The Official Refutation of Dr. Robert Koch's Theory of Cholera and Commas.

The following Memorandum has been drawn up by a Committee convened by the Secretary of State for India, for the purpose of taking into consideration a Report by Drs. E. Klein and Henage Gibbes, entitled "An Inquiry into the Etiology of Asiatic Cholera." The members of this Committee were—Dr. William Aitken, F.R.S., Professor of Pathology, Army Medical School; Dr. J. Burdon-Sanderson, LL.D., F.R.S., Waynflete Professor of Physiology, Oxford; Dr. Norman Chevers, C.I.E., Deputy-Surgeon General, late Principal and Professor of Medicine, Medical College, Calcutta; Dr. F. de Chaumont, F.R.S., Professor of Hygiene, Army Medical School; Sir Joseph Fayrer, K.C.S.I., LL.D., F.R.S., Surgeon-General, Honorary Physician to Her Majesty the Queen and to His Royal Highness the Prince of Wales, Physician to the Council of India; Sir William W. Gull, D.C.L., LL.D., F.R.S., Physician Extraordinary to Her Majesty the Queen, Physician in Ordinary to His Royal Highness the Prince of Wales; Sir William W. Gull, D.C.L., LL.D., F.R.S., Physician Extraordinary to Her Majesty the Queen, Physician in Ordinary to His Royal Highness the Prince of Wales; Sir William W. Gull, D.C.L., LL.D., F.R.S., Physician Extraordinary to Her Majesty the Queen, Physician in Ordinary to His Royal Highness the Prince of Wales, President of the Royal College of Physicians; Dr. Timothy Richards Lewis, Surgeon-Major, Assistant-Professor of Pathology, Army Medical School; Dr. John Macpherson, Inspector-General of Hospitals (retired); Dr. Jeffery A. Marston, Deputy Surgeon-General, Head of Sanitary Branch, Army Medical Department; Sir William R. E. Smart, K.C.B.,
The epidemic outbreak of cholera which occurred in Egypt about two years ago gave a fresh impetus to the study of the etiology and pathology of the disease, and special measures were taken by the Governments of Germany and France, as well as by our own, to elucidate the matter during the continuance of the epidemic. The labours of the German Commission (of which Dr. Robert Koch was the chief) attracted exceptional attention, from the circumstance that it was believed that a specific organism—a bacillus, resembling one which had been found in glanders—had been discovered by them, which warranted the assumption that further study would be likely to demonstrate that it was the special cause of the disease.

With this object in view, the German Commission proceeded to India towards the latter end of 1883, and early in 1884 Dr. Robert Koch announced that this organism—now described, however, as curved, or comma-shaped, and not straight—must in reality be looked upon as the essential cause of cholera, on the grounds, principally, that it was always present in the alvine discharges in this disease, and in the mucous tissue of the lower part of the small intestine; that it was not to be found under any other conditions; and that a causal connexion between the organism and the disease had been demonstrated by the circumstances that comma-shaped organisms had been found in a tank in Calcutta near a village in which the people suffered from cholera, and that the disease diminished simultaneously with the diminution of the commas from the water of the tank.

As it was obvious that, in view of the new light which was very generally supposed to have been shed on the etiology of cholera, other prophylactic and curative measures would have to be adopted in the event of the statements being confirmed, and that harm might result were such measures resorted to on erroneous grounds, Sir Joseph Fayrer (in his
capacity as Physician to the Council of India) suggested to the Secretary of State in May, 1884, that the Government should institute a special inquiry into the whole subject. This proposal was acceded to, and it was arranged that two gentlemen, who were exceptionally well qualified to conduct researches of this character, Drs. Klein and Gibbes, should proceed to India at their earliest convenience. Every possible assistance was to be accorded to them, both at home and in India, for the prosecution of their investigations, and they were instructed to furnish a report to the Government on the conclusion of their labours, which was afterwards to be submitted to the consideration and final judgment of a Committee appointed by the Secretary of State for India in Council.

