

The loss of terrestrial heat by radiation is now exceedingly small. But small as this loss is, it cannot take place without producing contraction, and Cordier long since calculated that supposing five volcanic eruptions to take place annually, it would take a century to eject so much lava as would shorten the radius of the earth to the extent of 1 mm., or about  $\frac{1}{25}$  inch.

I therefore conclude that the hypothesis originally propounded, namely, that volcanic phenomena are dependent on the effect of secular refrigeration is, with certain modifications, the one that best meets the necessities of the problem.

“Preliminary Report on the Pathology of Cholera Asiatica (as observed in Spain, 1885).” By C. S. ROY, F.R.S., J. GRAHAM BROWN, M.D., &c., and C. S. SHERRINGTON, M.B.  
Received and read June 10, 1886.

The differences of opinion among pathologists as to the relation of certain micro-organisms,—and more especially of a curved bacillus described by Koch—to Cholera Asiatica, led to our being deputed last summer, by the Association for the Promotion of Research in Medicine, acting in conjunction with the Royal Society and University of Cambridge, to proceed to Spain to make further investigations on the subject.

In Madrid we were able to make autopsies on twenty-five typical cases of cholera, the *post-mortem* examinations being made in many of them either immediately after death or within very few hours of it. Our attention was at first directed chiefly to the relation of the comma bacillus of Koch to Cholera Asiatica. Early in our inquiries we were struck by the fact that Koch's comma bacillus is not discoverable in the intestinal contents of all cases of cholera. We employed much time and care in the examination of thin dried films of the mucous flakes and fluid contained in the intestine, these films being stained by methods which we knew to be well fitted to show the comma bacillus if that micro-organism were present. Such films from one or two fatal cholera cases showed that the intestinal contents contained enormously larger numbers of comma bacilli than of other parasites. In some of the cases the comma bacillus, though certainly present, was not the most marked feature in the preparation, and in certain of these cases we were only able to find these bacilli after prolonged and careful searching. In many cases of undoubted Cholera Asiatica where death occurred before the reaction stage had set in, we were unable to detect comma bacilli in any of the films or cultures prepared from the intestinal contents taken from different parts of the alimentary canal.

We made also an enormous number of plate cultivations in gelatine and agar-agar, the cultivating media employed being prepared in the manner recommended by Koch. These cultures gave results corresponding with those obtained from examination of the dried films above referred to. In a few cases the majority of the colonies which grew in the gelatine were composed of comma bacilli. In others these were comparatively few in number, while in many of our plate cultures from the intestinal contents no colonies of comma bacilli presented themselves. The results both of the examination of films and of the plate cultures from the contents of the intestines are therefore opposed to the facts obtained by Koch. We do not think that the complete absence of the comma bacillus in the films and cultures of many of our cases can be explained by want of due care on our part.

When we came to the preparation and examination of sections of the wall of the intestine, the results we obtained were also different from those described by Koch. The tissues intended for histological examination were placed in absolute alcohol while the autopsy was being made, and the staining method which we chiefly employed was that used by Koch with methylene-blue, which method in our experience is well fitted to show the comma bacillus when it is present in the tissues.

Only in a few of our cases did we find the bacillus in question situated in the substance of the mucous membrane of the intestine, and in these cases it was present either in or close to the tubular glands of Lieberkühn or else close to the free surface of the mucous membrane. The situation of the bacilli in these cases was such as led us to the belief that it might easily have penetrated the epithelium either after death or in the few hours preceding death. In the great majority of our cases careful and conscientious search did not enable us to discover any comma bacilli in the mucous membrane of the intestine, nor indeed in any of the tissues or organs which we examined. Under these circumstances we did not think it necessary to make special investigations on the pathogenic effects of the comma bacillus when administered to the lower animals. We have not been able to convince ourselves that the pathogenic effects which Koch, Van Ermengem, and others find to result when comma bacilli are given to certain animals are identical with the phenomena which characterise *Cholera Asiatica* in man.

Further, the complete absence of comma bacilli, both in the contents of the intestine and in the tissue of many of our cases, makes it impossible for us to accept Koch's views as to the causal relation of the bacillus in question with *Cholera Asiatica*.

