REMARKS

ON

THE PREVENTION OF HYDROPHOBIA BY
M. PASTEUR'S TREATMENT.

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THE disease which is popularly called hydrophobia is one which from the days of Aristotle has attracted the attention of medical men. They, as well as the general public, had been struck by its remarkable peculiarities, and, during many centuries, popular credulity surrounded the disease with fabulous stories, some of which are believed even now, whilst others have left their trace as popular sayings and proverbs. And yet hydrophobia is in some parts of the country by no means frequently met with. There are many medical men who have never seen a case, or who have seen one or two at most, in the course of a long and busy lifetime, during which they may have watched hundreds die of typhoid fever, phthisis, and other infectious diseases. The chief interest of hydrophobia, however, lies in the fact that the fate of human beings inoculated with the hydrophobic virus remains doubtful for some considerable time after the bite. The friends and the medical attendant of a patient bitten by a hydrophobic animal know that the life of that man may suddenly come to an end. During a period extending over many months—over a year even—that man has to wait, believing that nothing can be done for him to prevent the breaking out of the disease. He knows, of course, that he has many chances of escaping, but that, if the first symptoms make their appearance, he is hopelessly doomed to a most painful and horrible death. The medical man who may have cauterised or even sucked the wound, until recently believed that so far his work was at an end, and that all he could do was to wait, and, if the symptoms set in, to mitigate as much as he was able the sufferings preceding the inevitable end.

We need not wonder, then, that when in 1885 M. Pasteur stated, at the Académie des Sciences de Paris, that he had discovered a method to prevent the occurrence of hydrophobia after a bite, the medical and public press rang with the news. But although patients flocked from all parts of the world to the Laboratory of M. Pasteur, in the Rue d'Ulm, many scientific men openly expressed their doubts as to the value of the treatment. Since 1885, however, the number of people who have submitted themselves to the preventive treatment for hydrophobia exceeds 9,000. Over twenty antirabic institutes have been built in various parts of the world, in which patients have been inoculated by independent observers. From the data collected in the statistics published by the directors of these establishments, it is possible now to form a correct opinion as to the value of M. Pasteur's treatment.

Another set of opponents have relentlessly attacked M. Pasteur because his knowledge has been acquired by means of experiments on animals. Let me say at once that it is not my intention to waste the time of this Association by discussing this last kind of opposition, but at the same time it will be necessary for me to show how this newly-gained knowledge has been acquired.

A few minutes must be devoted to the description of the most important clinical phenomena of the disease and to studying the localisations of the virus in man and animals.

The modes of obtaining the virus will occupy us next, and after the process of inoculation has been fully explained, the theory of antirabic vaccination will be entered into.

Lastly, an account of the results of the treatment, as shown by the statistics published by the different antirabic institutes, will conclude this paper.

Hydrophobia is a specific infectious disease. As far as we know, it never originates *de novo*, but is always propagated from one animal to another by inoculation. The virus is a particulate virus, and is most probably a living micro-organism. Several observers have described micro-organisms in the spinal cord, and

even in the organs of animals and men dead of hydrophobia, but unfortunately the attempts of others to see these micro-organisms again or to cultivate them have failed. Unlike ordinary putrefactive micro-organisms, it is endowed with very little power of resistance, being easily destroyed by heat, drying, or sunlight. It is destroyed by exposure to sunlight in fourteen to thirty hours; steam at 100° C. destroys it in thirty minutes. A temperature of 50° to 60° C. in one hour; of 45° C. in twenty-four hours; of 58° for one hour; and of 62° C. for four minutes completely destroys its virulent properties. The oxygen of the air seems to have a very deleterious effect on it, as when kept in closed sealed tubes it remains virulent for three or four weeks even in the heat of summer. Low temperatures (30° C.) have no effect on it.

The effects of drying the virus will be explained further on.

Experimentally it has been demonstrated that rabies may be successfully inoculated by injecting the virus obtained from the central nervous system of an animal which has died of rabies (rabbits, dogs, etc.) under the skin of another animal, or into its veins, into the peritoneum, into the muscles, eye, or under the dura mater after trephining. Of these various modes of inoculation there is only one which is absolutely certain to reproduce the disease, namely, inoculation under the dura mater. That method is successful in a hundred per cent. of the cases so treated. Whether herbivora (rabbits) or carnivora (dogs) be used for these experiments, all the other modes of inoculation, excepting perhaps the introduction of the virus into the anterior chamber of the eye, are occasionally unsuccessful (Pasteur).

The wound through which the pure virus is introduced heals in a perfectly normal manner as a rule. Many observers have stated that wounds produced by the bite of a mad dog heal slowly, and only seldom by first intention. That statement is correct, but this delay in healing is simply due to the fact that the saliva, even of a healthy animal, contains numerous other micro-organisms, which are introduced together with the hydrophobic virus into the wound. A wound produced by a bite of any animal is practically always a septic one. When the pure hydrophobic virus is used the wound heals by first intention in man and in animals.