4. Drs. Klein and Gibbes embarked for India on August 6, 1884, and visited Bombay, Calcutta, and other cities in that country for the purpose of studying the disease. They left again for England on December 12, 1884, and towards the end of March, 1885, submitted an account of their researches to the Secretary of State for India.

5. Such, briefly stated, appear to be the main incidents which have given rise to the preparation of the report, which has been submitted to the consideration of this Committee, copies of which were placed in the hands of the members under cover of India Office letter of June 17, 1885. The 'Proceedings' will be found to contain a brief summary of the remarks made by individual members at the meetings, together with some notes bearing on the subject under discussion which were handed to the secretary, and are reproduced in the form of an appendix.

6. While fully accepting the truth of the statement that choleraic dejections are generally characterised by the presence of comma-shaped organisms, as maintained by Dr. Koch, a perusal of the report shows that Drs. Klein and Gibbes directly traverse several of Dr. Koch’s conclusions, and, in some cases, his statements as to assumed matters of fact. Indeed, the correctness of what may be conveniently described as Dr. Koch’s three main propositions is emphatically denied by Drs.
Klein and Gibbes. Stated shortly, Dr. Koch appears to maintain—first, that the number of comma-shaped organisms in the intestinal tissues and contents is in proportion to the acuteness of the attack, and that these organisms generate within the body a ferment by which the system is poisoned: second, that they are not found under any conditions other than in connection with cholera; and, third, that their presence in a tank which supplied certain cholera-affected villages in Calcutta with water was, practically, a proof of the causal connection between the organisms and the disease.

7. With regard to the first cited of these propositions, Drs. Klein and Gibbes write as follows:

"Comma-bacilli are present in the rice-water stools of cholera patients, but their number is subject to very great variations; while in some they are easily found, in others it is difficult to meet with one" (p. 6). . . "In order to explain the causation of the disease by the comma-bacillus, Koch assumes that, it being absent from the blood and present only in the small intestine, a chemical ferment, which is the actual poison, is secreted by it, and on the amount of this the severity and rapidity of the illness depend; in the typical acute cases a large amount of this chemical ferment is being produced, absorbed by the system, and therefore death rapidly ensues. And this, Koch states, is in accordance with the observation made by him that in these instances the comma-bacilli are so numerously found in the mucous membrane itself, particularly in the lower part of the ileum, that this appears almost like a pure cultivation of the bacilli. If this were really the case—viz. if it could be shown that in acute typical cases of cholera not only the flakes composed of the detached epithelium and mucus, found in the cavity of the intestine and on the surface of the mucous membrane, but also, as Koch states, the superficial layers of the mucous membrane of the congested ileum, are loaded with comma-bacilli and nothing else, this would be a remarkable fact, and there would be strong grounds for believing that the comma-bacilli must in some way or another be related to the morbid process, although it would not neces-
necessarily follow that these bacilli must, as a conditio sine quâ non, be the actual cause of the disorder.

“Now, our observations are in direct opposition to these statements of Koch. It is difficult to explain how such a statement could have been made. Several cases of acute typical cholera were subjects of post-mortem examination. Death had followed in some within from sixteen to twenty-eight, in others from eight to twelve hours; the post-mortem was made in some within one, in others within half or a quarter of an hour. The ileum, and, as a matter of fact, the whole of the small intestine, was either slightly and uniformly injected and its mucous membrane slightly tumefied, the cavity both of the jejunum and ileum being filled with clear watery fluid in which were suspended large numbers of the typical flakes; there was no difference noticeable in this respect between the lower part of the ileum and the rest of the small intestine. In a few cases in the lower portion of the ileum the solitary follicles and Peyer’s glands were distinct, and presented either a slight redness or only redness at the margin. Koch’s statement that in acute typical cases of cholera the Peyer’s glands and solitary glands of the ileum are enlarged, and on naked-eye inspection already visible by a slight injection of their marginal portion, is not confirmed by our observations, since several acute typical cases came under our observation in which such a condition was not noticeable, that is to say, cases coming under the category of the pure typical cases of Koch in which the mucous membrane ought to be almost ‘a pure culture of comma-bacilli’” (pp. 7, 8).

