be the cause of the disease. Dr. Koch has given in his report the only three possible hypotheses which may be formed from these facts.

In the first place, one might say that the choleraic process favours the growth of these bacilli, by providing a medium in which they can grow more rapidly than other forms of bacteria. But this hypothesis would imply that these organisms are normally very widely distributed throughout the world, which, as we have seen, is not the case. It is absurd, and, indeed, it is against the facts, to suppose that cholera-bacilli are constantly present in every individual, and yet are in such small numbers that they cannot be detected, for we know that cholera-dejecta are not the only soil on which these organisms can grow luxuriantly; they grow readily in all sorts of putrescible materials, and if they are constantly present in every individual, they must of necessity often meet with soil, either inside or outside the body, in which they can grow well. It is difficult, also, to see how they can prolong their existence if they can only grow with difficulty, and in small numbers, except when the patient is suffering from Asiatic cholera. Nor is it possible to imagine what their function in the economy of Nature could be under these circumstances, for every one of these bacteria has its proper function. Besides, considering the enormous amount of material that has now been examined for them, they would certainly have been found by this time. This hypothesis may, therefore, be dismissed, and the other two considered.

In the first place, it might be said that, as the result of the choleraic process, some common and well known form of organism changes its characters, and becomes converted into the cholera-bacillus; or, in the second place, it must be concluded that the cholera-bacillus is, in some way or other, causally connected with the disease.

The first conception is quite inadmissible in the present state of our knowledge. We are here brought face to face with the question of the conversion of one form of micro-organism into another. This, though possible on the evolution-theory, is contrary to all carefully observed facts with regard to bacteria, and, for this reason, it must be proved beyond a doubt before it can be accepted in any case. The evolution-theory is all very well, but it is still only a theory, however probable, and it must not be put in opposition to facts. But, even on the evolution-theory, it is hardly possible to admit this view; for change on the evolution-theory—such change as involves complete loss of original characters and acquisition of new ones—requires a long time, a great number of generations.

Now what is a generation? In the case of the higher plants, it would be reckoned from seed to seed. The formation of each new cell does not imply a new generation. And so, in the case of the spore-bearing bacteria, I should be inclined to reckon the generation from spore to spore, and not the mere division of the rods, which seems to me more comparable to the formation of new cells in the same generation. But if one reckon the whole cycle of changes from the sprouting of one spore to the formation of new spores as a generation, then the idea that one spore-bearing bacterium can be converted into another in a few hours or days, is quite untenable.

In the case of the cholera-bacillus, I doubt whether the complete cycle is yet known; but, so far as our information goes, it probably extends from the early stage, when the bacillus is almost straight, to the curved stage, and thence to the spirillar stage. But this cycle takes a considerable time; and the idea that a sufficient number of these cycles occur in a single case of cholera to convert one organism into another is quite out of the question. But, even granting that the formation of each new cell is a generation, there is still not time for conversion of one organism into another. Take case No. 2 as an example. Here, in twenty-four hours from the first symptoms of the disease, there were already innumerable myriads of cholera-bacilli in the dejecta; hence, on the view we are considering, this change must have occurred a considerable time previously; in fact, within a very few hours of the commencement of the choleraic process, in a period

of time too short, so far as we can judge, for the occurrence of change. And then, again, the cholera-bacillus can be grown through a large number of generations extending over months, and it does not show the slightest evidence of change. My own cultivations retain precisely the same characters as when they were first obtained five months ago. And yet, if this organism be so very unstable, that a few hours in a cholera-patient suffice to change its characters, one would expect that it would again revert to its original characters, more especially as it has been grown under a great variety of different conditions. The attenuation of anthrax-bacilli is not a case in point, as there there is no alteration in form and other characters, but only loss of pathogenic properties. The only instance which could be adduced is Buchner's experiments, in which he thought that he had converted the innocent hay-bacillus into the virulent bacillus-anthraxis, and *vice versa*; but these experiments have been repeated by various observers, amongst others by Dr. Klein, and the conclusion came to was that Buchner's results were due to accidental contamination of his cultivations, and not to conversion of one organism into another; and Dr. Klein has published a number of other observations on other bacteria to show that a change of this kind does not occur. But I need not refer further to this view, against which all experimental evidence is unanimous, and in support of which no reliable facts are known.

We are then left with the other alternative, namely, that, so far as our present knowledge goes, there is no other probable explanation of these two leading facts than that the cholera-bacillus is, in some way or other, causally connected with Asiatic cholera. There are, moreover, various other facts which favour this view, in addition to the difficulty of finding any other probable explanation of the exclusive association of this organism with Asiatic cholera.

