TRANSLATION OF AN ADDRESS ON THE GERM THEORY.

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GENTLEMEN: I had no intention of addressing this admirable Congress, which brings together the most eminent medical men in the world, and the great success of which does so much credit to its principal organizer, Mr. Mac Cormac. The good-will of your esteemed President has decided otherwise. How could one, in fact, resist the sympathetic words of that eminent man whose goodness of heart is associated in no small degree with great oratorical ability? Two motives have brought me to London. The first was to gain instruction, to profit by your learned discussions; and the second was to ascertain the place now occupied in medicine and surgery by the germ theory. Certainly I shall return to Paris well satisfied. During the past week I have learned much. I carry away with me the conviction that the English people are a great people, and as for the influence of the new doctrine, I have been not only struck by the progress it has made, but by its triumph. I should be guilty of ingratitude and of false modesty if I did not accept the welcome I have received among you and in English society as a mark of homage paid to my labours during the past five-and-twenty years upon the nature of ferments—their life and their nutrition, their preparation in a pure state by the introduction of organisms (*ensemencement*) under natural and artificial conditions — labours which have established the principles and the methods of microbie (microbism), if the expression is allowable. Your cordial

[1] Liberty, Equality, and Fraternity, by James Fitz James Stephen, N. Y. 1873, p. 178.

welcome has revived within me the lively feeling of satisfaction I experienced when your great surgeon Lister declared that my publication in 1857 on milk fermentation had inspired him with his first ideas on his valuable surgical method. You have reawakened the pleasure I felt when our eminent physician Dr. Davaine declared that his labours upon charbon (splenic fever or malignant pustule) had been suggested by my studies on butyric fermentation and the vibrion which is characteristic of it. Gentlemen, I am happy to be able to thank you by bringing to your notice a new advance in the study of microbie as applied to the prevention of transmissible diseases—diseases which for the most part are fraught with terrible consequences, both for man and domestic animals. The subject of my communication is vaccination in relation to chicken cholera and splenic fever, and a statement of the method by which we have arrived at these results—a method the fruitfulness of which inspires me with boundless anticipations. Before discussing the question of splenic fever vaccine, which is the most important, permit me to recall the results of my investigations of chicken cholera. It is through this inquiry that new and highly important principles have been introduced into science concerning the virus or contagious quality of transmissible diseases. More than once in what I am about to say I shall employ the expression virus-culture, as formerly, in my investigations on fermentation, I used the expressions, the culture of milk ferment, the culture of the butyric vibrion, etc.

Let us take, then, a fowl which is about to die of chicken cholera, and let us dip the end of a delicate glass rod in the blood of the fowl with the usual precautions, upon which I need not here dwell. Let us then touch with this charged point some *bouillon de poule*, very clear, but first of all rendered sterile under a temperature of about 115° Centigrade, and under conditions in which neither the outer air nor the vases employed can introduce exterior germs—those germs which are in the air, or on the surface of all objects. In a short time, if the little culture vase is placed in a temperature of 25° to 35°, you will see the liquid become turbid, and full of tiny microbes, shaped like the figure 8, but often so small that under a high magnifying power they appear like points. Take from this vase a drop as small as you please, no more than can be carried on the point of a glass rod as sharp as a needle, and touch with this point a fresh quantity of sterilized *bouillon de poule* placed in a second vase, and the same phenomenon is produced. You deal in the same way with a third culture vase, with a fourth, and so on to a hundred, or even a thousand, and invariably within a few hours the culture liquid becomes turbid and filled with the same minute organisms. At the end of two or three days' exposure to a temperature of about 30° C. the thickness of the liquid disappears, and a sediment is formed at the bottom of the vase. This signifies that the development of the minute organism has ceased—in other words, all the little points which caused the turbid appearance of the liquid have fallen to the bottom of the vase, and things will remain in this condition for a longer or shorter time, for months even, without either the liquid or the deposit undergoing any visible modification, inasmuch as we have taken care to exclude the germs of the atmosphere. A little stopper of cotton sifts the air which enters or issues from the vase through changes of temperature. Let us take one of our series of culture preparations—the hundredth or the thousandth, for instance—and compare it in respect to its virulence with the blood of a fowl which has died of cholera; in other words, let us inoculate under the skin ten fowls, for instance, each separately with a tiny drop of infectious blood, and ten others with a similar quantity of the liquid in which the deposit has first been shaken up. Strange to say, the latter ten fowls will die as quickly and with the same symptoms as the former ten; the blood of all will be found to contain after death the same minute infectious