“That the comma-bacilli should in some cases of cholera, particularly those with typical rice-water stools, with or without many mucous flakes, be very abundant may simply mean that here the comma-bacillus finds the most suitable conditions for growth, more suitable than any other bacillus, although, as a matter of fact, we have not found that, except in a few cases, it always predominates over other bacilli, particularly very short, thin, straight bacilli, to be mentioned below. The statement of Koch that, in acute typical cases, the comma-
bacilli are found chiefly and almost exclusively in the mucus flakes of the lower part of the ileum—a statement borne out by our observations—does not harmonise, it appears, with the assumption that the comma-bacilli are the cause of the disease, since, in several acute typical cases, there is no difference as regards the aspect of the intestine, the amount of fluid and flakes contained in the cavity of the intestine, and the anatomical changes of the membrane between the lower and upper portions of the ileum as well as jejunum” (p. 7).

“Fine sections made of the mucous membrane of the above typical acute cases of cholera, after hardening the intestines in alcohol or Müller’s fluid, particularly the first (also used by Koch), and stained in various aniline dyes (gentian violet, in several modifications, Spiller’s purple, methyl blue, magenta, after Ehrlich’s, Weigert’s, Koch’s, and other methods), revealed the total absence of comma-bacilli from the mucous membrane itself, from the tissue of the villi, from the Lieberkühn’s follicles, and from the lymphatic tissue of the Peyer’s and solitary glands; the epithelium of the surface of the villi having become detached, during life has not generally kept its place in the hardened intestine but in many places the epithelium of the surface as well as that of the Lieberkühn’s follicles, although loosened and slightly raised from the mucous membrane, had nevertheless kept its position and was fixed during the hardening; and in these places the comma-bacilli or any other organisms are conspicuous by their absence; they are nowhere to be found, they are simply absent” (page 9).

“Some of the ardent supporters of Koch’s theory, after it has been shown that the mucous membrane of the ileum or of any other part in the acute cases of cholera, provided the examination be made immediately or very soon after death, is absolutely free of comma-bacilli, might and probably will, nevertheless, cling to the comma-bacilli as the cause of cholera, saying,—‘But the comma-bacilli are present in the cavity of the intestine, and although absent from the mucosa itself might nevertheless be the producers of the chemical ferment, seeing that they are present in such large numbers.’ As answer to
this it may be repeated:—(1) That there are acute cases in which the comma-bacilli are very scarce indeed, even after the disease has well set in; that they should have been present in sufficiently large numbers in the lower part of the ileum before the symptoms appeared, in order to produce the large amount of chemical ferment which is to be absorbed—for this is what is meant by absorption of the chemical ferment, for no absorption can go on in an intestine during the attack itself, when the wall of the stomach and intestines discharge such enormous quantities of fluid as fast as they can—must be evident to every one to be an absurdity; an assumption of this kind would imply that the comma-bacilli are present in the fecal matter in the lower part of the ileum before the setting in of the disease, and consequently they would have to remain here long enough to produce the virus, but for such an assumption there is not a tittle of evidence, and all our knowledge of the physiology of the intestine is against it; (2) that the whole of the small intestine presents in some acute typical cases the same appearances—viz. slight congestion, the cavity filled with clear fluid, in which are suspended the typical mucus flakes, and the great scarcity indeed of comma-bacilli in the flakes taken from the jejunum and upper part of the ileum; and (3) that the comma-baccilli are present only in dead tissues—for the mucus flakes are in all respects dead tissue, and they are found more numerously the lower down we go in the cavity of the ileum; these two facts point clearly to the comma-bacilli being putrefactive organisms” (page 11).