At the Pasteur Institute, where between 100 and 200 subcutaneous injections are made every day in man abscesses are of exceedingly rare occurrence. The wounds of rabbits, when the pure hydrophobic virus is injected under the skull, invariably heal by first intention, provided efficient antiseptic precautions have been taken during the necessary operation.

The period of incubation, that is, the time elapsing between the date of the bite and that at which the first symptoms set in, varies in man. Cases have been reported in which hydrophobia is supposed to have occurred on the same day, the next day, or within a week after the bite. These were most probably cases of acute mania or tetanus (Hunter), and may be safely excluded from statistics of hydrophobia.

A period of thirteen days (Tardieu, Jouffroy) is the shortest space of time at which the symptoms of hydrophobia make their appearance after a bite. Inquiries made by the Conseil du Comité d'Hygiène show that, of 170 deaths occurring after bites from rabid animals during a period extending over ten years (1862-1872), 38 occurred within the first month, 112 before the end of the second, 147 within three months, 158 within four months, 6 deaths occurred during the fifth month, 4 during the sixth, and 2 during the eighth. Occasionally the period of incubation extends over a year. Valentin has published a case in which hydrophobia made its appearance eighteen months after the inoculation. Disser has seen death follow fifteen months after a bite, and I know myself of a death which occurred more than fifteen months after a superficial bite of a rabid dog. In the *Annales de l'Institut Pasteur* will be found the history of a man who died twenty-seven months after being bitten by a rabid dog. The period of incubation seems to be shorter in young people. It is distinctly shorter after face bites than after bites in the limbs. In the report of the Comité d'Hygiène of 139 cases of deaths by hydrophobia, the average duration of life after face bites is found to have been 48 days; after bites in the limbs, 69 days. Although the average duration of life after fatal face bites is stated to be 48 days, it is nevertheless in many cases far shorter, and death frequently results within one month of the bite, as we shall see when we study the statistics published by the different antirabic institutes.

The symptoms of rabies in man have been so well described by numerous observers, that it is needless to speak of them at length. They may be divided into three stages: the first is characterised

by melancholia, together with pains which often start from the wound, though not always so; the second is the so-called convulsive state, in which the symptom hydrophobia, that is, the fear of water, is often very prominent. But hydrophobia is only a symptom, which may be slight or may be even totally absent during the whole course of the disease; a fact which Morgagni in the eighteenth century had already noted. In dogs this particular symptom is for the most part absent. A rabid dog does not fear water; it puts its head under water, but is unable to drink, on account of the pharyngeal spasms, or of the paralysis of the lower jaw. Man, in the majority of instances, does not fear water, but avoids it, because the effort of drinking, the sight, the sound, even the thought of water give rise to the most painful respiratory and pharyngeal spasms. In some cases a patient is able to drink with an effort right through the course of the disease. Sometimes the hydrophobia, a prominent symptom at first, completely disappears, and the patient is able to eat and drink, voraciously even, for some hours before the fatal termination.

Moreover, hydrophobia is a symptom which is present in other diseases, and therefore, although at the suggestion of our President to-day, I have called this disease up to now hydrophobia, merely because it is usually designated by this name, yet I hope that medical men will give up the term and call the disease by its proper name, "rabies," reserving the term hydrophobia for one of its most characteristic symptoms in man.

The third stage is characterised by progressive muscular weakness and by gradually increasing paralysis. At last the patient dies exhausted by the spasms, or more frequently through paralysis of the respiratory centre. The end is sometimes very sudden, and the patient falls down dead without any symptoms leading the looker-on to suppose the fatal termination to be so near.

In rabbits the course of the disease is, as a rule, different. The attacks of agitation are absent, and it begins by a paralysis of the posterior limbs, which gradually spreads to the trunk muscles and then to the anterior limbs. This paralytic form of rabies is frequently met with in the dog also (dumb madness), and has been occasionally described as occurring in man. Some of M. Pasteur's patients having died of the paralytic form of rabies after undergoing the preventive treatment, it was stated by some of his opponents that their deaths were due to the inoculation of the rabbit's virus. The answer to this accusation is that the virus taken from a dog suffering from the convulsive form of the disease may produce the paralytic variety when inoculated into another dog, and *vice versa*. Moreover, patients bitten by animals suffering from convulsive rabies have undoubtedly died of the paralytic form of the disease, even when they had not been subjected to any preventive treatment whatever. Gamaleia has recorded twenty deaths from paralytic rabies in patients bitten by rabid animals who had undergone no treatment. Indeed, this form of rabies appears to be far more common than it is generally believed to be, for, of ten patients who died of rabies at Odessa, four died of paralytic rabies (Gamaleia). Dr. Uffreduzzi, Mr. Horsley, and Dr. Bristowe have recently recorded similar cases, and I feel convinced, that now that attention has been drawn to the subject, like facts will shortly be put on record. It is a noteworthy fact that, although in ten out of twenty cases recorded by Gamaleia, paralysis began in the limbs injured by the bite, in seven others it did not make its first appearance on the bitten side. I cannot enter into the details of the progress of this form of the disease, and I must refer those who are interested in this subject to the paper by Gamaleia in the *Annales de l'Institut Pasteur* for 1888, and to Mr. Horsley's and Dr. Bristowe's papers.