At the same time we do not think that sufficient evidence has been adduced to prove satisfactorily that Koch's comma bacillus is identical

either with that described by Finkler and Prior as having been obtained from cases of Cholera nostras, or with those other forms of curved bacilli which have been found in the mouths of healthy persons, decayed teeth, cheese, &c. That it is pathogenic scarcely admits of doubt, in view of the evidence given by Koch and V. Ermengem. The view, however, that it is to be looked upon as the direct cause of cholera is, we think, incompatible with the results we obtained, as referred to above. Many points of similarity between Koch's and Finkler and Prior's comma bacillus, and the relation between the latter and Cholera nostras, have led us to consider the possibility of the former of the two being the cause of the so-called premonitory diarrhoea which is so frequently, if not constantly found accompanying epidemics of Asiatic cholera. The frequency with which the comma bacillus of Koch is to be found in cases of cholera makes it, we think, almost certain that it has some relation to the disease in question. That the so-called premonitory diarrhoea of cholera cannot be looked upon as a mild form of Asiatic cholera we feel convinced from our own observations in Spain. At the same time we think it must be looked upon as a predisposing cause of Asiatic cholera. It seems to us by no means improbable that Koch's comma bacillus may be the cause of this so-called premonitory diarrhoea, and that its frequent presence in fatal cholera cases may be due to true cholera having supervened. Unfortunately while in Spain our researches were not sufficiently complete to enable us to decide that Koch's comma bacillus could not be looked upon as the direct cause of cholera, and our attention, therefore, was not directed to the question of its being found in the dejecta of persons suffering from the so-called premonitory diarrhoea. This is a question which we believe well worthy of further investigation.

As to the straight bacilli obtained by Emmerich from the blood and organs of fatal cholera cases, our results, by use of similar methods to those employed by Emmerich, do not enable us to confirm those of that observer. The cultivating media in which we placed drops of blood, or portions of the kidney, liver, and other organs from cholera cases, remained sterile. We cannot, therefore, accept the bacillus of Emmerich as the cause of Cholera Asiatica, and see no difficulty in explaining the pathogenic effects which he observed on introduction of his bacillus into certain of the lower animals as being due to a form of Septicæmia.

The straight bacillus described by Klein in his Report of the Indian Cholera Commission, is much smaller than that found by Emmerich; and we know of no reason for believing the two to be identical. As Klein has not claimed for the bacillus found by him any causal relation to cholera, we need only say here that we have not been able to recognise it in any of our preparations.

The pleomorphism of the comma bacillus which Ferran described in his article in the "*Zeitschr. f. Klin. Med.*" of last year, and the method of inoculation for protection against cholera, largely employed in Spain, attracted our attention while in that country. We had an opportunity of examining with the microscope the cultures sent, at the request of the Government, from Ferran's laboratory, to be employed in inoculating troops. These cultures were under the care of agents duly authorised by Ferran. We found them to contain several forms of bacilli and micrococci, but we did not discover either comma bacilli or any of the peronospora-like bodies described by Ferran to be present in his protective inoculation fluid. We need only say further that the facts which came to our knowledge regarding the protective power of Ferran's inoculations are by no means in accordance with the statements made by that observer. The inoculation of such fluids as we saw in the hands of Ferran's agents must expose the recipient to serious peril of septicæmic infection. The theory, moreover, on which Ferran's system is based, *e.g.*, that one attack of cholera protects against a second attack of the same disease, is entirely opposed to the facts which came under our notice in Spain. As, however, we did not personally meet with Dr. Ferran, we have no right to affirm that the cultivations when they left his hands were impure; we believe indeed that the small swellings described by him in cultivating the comma bacillus under certain conditions—and which are found in the course of the spirillum—rest upon correct enough observations. They have been seen by others, and are apparently degenerative changes. Large peronospora forms described by Ferran we knew of no reason to accept as being possible modifications of the comma bacillus.

With regard to the macro- and micro-scopic morbid changes to be found in fatal cholera cases, our observations are completely in accord with the classical description given by Strauss, Nocard, Roux, and Thuiller. With regard to the comma bacillus, the observations of Strauss, in which he was unable to satisfy himself of the causal relation between the comma bacillus of Koch and Asiatic cholera are also fully accordant with our own investigations.

Although specially commissioned to investigate the relation between Koch's comma bacillus and Asiatic cholera, we naturally turned our attention to the pathology of the disease as well as to its etiology.