“The blood of cholera patients has been carefully examined in the fresh state, on stained specimens, and by cultivation; the blood was obtained according to the usual approved method from patients in various stages of the disease, from ten hours after seizure to forty-eight hours, and in no one single instance could the presence of any kind of bacterium or other organism be shown to exist in the blood. The preparations examined fresh, those examined after staining with aniline dyes, revealed nothing that could be identified either as extraneous matter, or as in any way indicating a specific morphological
change; all assertions to the contrary must be put down as based on imperfect method of examination or insufficient acquaintance with the appearances of blood in health and disease” (page 16).

“Numerous cultivations were made with the juice of the mesenteric glands, but no trace of bacteria was obtained, except in those tubes in which clearly and unmistakably putrefactive micrococci or putrefactive thickish bacilli had found their entrance. Thus, then, as regards the blood and tissues, the conclusion is imperative that no kind of bacteria are present in patients suffering from cholera” (page 17).

8. The foregoing extracts, especially when taken in connection with observations recorded by other observers, appear to justify the inference that no direct relation exists between the number of comma-shaped organisms associated with the choleraic process and the gravity of the disease, and that these organisms are not found in the blood or tissues, and are not ordinarily, if ever, to be found in the tissues of any part of the intestinal canal in even the most acute cases of cholera when the post-mortem examination is made immediately after death.

9. Passing on to the second of the above formulated propositions—that comma-bacilli are not found under any conditions other than cholera—Drs. Klein and Gibbes assert that “this cholera bacillus, or at any rate one that in morphological respects appears identical with it, occurs also in the stools of cases of diarrhœa. In an epidemic of diarrhœa that occurred in the autumn of 1883 in Cornwall, the stools of the patients contained . . . curved organisms which it is impossible to distinguish from the comma-bacillus of cholera stools; in size they are the same, in being curved they are the same, and, just as is the case with the choleraic comma-bacilli, some examples are either slightly pointed at the ends or blunt. They occurred not less numerously than they are sometimes found in cholera stools” (page 7). They were also met with in cases of dysentery and enteric catarrh, and “in a case of chronic phthisis of which a post-mortem examination was made, the mucus of the small intestine, although
free of any tubercle bacilli, contained, besides other putrefactive organisms, also comma-bacilli, and in this case they were so distinct that there was no difficulty in identifying them, and they were as numerous as in many cholera stools that we have examined. In the stool of a case of diarrhœa of a child suffering from chronic peritonitis (February, 1882) there are present in specimens stained with Spiller's purple numbers of comma-bacilli which it is impossible to distinguish from choleræic comma-bacilli; in size, shape, and general aspect they appear identical. On the whole, then, we maintain, contrary to Koch's emphatic statement, that the comma-bacilli occur also in cases of intestinal disease other than cholera" (page 7).

10. Both before and since this report was written evidence of a like character has been adduced, but it is to be borne in mind that, in at least some instances, such, for example, as the comma-shaped organisms which have been found associated with the cases of so-called "cholera nostras" in Bonn, it has been stated that "although in size and form they resemble those of cholera, they are, nevertheless, not identical with them." Drs. Klein and Gibbes draw attention to the fact, which had been recently pointed out, that comma-shaped bacilli, similar in appearance to those found in cholera, are ordinarily present in certain parts of the alimentary tract in health; and, as will be seen by a reference to our 'Proceedings,' there is reason to assume that these comma-shaped organisms present themselves under two, if not three, forms in the mouth alone. It has latterly been shown by Miller that at least one of these forms can be cultivated, though isolating it in the first instance appears to have been a difficult task; and we are informed that Dr. Klein (apparently since the submission of the report) has succeeded in cultivating either this or one of the other forms of mouth-commas, and has, moreover, demonstrated that its action on the media in which it grows is identical with that of the comma-bacillus as derived directly from a case of cholera. That the two forms are absolutely identical does not, however, appear to have been definitely
established. Still the facts which have been brought to the notice of the Committee seem to point to the probability that the special organism to which such virulent properties are ascribed by Dr. Koch will, sooner or later, be demonstrated to be one or other of the various curved forms ordinarily found in the alimentary tract in health, the growth of which has been favoured by the exceptional conditions which exist in the intestine during an attack of cholera.