The prognosis of rabies in man, when once the first symptoms have made their appearance, is always fatal, and I do not know of any single authenticated case in which the patient has recovered. But the case is somewhat different in dogs. In 1881 M. Pasteur inoculated three dogs with rabies; two were seized shortly afterwards with the symptoms of the disease, and died. The third one showed the first symptoms and recovered. That third dog was trephined twice in 1882, and inoculated each time under the dura mater with the virus of rabies. That first mild attack, however, had vaccinated the animal against a further attack of rabies, so that the inoculations under the dura mater were followed by no evil effects. Although unique, this fact was one which helped to convince M. Pasteur that it was possible to vaccinate against rabies.

The *post-mortem* appearances in the central nervous system, peripheral nerves, and other organs of patients and animals dying

of rabies are so well known that it is unnecessary to describe them here. Moreover, there are other and far better means of settling the existence or non-existence of rabies, namely, by means of the experimental method. If a piece of the central nervous system of an animal, suspected to have died of rabies, be crushed with a little sterilised water, and a drop of this emulsion be then injected under the dura mater of a rabbit the symptoms of rabies, provided the man or animal really died of the disease, will shortly make their appearance in the inoculated animal, that is, in the majority of cases, within eighteen days.

The virus is present in the nerves, though not constantly so, and rabies has been produced by the inoculation of the blood (Uffreduzzi, Babes), of the urine (Bouchard), of the liver, kidneys, spleen, and salivary glands. The experiments of Bouchard are important, because they may possibly help to explain some cases of so-called spontaneous rabies in which the mode of inoculation cannot be traced. If a rabid animal passes its water on the ground another dog, with perhaps a small cut on one of its feet, passing over that spot may thus be inoculated with rabies.

But though occasionally found in most organs and most secretions of the body, including perhaps milk, it is often absent; whereas its presence can always be easily demonstrated in the cerebro-spinal axis. If a rabbit be trephined and inoculated under the dura mater with an emulsion made with the medulla of a rabid animal—a dog, for instance—the first symptoms of rabies appear, as a rule, within fifteen days; never in a shorter period than nine days. If an emulsion made with the medulla oblongata of this first rabbit be inoculated under the dura mater of a second the incubation period becomes shorter, say eleven days. If a third rabbit be now inoculated with the virus of the second, a fourth with the virus of the third, and if rabbits be thus inoculated successively from each other, the period of incubation becomes gradually shorter and shorter until it lasts only six to seven days. Eighty successive inoculations are necessary to produce the form of the disease characterised by the short incubation period. When the incubation period lasts only six to seven days the virus becomes what M. Pasteur calls "fixed," that is, the period of incubation is of six to seven days always, and the animal dies on the tenth day after inoculation. The importance of this fact cannot be over-estimated, for it was absolutely necessary, before a preventive treatment could be applied, to be provided with a constant and regular supply of virus of the same strength. At the Pasteur Institute, where patients are inoculated every day, one rabbit is trephined daily, and, as the animals always die on the tenth day, it supplies in its turn the virus necessary to the day's inoculations.

Now, if a spinal cord of a rabbit which has died after being inoculated under the dura mater with the fixed virus be hung up in a sterilised bottle, the air of which is dried by means of caustic potash placed at the bottom, and if it be kept at a temperature of 25° C. it is found that, when inoculated under the dura mater of another rabbit, after being dried during one day, it still reproduces rabies, but that the inoculated animal dies one or two days later than it would do if it had been inoculated with the fresh fixed virus.

If before inoculation it has been dried:

2 days it produces death in 11 to 17 days, postponing it for	1 to 2 days.
3 " " " 14 to 16 " " "	4 to 6 " "
4 " " " 12 to 15 " " "	2 to 5 " "
5 " " " 17 to 20 " " "	7 to 10 " "
6 " " " 12 to 22 " " "	2 to 12 " "
7 " " " 23 to 29 " " "	13 to 19 " "
8 " " " 24 to 27 " " "	14 to 17 " "
9 " " " 27 to 40 " " "	17 to 30 " "
10 " " " 32 to 36 " " "	22 to 26 " "
11 " " " 30 to 35 " " "	20 to 25 " "

These are the results of Dr. G. Bordoni Uffreduzzi, obtained after a long and careful series of researches. The spinal cord, dried twelve, thirteen, and fourteen days, contains the living micro-organism no longer; it is harmless. The spinal cords dried nine, ten, and eleven days often contain no active micro-organisms. This increasing length of the incubation period shows that the number of micro-organisms in the spinal cord steadily diminishes with each day's drying, until at last, after eleven days, sometimes even after eight days, the tissue contains no living micro-organisms at all.

The cerebro-spinal axis of an animal dead of rabies, however, does not only contain the micro-organism which produces the disease, but in it are to be found those substances which the micro-organisms have elaborated during their life in the spinal cord.