According to Dr. Koch, these organisms are present in greatest numbers in the most acute cases of the disease, and at an early stage. In the cases previously mentioned, it will be seen that they were most numerous in the dejecta from a case only ill twenty-four hours, and least numerous where the patient had been ill for four days and was recovering. Again, the experiments on animals show that, when this organism can grow in the intestine, it sets up a morbid process similar to cholera. In my own experiments, two definite cases of this kind occurred, and I have previously hinted that we will shortly have very striking evidence from Dr. Koch on this point. In fact, it seems as if he had found out why it is that the injections performed in the way I have previously described are so uncertain; and apparently, as I understand, he can now infect the animals with certainty with pure cultivations of the cholera-bacillus. I need not, therefore, enter into this matter of experiments on animals, for Dr. Koch's further report will be published very soon. Again, this organism is remarkable for the rapidity with which it is killed by drying; and Mr. Macnamara mentions, in his work on *Asiatic Cholera*, that, during the epidemic spread of the disease, districts suffering from drought were entirely passed over, although small-pox and other epidemics were raging freely in them. Again, Mr. Macnamara states, as the result of his very precise observations, that dilute acids—the gastric juice, for example—kills the virus of cholera; gastric juice, as we have seen, kills the cholera-bacillus very rapidly. He also came to the conclusion that decomposition destroys the virus of cholera, and Dr. Koch came to the same conclusion with regard to the cholera-bacillus. Then the way in which epidemics disappear from Europe would imply that the virus cannot be very tenacious of vitality; the cholera-bacillus has no spore or resting-stage, and soon dies when it has insufficient nutriment.

But, while there appears to be every reason for believing that without this bacillus Asiatic cholera could not occur, it is evident that this disease is one in which other factors play a most important part. It remains to be ascertained whether this bacillus stands on the same footing as other pathogenic bacteria—say, the bacillus anthracis. Inject anthrax-bacilli into an animal, and they will practically, with certainty, cause anthrax. Is the cholera-bacillus equally potent? May there not be some truth in Pettenkofer's views, and may not this bacillus only acquire its virulence in suitable soil outside the body? What is the meaning of the epidemic outbreaks of this disease, and why is it at times endemic without being epidemic? In fact, what other conditions come into play, and what is the importance of the share they take in the causation of the disease? That other conditions do play a very important part, is evident from the whole history of cholera, and I can only explain the great, and apparently hopeless, diversity of opinion among Indian observers, as to the contagiousness of the disease, by supposing that one observer has paid special attention to one set of conditions, and that another must have been specially struck by other conditions. These are the points which, it seems to me, now urgently require investigation; for, till

some conclusion is come to as to all the necessary conditions concerned in the process, we can hardly expect to be able to decide on the best and most practicable means of prevention and cure, although, no doubt, the knowledge gained by Dr. Koch's work must greatly advance matters.

(To be continued.)

A CLINICAL LECTURE ON SPINAL ABSCESS, AND ITS TREATMENT.

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GENTLEMEN,—There is a class of cases that very frequently comes before us in hospital-practice, in which there is still room for improvement in our methods of treatment. Spinal caries is a very common disease. It is not so common amongst the very poor as it is amongst the class just above them. The gutter-children are almost constantly out in the open air, and are as hardy as town-children can be. But amongst the children of parents who are too respectable to allow their children to play in the open streets, and who therefore keep them shut up in more or less unwholesome rooms, the diseases of a tubercular type are fearfully common, and amongst these cases are many of caries of some part of the spinal column. The spine is very liable to injury from falls and blows; and injuries of this kind, unless they be so severe that the patient is at once carried to a hospital, are not very likely to receive the care and rest which are in most cases essential to recovery, and disease is therefore a frequent result. Spinal caries soon results in deformity, from the destruction and absorption of the carious bone; and sooner or later that deformity, and the irritation which must be associated with it, promote the formation of an abscess. These abscesses in their early stages are often overlooked. Sometimes, very little treatment is adopted until the patients, not necessarily all children, are brought or come to the hospital with an abscess of considerable size. Several cases of this kind have been under treatment in the surgical wards from time to time. One was brought in almost moribund, from extensive caries and long continued suppuration, but the rest have gone to convalescent homes, with good promise of recovery. The last of these is the boy who leaves St. Matthew Ward to-day, a most satisfactory example of what may be done for this class of cases, and affording us a suitable text for our lecture to-day.

Now there is some difficulty in recognising the beginnings of these abscesses. They are naturally chronic and insidious. They may commence, as you know, in almost any position around the carious bone, and sometimes at a little distance from it. When once they begin, the pus may travel in a good many different directions, and finally point in some part remote from the source of irritation. When the abscesses travel backwards, they will soon become evident in the back by swelling and fluctuation on one side, or sometimes on both sides, of the spinal column. There is no excuse for not recognising these early. In the majority of cases, however, the abscesses commence in the neighbourhood of the bodies of the vertebrae, and will not be recognised either until they have attained a large size, or until they have extended downwards, and have approached the surface in the loin, in the groin above Poupart's ligament, in the perineum, in the upper part of the thigh, and even, occasionally, in some other part of the thigh or leg. These abscesses sometimes burst into the rectum, or may burrow through the obturator foramen to the back of the thigh, and point behind the great trochanter. The abscess will usually receive a different name in each position, but the disease is the same in all, and the treatment must be on the same principles.

In two of the cases that have been under treatment the abscesses had travelled backwards, and were found as dorsal abscesses on one side of the spine. In three, the collections of pus were psoas abscesses, and presented in the upper part of the thigh, in front of the insertion of the psoas muscle. And in the case before us there were the remains of a psoas abscess on one side, with a large similar abscess on the other side, but presenting above Poupart's ligament.

Before speaking to you of the treatment of these abscesses, let me impress upon you the importance of preventing their formation by the