11. As regards the third point—the evidence as to the causal connection between the comma-shaped organisms and cholera—perhaps the most striking circumstance which gave support to the theory advanced by the German Commission in India was that referred to by Dr. Koch, that, when visiting one of the native quarters in the suburbs of Calcutta, in which an outbreak of the disease had occurred, he discovered comma-shaped bacilli in the village tank, and, further, that the disease diminished simultaneously with the diminution of the commas in the water.

12. Regarding this phase of the question, Drs. Klein and Gibbes write:

"We have had the opportunity, in connection with Dr. D. D. Cunningham, to make an examination of the water of some of the tanks in Calcutta, with reference to this very question of the comma-bacilli.

"The same tank that plays such a conspicuous part in Koch's report above mentioned was visited on the 26th November. It is surrounded by native huts in which about 200 families are living. There had occurred one case of cholera in this bustee about the first week of the month of November. The water of this tank was very dirty, particularly all along the shore, and the people around the tank, as is customary, made use of the water for all and every kind of domestic and other purposes, including drinking.

"A sample of this water was taken from near the shore, where it appeared particularly impure, about twenty yards from the house in which the cholera case had occurred, and the microscopic examination revealed undoubted comma-
bacilli, identical in every respect with those found in cholerae dejecta. Notwithstanding their presence in this water, and notwithstanding the extensive use the 200 families were constantly making of it, there has been no outbreak of cholera. Now, we have in this instance an experiment performed by nature on a scale large enough to serve as an absolute and exact one. This water had been contaminated with choleraic evacuations, and of course with the comma-bacilli, and it was used extensively by many human beings for several weeks. If, to speak with Koch, the comma-bacilli were the cause and essence of cholera, how is it that not one person among so many has, until the middle of December, contracted the disease? Clearly because the water did not contain the cholera virus, and because this latter has nothing to do with the comma-bacilli’’ (p. 36).

Other instances are cited of the occurrence of comma-bacilli in tanks wholly unassociated with any recent outbreak of cholera, and, taken altogether, the evidence adduced is strikingly opposed to the correctness of the interpretation which Koch had proposed as to the connection of the disease with water of this character, unless, as a result of seasonal and other influences, the comma-shaped organisms found by Dr. Klein in November were different from those found by Dr. Koch in February. As it is not explicitly stated that Drs. Klein and Gibbes subjected the “commas” from these tanks to the test of cultivation, it could not be accepted as established that they were identical with those of cholera; but, on the contrary, they may have been identical with those discovered by Dr. Koch in some water near the Salt-water Lakes (a few miles out of Calcutta), which he found by cultivation to be physiologically different from the comma-shaped organism of cholera. The secretary, however, has ascertained from Dr. Klein that, although it is not distinctly stated in the report that these tank-commas were cultivated, nevertheless, as a matter of fact, they had been, and were found to be identical with Dr. Koch’s choleraic commas, so that this phase of the question may be looked upon as disposed of.
13. The only other evidence which has been adduced in favour of a causal connection between this organism and the disease is that acquired by means of experiments with animals. Referring to researches of this character which were performed by the German Commission and by other observers, as well as by themselves, Drs. Klein and Gibbes say:

"When in Egypt and Calcutta, Koch performed a large number of experiments by feeding, subcutaneous and intravenous injection, as well as injection into the duodenum with rice-water stools and with pure cultivations of comma-bacilli, on rodents, carnivorous animals, and monkeys, and obtained no result, and his inquiries among the people led him to the conclusion that no case was known of a domestic animal having taken cholera, and he therefore came to the conclusion that cholera is not transmissible to the lower animals. He made, however, the observation that animals (rodents) may die of septicæmia after inoculation with rice-water stools, and that the comma-bacilli are capable of multiplication within the animals inoculated, without, however, producing cholera. Since his return to Berlin he maintained that he has been able to confirm the assertions of Nicati and Rietsch—viz. that injection of the comma-bacilli into the duodenum of dogs and guinea-pigs led to death with multiplication of the comma-bacilli, and he therefore considers it proved that the comma-bacilli are pathogenic organisms.