The yeast plant, growing in a solution of sugar, will produce

alcohol, carbonic acid, etc.; other micro-organisms give rise to colouring matters (bacillus prodigiosus, pyocyanus). In fact, every living micro-organism excretes substances as a result of its life, just as higher animals excrete a certain quantity of urea, carbonic acid, etc., every day. We know now, since the experiments of Salmon and Smith, of Charrin, of Chamberland and Roux, of Chantemesse and Widal, that some pathogenic micro-organisms when growing in suitable mediums may produce chemical substances which, when injected into an animal, enable that animal to resist the action of the specific micro-organism producing the disease.

To take an example: If the micro-organism which, when inoculated, produces that horrible disease called "malignant oedema," be allowed to grow in beef-broth at a proper temperature, and if, after a time, the fluid in which it has lived be carefully heated to 110° C., so that all the micro-organisms in it are killed, the fluid will contain nothing but dead micro-organisms and the soluble substances produced by these micro-organisms during their life in the beef broth. If some of this fluid be injected into a guinea-pig, and if two or three days afterwards the bacillus of malignant oedema be inoculated into the same animal, it will be found that the micro-organism is unable to produce malignant oedema in that guinea-pig. The guinea-pig, in one word, has been previously vaccinated by the sterilised fluid. The same organisms, taken from the same culture, which have proved harmless to the first vaccinated animal, will kill another animal of the same breed in eighteen hours if that animal has not previously been vaccinated by the injection of the sterilised fluid.

Although M. Pasteur never isolated these vaccinating substances himself, yet he was the first to point out that vaccination could most probably be accomplished by means of chemical substances, and in his famous letter to M. Duclaux, published in the first volume of the *Annales de l'Institut Pasteur*, he pointed out the probability of the existence of such vaccinating substances, and he thus opened a new field for original research.

If an emulsion of the spinal cord of a rabbit which has just died of rabies be injected under the skin of a dog, two things are introduced; first, the micro-organisms of hydrophobia; and secondly, the poisons elaborated by the same micro-organisms during their life in the spinal cord. Remember, now, that a period of fourteen days at least must elapse before that living micro-organism is able to give rise to the first symptoms of rabies. The chemical substance, however, probably produces its vaccinating effect at once, or within a short period after its injection, so that, when the disease ought to break out, the animal has already been rendered capable of resisting the action of its specific organism through the absorption of this chemical vaccinating substance.

If two or three drops of an emulsion of the spinal cord of a rabbit just dead of rabies be injected under the skin of a dog, a small number of organisms and a very small quantity of the vaccinating poisons are injected, and rabies will almost certainly follow. If, on the other hand, a very large quantity of the same emulsion be injected (one to ten, twenty, thirty cubic centimètres, or more), a large number of micro-organisms are introduced, but at the same time a large quantity of the vaccinating substance is injected as well. And M. Pasteur, and after him Bardach, have proved that it is possible to vaccinate dogs against rabies by introducing into their system one, five, ten, fifteen, twenty, or thirty cubic centimètres of an emulsion made with the fresh spinal cord of a rabbit, immediately after its death from rabies. The only possible explanation of this fact is, that vaccination in these cases is due to the large quantities of soluble vaccinating substances introduced with each injection. Unfortunately, that mode of vaccination frequently fails, and hence it cannot be applied to man.

M. Pasteur, however, got over the difficulty in the following way. You will remember that the inoculation of a spinal cord, which has been dried for fourteen, thirteen, and twelve days, at a temperature of 25° C., no longer produces rabies in an animal inoculated with it. Cords dried during twelve, eleven, and ten days contain far fewer micro-organisms, sometimes none, but they still contain some amount of vaccinating substance; and, indeed, M. Pasteur has proved this to be so, as he has been able to vaccinate dogs with the emulsion of dried spinal cords of rabid animals, which were proved to no longer contain any living micro-organisms, but still contained the vaccinating substances. If, therefore, a man be inoculated on the first day of treatment with an emulsion of a spinal cord dried during fourteen days, and with a spinal cord thirteen days old, on the second day with one twelve

days old, he has during that period of time been inoculated with vaccinating substance alone, without any active micro-organisms. It must be remembered also that the emulsion of the eleven days spinal cord which is then inoculated, even if micro-organisms be present in it, contains a large dose of vaccinating substance. If, then, every day the number of micro-organisms injected for preventive treatment becomes greater and greater, at the same time more and more vaccinating substance is introduced with each injection.

SIMPLE METHOD

N.B. EACH DOT STANDS FOR ONE INOCULATION.

In the simple method employed by M. Pasteur, he injects on the first day an emulsion made with the spinal cord dried during fourteen days, and with one dried thirteen days; on the second day, an emulsion made with one dried during twelve days and with one dried eleven days; on the third, with one dried ten days and nine days, etc.

Several deaths having occurred when this method was used after severe bites by wolves or face bites by other animals, M. Pasteur came to the conclusion that the method used was not powerful enough, and he therefore invented and used a second or intensive method. The simple method has also been modified, and the two methods now in use at the Pasteur Institute at Paris are explained by the diagrams.

The intensive method is chiefly used for face bites. The incubation period in the case of face bites is often extremely short, and hence it is necessary to inject large quantities of vaccinating substance as soon as possible. Whereas in the simple method the cord dried six days is only injected on the fifth day, in the intensive treatment it is injected on the third day; the other differences in the two modes of treatment are best seen on studying the tables. Each injection consists of about $\frac{1}{2}$ a cubic centimètre of spinal cord crushed in 2 cubic centimètres of sterilised beef tea.