That the hypersecretion from the mucous membrane of the stomach and intestines in cases of cholera is not due to catarrh, is abundantly shown both by the chemical characters of the dejecta of cholera and by the absence in the mucous membrane, on examination after death, of the anatomical changes which occur in catarrh. That it is not due to any irritant present in the contents of the intestine we think may safely be concluded from the absence of necrosis (ulceration), as well as the absence of any well-marked inflammatory

change in the mucosa. The experiments of Moreau, who found well-marked hypersecretion of the mucous membrane of the small intestine, resulting from section of its nerves, seems to us to have a very important bearing on the pathology of the disease in question. The chemical characters of the fluid so abundantly secreted during the few first hours following section of the nerves of the isolated loop of intestine are, as shown by Kühne, practically identical with those of the dejecta of cholera cases. That the hypersecretion from the intestine in cholera, with the more or less complete arrest of the power of absorption by the mucosa, is the cause of the thickening of the blood and the drying of the tissues there can be little doubt. Everything seems to point towards the assumption that the chief symptoms and signs of cholera, as well as the frequent fatal termination of that disease, is due to the escape of fluid from the vessels into the intestine. The pathology of cholera is therefore centred in the question as to what is the cause of this intestinal secretion and diminished power of absorption. We have repeated Moreau's experiments more than once with the view of observing for ourselves how far the fluid contained in the isolated loop of the intestine resembles the intestinal contents of fatal cholera cases. The results of these experiments are such as to impress us strongly with the conviction that the characters of the paralytic secretion following section of the nerves to the intestine are practically identical with those of the contents of the intestine in cases of cholera. With regard to the question whether or not the epithelium covering the free surface of the mucosa is simply less firmly attached than in the normal intestine, or whether it be actually detached before death, our observations tend on the whole towards the first-named of the two possibilities.

The pathology of cholera, we are of opinion, can be best explained by some cause acting on the glands or nerves of the intestine, and producing effects similar to those which result from paralysis of the intestinal nerves. This conclusion makes it probable that the cause of the disease, if discoverable by the microscope, is to be found either in the mucosa itself, in the nerves running in the mesentery, or in the ganglia from which those nerves proceed.

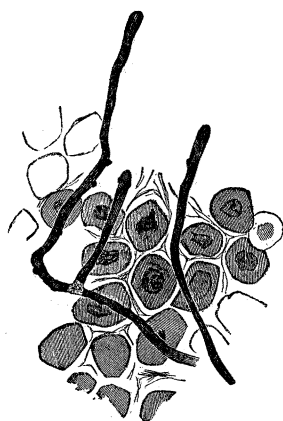
Soon after our return from Spain our inability to confirm Koch's views as to the causal relation of the comma bacillus to cholera induced us to look with care for any other parasite, the presence of which might be supposed capable of causing the disease in question. In the course of this work, which occupied many months, we observed in sections of the intestinal wall, prepared and stained in the different ways which we thought best fitted to make evident any micro-organisms present in the tissue, granules the characters of which arrested our attention. These granules, which vary much in size, were for the most part smaller than the nuclei of the surrounding

cells—which they resembled in the degree to which they were stained with fuchsine, methylene-blue, and other aniline dyes—that they had one or more processes proceeding from them, we were always able to observe; but these processes, being unstained, could not be followed by us in the tissues. It was only where in a specimen of a kidney we saw several of these granules lying in the lymph space outside the membrana propria of a convoluted tubule that we could see against the clear background the arrangement of the filaments which we had noticed proceed from the granules in other specimens. We could then see that delicate filaments connected the granules one with another in a manner so striking that the possibility was forced on us of the structure in question being a vegetal parasite. As we ourselves know no more regarding the morphology of the lower vegetal micro-organisms than is known ordinarily to the pathologist, we judged it best to show the specimen to Mr. Vines and Mr. Gardiner, whom we thought well fitted to assist us in the question whether or no we had before us a vegetal parasite, and if so of what kind. They at once informed us that forms such as the one we showed them were characteristic of the Chytridiaceæ, an order which includes many rapidly growing and virulent parasites of vegetables. They informed us, moreover, that they should not expect the envelope of such parasites to give the ordinary cellulose reactions; and also that in their opinion some method of staining in methylene-blue would be found best fitted to differentiate such a micro-organism from the surrounding tissues. The necessity which we felt of finding some method which would stain the mycelium-like threads of this structure before its presence could be demonstrated in the tissues of cholera cases, led us to spend much time experimenting with the different methods of staining in methylene-blue which we thought might be of use for this purpose. After many failures, we found that it was possible, by using a method almost identical with that of Löffler, to stain with methylene-blue the micro-organism in question, although even with this method considerable care is required to stain satisfactorily the filaments of which it is partly composed. When observed in a successfully stained preparation, it is impossible to doubt that the structures referred to are parasitic, which will, we believe, be admitted on examination of the specimens which we show at this meeting. The difficulty of staining the parasite satisfactorily, and the fact that, so far as we know, Löffler's method has not been employed to stain sections of tissues taken from fatal cholera cases, sufficiently explains to our minds why a parasite having so striking a form could have been overlooked by the many competent observers who have sought for micro-parasites in the tissues of fatal cholera cases. That its presence in our specimens could not be explained by accidental contamination after removing the tissues from the body we have satisfied ourselves by

most careful precautions. During the autopsy pieces of the intestinal wall and of the other organs are placed in absolute alcohol, and all the fluids through which the tissue and sections required to be passed for the purpose of cutting, staining, &c., well boiled and protected from the invasion of vegetable organisms by boiling and the addition of thymol.