organisms. This equality, so to speak, in the virulence both of the culture preparation and of the blood is due to an apparently futile circumstance. I have made a hundred culture preparations—at least, I have understood that this was done—without leaving any considerable interval between the impregnations. Well, here we have the cause of the equality in the virulence. Let us now repeat exactly our successive cultures with this single difference, that we pass from one culture to that which follows it—from the hundredth to, say, the hundred and first, at intervals of a fortnight, a month, two months, three months, or ten months. If, now, we compare the virulence of the successive cultures, a great change will be observed. It will be readily seen from an inoculation of a series of ten fowls that the virulence of one culture differs from that of the blood and from that of a preceding culture when a sufficiently long interval elapses between the impregnation of one culture with the microbe of the preceding. More than that, we may recognize by this mode of observation that it is possible to prepare cultures of varying degrees of virulence. One preparation will kill eight fowls out of ten, another five out of ten, another one out of ten, another none at all, although the microbe may still be cultivated. In fact, what is no less strange, if you take each of these cultures of attenuated virulence as a point of departure in the preparation of successive cultures and without appreciable interval in the impregnation, the whole series of these cultures will reproduce the attenuated virulence of that which has served as the starting point. Similarly, where the virulence is null it produces no effect. How, then, it may be asked, are the effects of these attenuating virulences revealed in the fowls? They are revealed by a local disorder, by a morbid modification more or less profound in a muscle, if it is a muscle which has been inoculated with the virus. The muscle is filled with microbes which are easily recognized because the attenuated microbes have almost the bulk, the form, and the appearance of the most virulent microbes. But why is not the local disorder followed by death? For the moment let us answer by a statement of facts. They are these: the local disorder ceases of itself more or less speedily, the microbe is absorbed and digested, if one may say so, and little by little the muscle regains its normal condition. Then the disease has disappeared. When we inoculate with the microbe the virulence of which is null there is not even local disorder, the *naturæ medicatrix* carries it off at once, and here, indeed, we see the influence of the resistance of life, since this microbe, the virulence of which is null, multiplies itself. A little further, and we touch the principle of vaccination. When the fowls have been rendered sufficiently ill by the attenuated virus which the vital resistance has arrested in its development, they will, when inoculated with virulent virus, suffer no evil effects, or only effects of a passing character. In fact, they no longer die from the mortal virus, and for a time sufficiently long, which in some cases may exceed a year, chicken cholera cannot touch them, especially under the ordinary conditions of contagion which exist in fowl-houses. At this critical point of our manipulation—that is to say, in this interval of time which we have placed between two cultures, and which causes the attenuation—what occurs? I shall show you that in this interval the agent which intervenes is the oxygen of the air. Nothing more easily admits of proof. Let us produce a culture in a tube containing very little air, and close this tube with an enameller's lamp. The microbe in developing itself will speedily take all the oxygen of the tube and of the liquid, after which it will be quite free from contact with oxygen. In this case it does not appear that the microbe becomes appreciably attenuated, even after a great lapse of time. The oxygen of the air, then, would seem to be a possible modifying agent of the virulence of the microbe of chicken cholera—that is to say, it may modify more or less the facility of its development in the body of animals. May we not be here in presence of a general law applicable to all kinds of virus? What benefits may not be the result? We may hope to discover in this way the vaccine of all virulent diseases; and what is more natural than to begin our investigation of the vaccine of what we in French call charbon, what you in England call splenic fever, and what in Russia is known as the Siberian pest, and in Germany as the Milzbrand. In this new investigation I have had the assistance of two devoted young *savants*—MM. Chamberland and Roux. At the outset we were met by a difficulty. Among the inferior organisms, all do not resolve themselves into those corpuscle germs which I was the first to point out as one of the forms of their possible development. Many infectious microbes do not resolve themselves in their cultures into corpuscle germs. Such is equally the case with beer yeast, which we do not see develop itself usually in breweries, for instance, except by a sort of scissiparity. One cell makes two or more, which form themselves in wreaths; the cells become detached, and the process recommences. In these cells real germs are not usually seen. The microbe of chicken cholera and many others behave in this way, so much so that the cultures of this microbe, although they may last for months without losing their power of fresh cultivation, perish finally like beer yeast which has exhausted all its aliments. The anthracoid microbe in artificial cultures behaves very differently. In the blood of animals, as in cultures, it is found in translucid filaments more or less segmented. This blood or these cultures freely exposed to air, instead