It is interesting to know how complications such as abscesses, erysipelas, etc., are avoided in these injections. In the first place, the syringes in use are carefully sterilised each day by prolonged boiling. After each injection the needle is dipped into oil heated to a temperature of 105° to 110° C., thus providing against the inoculation of syphilis and other diseases. Further, the cords which, when crushed, are to be injected, are proved to be free of all the micro-organisms of putrefaction in the following manner: one piece of each cord is placed in sterilised beef broth and kept for twenty-four hours at a temperature of 38° C., the cord being only used if the beef broth in which a portion of it has been placed remains perfectly aseptic. I may state that I have seen many thousands of inoculations at the Pasteur Institute without ever seeing an abscess.

The injections are made into the subcutaneous tissue of the abdomen. The patients occasionally complain on the second or third day of a little tenderness and redness. This entirely disappears on a hot poultice being applied every night after a warm bath. They feel no evil effects whatsoever either during or after the treatment.

INTENSIVE METHOD

N.B. EACH DOT STANDS FOR ONE INOCULATION

We now come to the question of the real value of M. Pasteur's treatment, and I think the question you wish me to answer is the following one. Supposing one of my patients or myself to have been bitten by a rabid animal, would the chances of life be greater by trusting to luck, or by at once going to be inoculated according to M. Pasteur's methods? In order to answer that question fully, it is necessary to know what the average mortality used to be in people bitten by rabid animals before the invention of M. Pasteur's treatment. Statistics of deaths occurring among patients bitten by rabid animals, and who declined to undergo M. Pasteur's treatment, must also be studied. There are several series of statistics which were published before the discovery of M. Pasteur, and some which have been made independently of M. Pasteur since his first publications. It is necessary to make a distinction between the people bitten by dogs, cats, and other domestic animals on the one hand, and people bitten by wolves. Now, in the first class of cases the mortality has been variously estimated. Faber has tabulated the cases of 145 people bitten by rabid animals in the kingdom of Wurtemberg, and he found that the mortality amounted to 19 per cent. At the General Hospital in Vienna, in 1860, it was found that of 115 persons bitten by rabid animals 25 died (mortality 21.73 per cent.). Leblanc states that of 32 people bitten by dogs undoubtedly rabid 5 died (mortality 15.82 per cent.). During the year 1887, 44 people bitten in Paris by rabid animals declined to undergo M. Pasteur's treatment, and 7 of them died (mortality 15.9 per cent.). Other statistics show a mortality varying between 20 and 50 per cent., but these numbers are probably too high because they are derived from official reports, the officers of the State being more likely to know of the fatal cases than of those which ended in recovery, and I shall, for the sake of argument, assume the mortality to be 15 per cent.

On the other hand, in the case of wolf bites, the statistics of Renauld, Vallet, du Mesnil, Bombarda, and Gamaleia, comprising together 1,296 cases of wolf bites, show a mortality of 60 to 64 per cent. Thus, for instance, one wolf at Ewanguliezenc, in Russia, bit 35 men and 23 women. The wounds were cauterised with caustic potash, but, nevertheless, 24 men and 15 women died (mortality 67.24 per cent.) within six months. The mortality also varies according to the part of the body which has been bitten. The statistics of the Comité d'Hygiène from 1862 to 1872 show that of people bitten on the face 88 per cent. died (50 cases); on the hands 67.25 per cent. died (113 cases); on the upper limbs 30 per cent. (40 cases); on the lower limbs 21.21 per cent. died (33 cases); on the trunk 31.81 per cent. died (22 cases); on the face and hands 2 men died out of 8 persons bitten.

This mortality is probably far too high, because it stands to reason that an official body like the Comité d'Hygiène would be at once informed of the fatal bites, but would take no notice of most of the cases which end in recovery. At the same time these figures show that face bites are far more dangerous to life than wounds in other parts of the body. Indeed, according to Leblanc's statistics, comprising, it is true, only very few cases, the mortality after face bites amounts to 80 per cent.

The statistics taken at the Pasteur Institute are made in the following way: Careful inquiries are made from each patient as to whether the animal which has bitten him was rabid or not. Whenever possible the head of the dog, cat, or other animal which has inflicted the wounds is sent to M. Pasteur's laboratory. An emulsion is made with the brain of that animal, and injected under the dura mater of a rabbit. If it is not possible to send the head, a certificate from a veterinary surgeon who has seen the animal is obtained, and at the same time careful inquiries are made as to the number of persons and animals which the rabid

beast may have bitten. The statistical tables are then divided into three columns. In the first column (A) are placed all the people who have been bitten by animals which have been proved to be rabid, the proof being by the inoculation from some part of the central nervous system of the biting animal reproducing rabies when inoculated into a guinea-pig or a rabbit. In this column are also placed people who have been bitten by an animal which has bitten other people or animals who have died of rabies. In the second column (B) are reckoned people who have been bitten by animals certified to be rabid by veterinary surgeons. In the third column (C) we find those who have been bitten by animals suspected of being rabid.