The micro-organism which we find in our specimens from cholera cases is composed of terminal or nodal swellings connected by filaments varying greatly in thickness, and showing no differentiation into component cells.

FIG. 1.



Mucous membrane of small intestine from Case XIV, showing a portion of deep part of mucosa (Powell and Lealand  $\frac{1}{12}$  oil immersion).

FIG. 2.



Similar section from Case XXIV ( $\frac{1}{12}$  oil immersion).

Frequently also we have seen exceedingly fine filaments extending from the granules, like those which form so marked a characteristic of many of the Chytridiaceæ. Stained with methylene-blue, the granules and filaments take on the colouring matter to a fairly equal degree, although with fuchsine, followed by diluted nitric acid, the filaments become decolorised before the granules. The globular enlargements referred to vary in size from knot-like swellings on the mycelium, causing simply an inequality in the thickness of the latter, to bodies as large and in some cases even larger than the nuclei of the surrounding cells. In this abstract, in which we cannot give satisfactory illustrations, we need not say more regarding the morphology of the parasite than that it differs considerably in appearance in different cases, always, however, within the limits included in the above description, and that there are frequently present minute, round,

unstained and stained spaces or bodies in the granules and mycelium, which suggest the possibility of spores being present. The development of zoosporangia from the terminal granules, such as are described in some forms of the Chytridiaceæ, we have never seen in our specimens. In every one of our twenty-five cases of Asiatic cholera we have found a parasite having the above-described characters lying in the mucous membrane of the intestine. It is found at various depths of the mucosa, its distance from the free surface, the absence of other micro-organisms, and the precautions taken to prevent post-mortem contamination, make it evident that it must have been present there during life. We find, moreover, that the luxuriance of its growth goes, speaking very roughly, hand in hand with the degree of the histological changes in the structure of the mucous membrane, which are found unequally distributed in the mucosa of the small intestine in fatal cholera cases. In some of our cases we have found it in or between the epithelial cells of the tubular glands of the intestine.

As to its presence in other organs and tissues, we have satisfied ourselves of its presence in the kidney in some of our cases. That it occurs in the blood-vessels in some cases we have also convinced ourselves, and think it possible that the filaments and bodies described by Strauss as growing from the blood corpuscles may have been the micro-organism which is above described.

The time required for the successful staining of this micro-organism has prevented us as yet from making a systematic examination of the kidney and other organs in all of our cholera cases, so that we are not at present in a position to say in what organs besides the mucous membrane of the small intestine it is frequently or constantly present. We have seen it, however, both in the liver and kidneys, as well as in the intestinal wall. As to the question whether this parasite can be cultivated artificially, our observations are unfortunately very unsatisfactory. While in Spain we made a very large number of cultivations from the contents of the intestine, from the blood and tissues, but found it impossible to investigate the life history of all the micro-parasites which we encountered. Our *à priori* belief was that the parasitic cause of cholera, if it exist (which we thought exceedingly probable), must belong to the class of the Schizomycetes. Our attention, therefore, was almost exclusively directed to the bacilli, bacteria, and micrococci, which grew in our plate cultivations, other micro-organisms receiving little or no attention. We may, very possibly, have grown the parasite which we afterwards found in the wall of the intestine, passing it over, however, as being a very improbable cause of the disease. It appears to us by no means necessary that this micro-organism will grow readily in the alkaline cultivating media which Koch found best suited for his



comma bacillus, and we would suggest to future observers that possibly acid media may be found better suited for the growth of this parasite. As to whether the micro-organism is frequently or constantly present in the contents of the intestine, our cultivations as above-mentioned are of no value. Nor does our examination of stained films enable us to speak definitely for or against the presence of this parasite. In the intestinal contents or the dejecta of cholera cases, we have seen appearances which resembled in many points the characters of the micro-organism in question; none of our films, however, show structures which are *unmistakeably* identical with those found by us in the substance of the mucous membrane.

We have only to add that not having cultivated this micro-organism artificially, we claim no right to say that it is the cause of Asiatic cholera. All we have to say is, that we have found it present in certain tissues of all the cholera cases which we had the opportunity of examining. Further investigation must decide whether or not it can be looked upon as the direct cause of the disease.

