the relations of these to the anatomical structures affected by such cause, exemplifies the rise to the dignity of a science.

"Knowledge is Power": but what of half-knowledge?

Microscopic discovery of an otherwise invisible parasite has enabled the practitioner to administer the remedies applicable to arrest or annihilate the cause of a direful malady; such knowledge gives also that of the stage beyond which there is no direct or specific remedy. In such phase of medicine, he can act with confidence and prophesy with certainty. Finally, I would refer to another test which, by the analogy of established sciences, bears upon my present subject.

When chemistry was struggling to its goal, a mockery disguised in its rags obtained the confidence of a majority, under the name of alchemy. It was long ere the professors of this pseudo-science lost the patronage of the rich and great, on whose credulity they battered. The extinction of the transmuters is an evidence, small, indeed, but significant, of the true and trustworthy status of the branch of experimental research to which the gifted, single-minded men devoted themselves, to raise chemistry to the status of a science.

Prior to, and for some time after, the promulgation of the Copernican theory, astrology continued to hold its ground against astronomy. The "caster of nativities" was patronised by monarchs, ministers, men of wealth, and lords of fair estates long after the periods disgraced by the persecution of Galileo, and by the cold neglect of Kepler. Finally, arose a Newton; and to the higher evidences of a "science of the stars," I may here add the lower one of the extinction of astrology or its relegation to some obscure almanac.

Are there, then, we may ask, at the present date, practitioners, professors of curative methods, analogous, in medicine, to the astrologers and alchemists at former periods of astronomy and chemistry? Do they, in like manner, obtain countenance and support, as did those empirics, from Prime Ministers and non-scientific people of rank and fortune.

In the degree in which the unlicensed dentist, the bone-setter, the mesmeriser, and homœopathist may flourish or get means of subsistence, may be estimated, in some degree, the stage at which inductive medicine has reached, on its rapidly advancing career, to the status of a science.

AN ADDRESS

ON

VACCINATION IN RELATION TO CHICKEN CHOLERA AND SPLENIC FEVER.*

BY M. PASTEUR, PARIS.

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 organiser, Mr. Mac Cormac. The goodwill 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 is 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* (microbiotism), if the expression is allowable. Your cordial 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

* We have availed ourselves of the excellent translation published in the *Times*, which, on comparing it with the MS. of M. Pasteur, we have found very accurate.

upon *charbon* (splenic fever or malignant pustules) had been suggested by my studies on butyric fermentation and the vibrio 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 micro-organisms 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 inoculation 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 vibrio, 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° cent. (239° Fahr.), 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 be placed in a temperature of 25° to 35° cent. (77° to 95° Fahr.), you will see the liquid become turbid and full of tiny micro-organisms, 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 sterilised *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° cent. (86° Fahr.), 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 trivial 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 micro-organism of the preceding. More than that, we may recognise 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 micro-organism may still be cultivated. In fact, what is no less strange, if you take each of these cultures of attenuated virulence at 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 attenuated 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 micro-organisms, which are easily recognised because the attenuated ones have almost the bulk, the form, and the appearance of the most virulent. 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 micro-organism 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 micro-organism the virulence of which is null there is not even local disorder; the *natura medicatrix* carries it off at once, and here, indeed, we see the influence of the resistance of life, since this micro-organism, 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 micro-organism in developing itself will speedily take all the oxygen of the tube and of the liquid, after which it will be perfectly free from contact with oxygen. In this case it does not appear that the micro-organism 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 micro-organism 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. Chamberlain 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 micro-organisms 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 fissiparous production. 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 micro-organism of chicken cholera and many others behave in this way, so much so that the cultures of this micro-organism, 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 micro-organism in artificial cultures behaves very differently. In the blood of animals, as in cultures, it is found in translucent 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 these corpuscles matter is absorbed, as I have represented it formerly in one of the plates of my work on the diseases 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 thradly 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 micro-organisms. 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 fission 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 micro-organism 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 micro-organism is no longer cultivable at 45° Cent. Its culture, however, is easy at 42° or 43° Cent., but in these conditions the micro-organism yields no spores. Consequently it is possible to maintain in contact with the pure air at 42° or 43°, a mycelian culture of bacteridia 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 micro-organism 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 micro-organism in chicken cholera. Besides, each of these conditions of attenuated virulence may be reproduced by culture; in fact, since the *charbon* does not recur a second time (*ne récidive pas*), each of our attenuated anthracoid micro-organisms constitutes for the superior micro-organism 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 20,000,000 francs. 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 micro-organism. The twenty-five inoculated sheep resisted the infection; the twenty-five non-inoculated sheep 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 matter. In the space of fifteen days, we have inoculated in the department 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 small-pox is for man. I have given to vaccination an extension which science, I hope, will accept as a homage paid to the merit, and to the immense services, rendered 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!

PROFESSOR CURTIUS has been appointed Rector, and Professor Westphal Dean of the Faculty of Medicine, in the University of Berlin.