During the period extending from November, 1885, to January, 1886, 2,164 human beings bitten by animals proved to be rabid were inoculated at M. Pasteur's Institute in Paris. Of these, 32 died (mortality 1.47 per cent.). On the other hand, 518 persons strongly suspected of rabies were submitted to the same treatment, and of these 3 died (mortality 0.58 per cent.). Notice that in the statistics are reckoned those even who died immediately after treatment, and before, in many cases at least, it could have had any beneficial effect. Amongst the 2,164 people, 214 were bitten in the face and head; of these, 186 had been bitten by animals proved to be rabid. Nine of the latter died, giving a mortality of 4.83 per cent. Notice, however, that 136 of these had been treated by the simple method. The mortality after the simple method amounted, therefore, to 6.61 per cent. Not satisfied with these results, M. Pasteur inoculated 50 by the intensive method; none of these 50 patients died. The mortality amongst people bitten in the hands was 1.22 per cent.; amongst those bitten in the limbs and body, 0.66 per cent., whereas the lowest mortality in persons not treated is 15 per cent.

Before proceeding with the statistics of the Pasteur Institute, I must say a few words of the statistics published in other countries, for the value of any particular mode of treatment is better judged when results obtained by independent observers are examined. Antirabic institutes have been established in a great many countries, and I give you the results as far as they are known.

Bujwid in the last six months of the year 1886 inoculated 104 people bitten by animals proved to be rabid, or which were most probably so. He lost 1 patient. He then tried a weaker treatment on 193 people; 8 of these died, amongst them being all those who had been bitten in the face. M. Bujwid then determined to give the intensive treatment a trial. He inoculated 370 people bitten by animals undoubtedly rabid; 4 of these were bitten by wolves in the face, 30 in the face by rabid dogs. All these 370 people are alive now, more than one year after the last inoculation. M. Bujwid, in a private letter to me dated July 29th, 1889, tells me that he has inoculated 146 people this year, of whom 1 has died. He also tells me that in his part of the country, and during his time of office at Warsaw, 31 people who were not inoculated died of rabies, although, as he remarks, very few people refuse to be inoculated nowadays after having been bitten.

At St. Petersburg, 484 people were inoculated from July 13th, 1886, to September 13th, 1888. The mortality is somewhat higher, being 2.68 per cent.

At Odessa, Dr. Gamaleia inoculated 324 people in 1886 by the simple method, mortality 3.39 per cent. In 1887, he inoculated 345 people by the intensive method, mortality 0.58 per cent., whilst in 1888 the mortality amongst 364 people amounted to 0.64 per cent. Dr. Bardach, the present director of the Institut Antirabique of Odessa, has been kind enough to send me the following information. Twenty-six people were inoculated after being bitten in the face by dogs proved to be rabid; of these one child, 7 years old, died. It is only fair to state that this unfortunate child arrived at Odessa fourteen days after the bite, and that it died on the nineteenth day after being bitten, that is, on the fifth day of treatment, before the latter would have produced any effect. All the patients who recovered had been most fearfully bitten, one of them having had the face almost torn off by eight dreadful bites, and bitten eleven times in the hand besides; another of them having had thirteen deep wounds inflicted by a rabid wolf in the face. Of the 333 other people inoculated by Dr. Bardach only two died (mortality 0.63 per cent.). Among the successful cases was one with thirty deep wounds, the results of bites from a wolf proved to be rabid. Among the 333 above mentioned were 7 men who had never been bitten, but who insisted on being inoculated as a preventive measure (mortality *nil*).

At Moscow Dr. Gwozdreff inoculated 107 persons in 1886 by

the simple method (mortality 8.40 per cent.). In 1887, with the intensive treatment, the mortality was 1.27 per cent. amongst 280 inoculated people. Dr. Jules Goldendach (Chef de l'Hôpital Empereur Alexandre III at Moscow), in a private letter, informs me that at Moscow, during the year 1888, 431 persons were inoculated according to M. Pasteur's method; 328 were bitten by rabid animals (mortality 1.82 per cent.), whilst of 70 bitten by wolves 10 died (mortality 14.28 per cent.); 3 of the deaths occurred in patients bitten in the face and head. One of them died only ten days after the treatment was finished, the 2 others dying during the progress of treatment, that is, before the preventive inoculations could have had any effect; 7 of the 11 deaths following wolf bites occurred in people bitten in the face and head, whilst 8 of them took place either during the progress of treatment or within 14 days after the last preventive inoculations, that is, 15, 19, 21, 24, 27, 28, 33, 44 days after the bite. Of the two others, 1 died 45 and the other 51 days after being bitten.

These Russian statistics are extremely interesting, for a great many of these patients were bitten by rabid wolves, and we know that after bites from these animals the mortality in non-inoculated people varies between 60 and 64 per cent. Gamaleia, in 1888, collected 119 cases of persons bitten by wolves and inoculated according to M. Pasteur's methods; of these, 8 died (mortality 6.72 per cent.). M. Pasteur's treatment, therefore, saved 63 of his people from a painful death.