"A large number of experiments were performed by one of us on rodents, cats, dogs, and monkeys by feeding, by subcutaneous, intraperitoneal, and intravenous injection, and by injection into the cavity of the upper part of the small intestine of mucus flakes of the ileum of typical acute cholera, and of pure cultivations of choleraic comma-bacilli and the small straight bacilli; the results of these experiments are described in the following pages" (pp. 19, 20).

"From all these experiments it follows that neither with mucus flakes taken from the ileum of acute cases of cholera nor with stools recent and old, nor with cultivations of comma-
bacilli or small bacilli, is it possible to produce in animals (mice, rats, cats, rabbits, and monkeys) any illness, be the introduction into the system carried out by feeding, by subcutaneous injection into the jugular vein, or by injection into the cavity of the intestine” (p. 24).

14. As regards lower animals, therefore, it seems to us that it has been demonstrated that neither the alvine dejections of cholera nor cultivations of isolated comma-bacilli, obtained from such dejecta are capable of producing cholera, nor even of producing systems undoubtedly of a choleraic type. On the other hand, there is no direct experimental evidence, so far as we are aware, that cholera can be induced in man by the introduction of a pure cultivation of comma-bacilli into his system; on the contrary, it is alleged that they have been swallowed with impunity.

15. The report under consideration deals with several other phases of the cholera question, but the portions referred to in the foregoing pages appear to be the most important. The investigations described, like most others recently undertaken with a view of elucidating the etiology of cholera, may, for the most part, be characterised as an attempt to confirm or refute the doctrine that the disease is caused by a microscopic comma-shaped organism. The results of these and of others of allied nature which have been brought to the special attention of the Committee may, briefly stated, be summed up as follows:

(a) That comma-shaped organisms are ordinarily present in the dejections of persons suffering from cholera.

(b) That they are not to be found in the blood nor in any of the tissues, including the mucosa of the small intestine when the latter is examined in a fresh condition.

(c) That comma-shaped organisms of closely allied morphological appearances are ordinarily present in different parts of the alimentary tract in health; that they are developed to an unusual extent in some of the diseases characterised by hyper-secretion of the intestine; and that there are grounds for assuming that when any predominant form is observed, it is in great measure attributable to the nature of such secretion.
That the comma-shaped bacilli ordinarily found in cholera do not induce that disease in the lower animals, and that there are no real grounds for assuming that they do so in man; while the circumstance that they have been found in tanks which constituted the ordinary water supply of adjacent villages unassociated with the presence of the disease goes to negative any such assumption.

16. Drs. Klein and Gibbes have made a valuable contribution to our knowledge of the bacterial organisms associated with cholera, though the evidence hitherto adduced does not warrant the conclusion that any of them bear a causative relation to the disease. As regards the question of its essential cause, the Committee are glad to learn that the Government of India are making further arrangements for having investigations, of a varied character, continuously conducted in that country under the direction of Dr. Douglas Cunningham.

17. Although the precise cause of cholera has not been ascertained, sufficient is known of the general character of the disease to serve as trustworthy basis for practical action, and the Committee feel that they ought not to separate without expressing their conviction that sanitary measures in their true sense, and sanitary measures alone, are the only trustworthy means to prevent outbreaks of the disease, and to restrain its spread and mitigate the severity when it is prevalent. Experience in Europe and in the East has shown that sanitary cordons and quarantine restrictions (under whatsoever form) are not only useless as means for arresting the progress of cholera, but positively injurious; and this not merely because of the many unavoidable hardships which their enforcement involves, but also because they tend to create alarm during periods of epidemics of the disease, and to divert public attention at other times from the necessity which constantly exists for the prosecution of sanitary measures of assured value—measures which, moreover, tend to mitigate the incidence of all forms of disease.

August 4th, 1885.