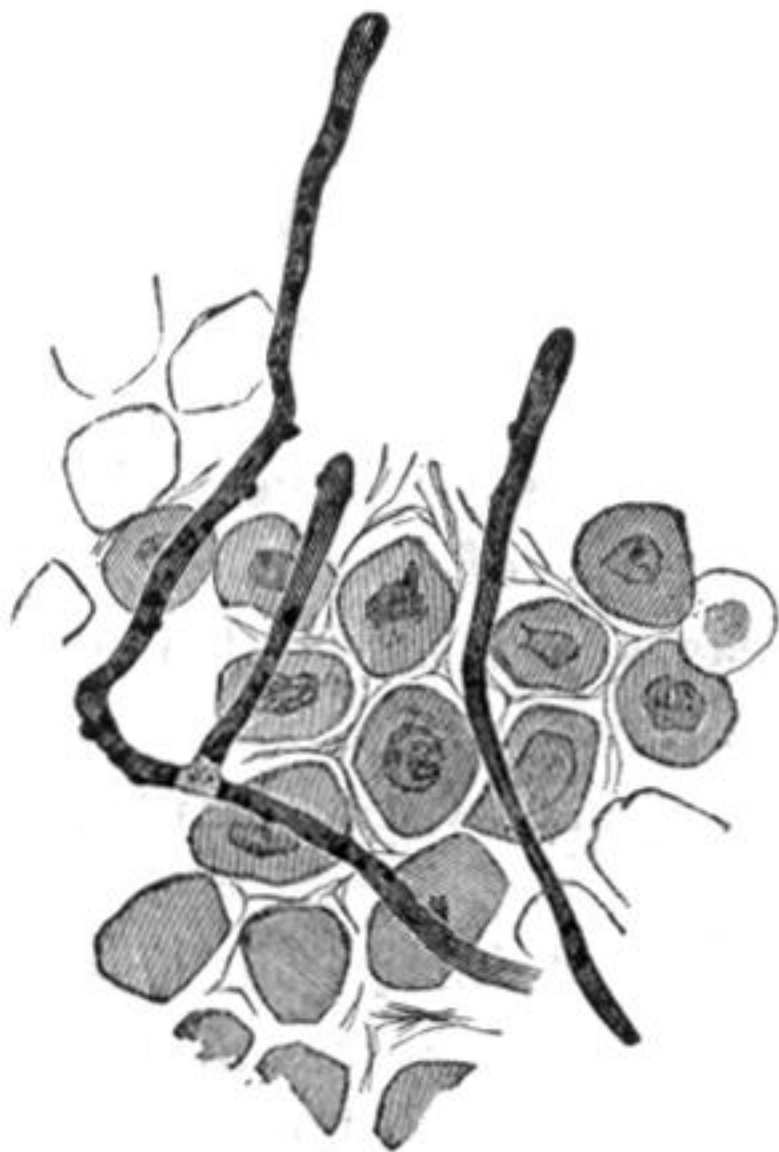
“An Instrument for the Speedy Volumetric Determination of Carbonic Acid.” By WILLIAM MARCET, M.D., F.R.S.  
Received June 9. Read June 10. Revised by the Author  
June 29, 1886,

[PLATE 2.]

The principle of this instrument is the absorption of carbonic acid in a closed receiver by potassium hydrate, and the accurate measurement of the volume of dry atmospheric air required to re-establish the atmospheric pressure after complete absorption. The volume of air used for that purpose will exactly correspond to that of the carbonic acid gas absorbed. It is obvious that whatever be the reading of the barometer, the volume of air corresponding to that of the carbonic acid absorbed, will give the correct proportion of carbonic acid in the air submitted to analysis; but to obtain the weight of the gas present, and its proportion by weight, it will be necessary to reduce both the volumes of air analysed and of carbonic acid found to their volume at 0° (C.), and under a pressure of 760 mm. of mercury. Hence the necessity of recording the height of the barometer at the time of the experiment, or one reading may suffice for a number of determinations.

The instrument resembles two small gasometers, and consists of two tanks and two bell-jars, or air-holders, each of the latter being made to hold half a cubic foot of air. The bell-jars hang on a metallic cord which connects them with each other, and passes over two pulleys,

FIG. 1.



Mucous membrane of small intestine from Case XIV, showing a portion of deep part of mucosa (Powell and Lealand  $\frac{1}{12}$  oil immersion).

FIG. 2.



Similar section from Case XXIV ( $\frac{1}{12}$  oil immersion).