In Italy, at Turin, Dr. Guido Bordonì Uffreduzzi has inoculated 531 persons, 486 patients having been bitten by animals undoubtedly rabid. Of these 10 died (mortality 1.88 per cent.). Here, again, we can judge of the value of the intensive treatment as compared with the simple method, for, on examining Dr. Uffreduzzi's statistics, we find that he submitted 373 persons to the simple treatment and that 9 of these died (2.54 per cent.); whereas of the 158 persons inoculated by the intensive method only 1 perished (0.56 per cent.). Of 43 patients bitten in the face and inoculated by him he only lost 1. At Lisbon Dr. Barateri has inoculated 335 persons up to November, 1888, and lost 2 patients (mortality 0.59 per cent.).

Dr. Luigi di Blasi has kindly sent me the following account of his inoculations at Palermo. He has inoculated 343 persons since March, 1887, 66 being treated by the simple (mortality 3.03 per cent.) and 277 by the intensive method (mortality 0.72 per cent.); 170 patients had been bitten by animals proved to be rabid. Of 21 patients bitten in the face 1 died; whilst of the 322 patients bitten in various parts of the body 3 perished.

At Naples Professor Cantani, assisted by Drs. di Vestea and Zagari, has inoculated 347 people, of whom 296 had been bitten by animals proved to be rabid (mortality 1.72 per cent.). It is noteworthy that, during a period of seven months, Professor Cantani had to close his antirabic institute for want of funds, M. Pasteur's opponents being very powerful at Naples. During that period, however, 9 persons died of rabies at Naples, and the Pasteur Institute had to be reopened.

At Constantinople 34 persons had been inoculated up to November, 1888, of whom not one has died.

At Havana Dr. Tamayo has inoculated 170 persons (mortality 0.60 per cent.).

I have shown you now conclusively, I hope, that M. Pasteur's treatment has given good results in other countries, and when applied by independent observers. Let us now return to M. Pasteur's own statistics. The following four tables will, better than any words of mine, show you the results of his inoculations:—

TABLE I.—January 1st to December 31st, 1887.

	A.	B.	C.
Number of persons inoculated ...	1778	1501	277
Mortality a.	1.34 per cent.	1.52 per cent.	0.78 per cent.
" b.	1.12 "	1.26 "	—
" c.	0.73 "	0.93 "	Nil.

TABLE II.—*Patients bitten in the Face and Head, and having undergone M. Pasteur's Treatment in Paris during the year 1887.*

	A.	B.	C.
Number of persons inoculated ...	145	127	18
Mortality <i>a.</i>	7.61 per cent.	7.87 per cent.	5.55 per cent.
" <i>b.</i>	4.18 "	4.72 "	Nil.
" <i>c.</i>	2.08 "	2.51 "	Nil.

TABLE III.—*January 1st to December 31st, 1888.*

	A.	B.	C.
Number of persons inoculated ...	1626	1371	255
Mortality <i>a.</i>	1.16 per cent.	1.31 per cent.	0.39 per cent.
" <i>b.</i>	0.79 "	0.94 "	Nil.
" <i>c.</i>	0.55 "	0.65 "	Nil.

TABLE IV.—*Patients bitten on the Face or Head, and having undergone M. Pasteur's Treatment during the year 1888.*

	A.	B.	C.
Number of persons inoculated ...	123	109	14
Mortality <i>a.</i>	7.33 per cent.	8.25 per cent.	Nil.
" <i>b.</i>	4.80 "	5.41 "	Nil.
" <i>c.</i>	2.44 "	2.75 "	Nil.

Explanations.—Column A. in each table includes all the cases inoculated at the Pasteur Institute during the year. Column B. includes only patients bitten by animals proved to be rabid at the time they inflicted the wound. (This corresponds to columns A. and B. in M. Pasteur's own tables.) Column C. gives the number of patients bitten by animals which, though presumably rabid, could not be proved to have been so.

Mortality *a.*—Total mortality, including patients dying during the progress of treatment. Mortality *b.*—Mortality after those who died during treatment have been excluded. Mortality *c.*—Mortality after those who died within fourteen days after the completion of treatment have been excluded. The lowest mortality in people bitten by rabid animals and not inoculated amounts to 15 per cent. at least.

One remarkable fact in this connection is that in the year 1887 350 people were bitten in Paris by rabid animals; 306 of these people were inoculated by M. Pasteur; 3 of them died = 0.97 per cent.; 44 trusted to luck, and declined to be inoculated, and of these 7 died. Mortality, 15.9 per cent. These facts were elucidated by careful inquiries made by Dr. Dujardin-Beaumetz, who is not in any way connected with the Pasteur Institute.

There is one question which I have not touched at all as yet, and it is this: Are there any cases on record in which it can be proved that death has followed as the result of M. Pasteur's treatment? I say, and I say it without the least hesitation, there are no such cases on record. Indeed, a great many of the men working under M. Pasteur in Paris, in the rabies department of his Institute, have been inoculated as a preventive measure. In fact, all the medical men, assistants in that department, who are skilled both in bacteriology and clinical medicine, have been inoculated, together with the laboratory attendant. Many medical men have done the same without feeling any evil effects either then or afterwards.