of continuing according to the first mode of generation, show at the end of forty-eight hours corpuscle germs distributed in series more or less regular along the filaments. All around those corpuscles matter is absorbed, as I have represented it formerly in one of the plates of my work on the disease of silkworms. Little by little all connection between them disappears, and presently they are reduced to nothing more than germ dust. If you make these corpuscles germinate, the new culture reproduces the virulence peculiar to the thready form which has produced these corpuscles, and this result is seen even after a long exposure of these germs to contact with air. Recently we discovered them in pits in which animals dead of splenic fever had been buried for twelve years, and their culture was as virulent as that from the blood of an animal recently dead. Here I regret extremely to be obliged to shorten my remarks. I should have had much pleasure in demonstrating that the anthracoid germs in the earth of pits in which animals have been buried are brought to the surface by earthworms, and that in this fact we may find the whole etiology of disease, inasmuch as the animals swallow these germs with their food. A great difficulty presents itself when we attempt to apply our method of attenuation by the oxygen of the air to the anthracoid microbes. The virulence establishing itself very quickly, often after four-and-twenty hours in an anthracoid germ which escapes the action of the air, it was impossible to think of discovering the vaccine of splenic fever in the conditions which had yielded that of chicken cholera. But was there, after all, reason to be discouraged? Certainly not; in fact, if you observe closely, you will find that there is no real difference between the mode of the generation of the anthracoid germ by scission and that of chicken cholera. We had therefore reason to hope that we might overcome the difficulty which stopped us by endeavouring to prevent the anthracoid microbe from producing corpuscle germs and to keep it in this condition in contact with oxygen for days, and weeks, and months. The experiment fortunately succeeded. In the ineffective (*neutre*) *bouillon de poule* the anthracoid microbe is no longer cultivable at 45° C. Its culture, however, is easy at 42° or 43°, but in these conditions the microbe yields no spores. Consequently it is possible to maintain in contact with the pure air at 42° or 43° a *mycélienne* culture of bacteria entirely free of germs. Then appear the very remarkable results which follow. In a month or six weeks the culture dies—that is to say, if one impregnates with it fresh *bouillon*, the latter is completely sterile. Up till that time life exists in the vase exposed to air and heat. If we examine the virulence of the culture at the end of two days, four days, six days, eight days, etc., it will be found that long before the death of the culture the microbe has lost all virulence, although still cultivable. Before this period it is found that the culture presents a series of attenuated virulences. Everything is similar to what happens in respect to the microbe in chicken cholera. Besides, each of these conditions of attenuated virulence may be reproduced by culture; in fact, since the charbon does not operate a second time (*ne récidive pas*), each of our attenuated anthracoid microbes constitutes for the superior microbe a vaccine—that is to say, a virus capable of producing a milder disease. Here, then, we have a method of preparing the vaccine of splenic fever. You will see presently the practical importance of this result, but what interests us more particularly is to observe that we have here a proof that we are in possession of a general method of preparing virus vaccine based upon the action of the oxygen and the air—that is to say, of a cosmic force existing everywhere on the surface of the globe. I regret to be unable from want of time to show you that all these attenuated forms of virus may very easily, by a physiological artifice, be made to recover their original maximum virulence. The method I have just explained of obtaining the vaccine of splenic fever was no sooner made known than it was very extensively employed to prevent the splenic affection. In France we lose every year by splenic fever animals of the value of 20,000,000f. I was asked to give a public demonstration of the results already mentioned. This experiment I may relate in a few words. Fifty sheep were placed at my disposition, of which twenty-five were vaccinated. A fortnight afterwards the fifty sheep were inoculated with the most virulent anthracoid microbe. The twenty-five vaccinated sheep resisted the infection; the twenty-five unvaccinated died of splenic fever within fifty hours. Since that time my energies have been taxed to meet the demands of farmers for supplies of this vaccine. In the space of fifteen days we have vaccinated in the departments surrounding Paris more than 20,000 sheep and a large number of cattle and horses. If I were not pressed for time I should bring to your notice two other kinds of virus attenuated by similar means. These experiments will be communicated by and by to the public. I cannot conclude, gentlemen, without expressing the great pleasure I feel at the thought that it is as a member of an international medical congress assembled in England that I make known the most recent results of vaccination upon a disease more terrible, perhaps, for domestic animals than smallpox is for man. I have given to vaccination an extension which science, I hope, will accept as homage paid to the merit and to the immense services tendered by one of the greatest men of England, Jenner. What a pleasure for me to do honour to this immortal name in this noble and hospitable city of London!—*Lancet*, Aug. 13, 1881.