What are we to conclude from this? What is our answer to the question which was put in the first place? I think it is simply this: "If I or one of my patients were bitten by a rabid dog, or by a dog suspected to be rabid, or if I held an official post in an antirabic institute, I should at once go myself, or send my patient to be inoculated." And that is the advice which M. Pasteur and all those who work with him give, and not only give, but have themselves followed.

Gentlemen, you have been told how this knowledge was acquired, and how it has been applied to man, so that now patients bitten by rabid animals have a great chance of recovery. I am very sorry that time does not allow me to do more, for it would have been interesting to see how M. Pasteur was led to his wonderful discovery. His method has only been the last step in a long list of researches on preventive inoculations in other diseases.

Rabies is a disease which has been known for centuries. On it the labours of clinical and veterinary men have been freely expended; and what is the result? Simply this, that rabies is almost unanimously pronounced to be an incurable disease. Then when there seems to be no hope, when the very idea of preventing rabies after a bite appears to be a chimera, the disease is studied by a man who knows little medicine or veterinary surgery, but who has spent his life in pursuing experimental investigations. He finds a method of inoculating the disease with certainty; he shows that the virus is in all probability a micro-organism, that it is always to be found in the cerebro-spinal axis, and that animals can be vaccinated against it; and, lastly, he applies to man that method which has been gained solely by means of experiments on animals, with the result that he and his pupils have been able to save more than 1,000 human lives.

M. Pasteur has taught medical men a great lesson, a lesson which many scientific men had in vain tried to enforce before him. It is that, although the healing art must necessarily make use of the data supplied to it by clinical observation, yet the present and future progress in medicine is and will be chiefly due to the application of experimental methods to its study; the most important of these methods consisting in experimenting upon the lower animals.

The PRESIDENT, in introducing Dr. Ruffer, stated that his reason for trying to obtain for the Section an authorised account of the most recent work and its results in the Pasteur Institute was that he desired that the Section should discuss the practical question, Should we, or should we not, recommend persons bitten by a rabid animal to undergo Pasteur's treatment? Dr. Ruffer's name was suggested to him by M. Pasteur.—Dr. ALFRED T. BRETT would like to state a few facts from personal experience. In forty years he had only seen two cases of hydrophobia. He lived at Watford, in Hertfordshire, and four months since a dog of Dr. Cayley became undoubtedly rabid. The muzzling order was made in Herts, but not then in Middlesex. A dog strayed into Herts and bit a boy. Dr. Brett was in Paris, and saw the Pasteur Institute; on returning he was told of the boy, and from information, and from the certificate of the Veterinary College, he came to the conclusion the dog was mad. Dr. Brett consulted Sir James Paget and the Professor of the Veterinary College, who advised the boy to be sent to Paris. Dr. Brett sent him. He stayed fourteen days, and the cost was £12. The board of guardians paid the expense. The boy was now quite well. The practical point was that it was of no use to have the muzzling order in one county and not in another. Dr. Brett had strong faith in the Pasteur treatment.—Dr. DRYSDALE (London) said he would like to commence his remarks by a reply to the question put by the President. If he were bitten by a rabid dog, he would at once submit himself without delay to the inoculation process of M. Pasteur. In 1886 he had first studied the plan in Paris, and since that date he had every summer spent a short time at the Pasteur Institute of Paris. He begged to be allowed to testify to the extreme honesty and care exhibited by all persons connected with that establishment in carrying out the difficult process invented by Pasteur. Although the statistics cited by Dr. Ruffer were full of important evidence as to the value of these inoculations, it was not these statistics that had convinced him that Pasteur had acquired the power of preventing the outbreak of hydrophobia. The physiological proof was the real one which had done so, just as he had been convinced of the value of vaccination in preventing small-pox by Jenner's early experiments, which consisted in first vaccinating a patient, and then in a month subsequently inoculating him with small-pox with no effect. Pasteur had done the same in the case of forty dogs which he had first inoculated with the preventive method, and had then inoculated them with virus under the dura mater without the occurrence of the disease, which under ordinary circumstances would inevitably have occurred. Under such circumstances, Pasteur was justified in assuming that a similar treatment would prevent the explosion of the fatal end of rabies in man by treating this disease of long incubation by a similar process, and the statistics brought forward by Dr. Ruffer were a splendid confirmation of the truth of the physiological theory. He could not help expressing his personal obligations to M. Pasteur as the greatest benefactor to mankind that had existed in this century since the days of Jenner, and he only regretted that the medical profession could not claim him as a member. In this country he had found, even recently, many very distinguished medical men still sceptical as to the advantages of Pasteur's pro-

cess, but he would ask such gentlemen to devote a little of their valuable time not only to reading the literature of the subject, but in acquainting themselves by personal inspection with the way in which the processes were carried out in the laboratories of Paris. The unwearied care, patience, and intelligence abounding on all sides in that Institute, he maintained, could not fail to bring conviction to the mind of all inquirers after truth that there was perfect honesty in all the work carried on by Drs. Grancher, Roux, and others in that establishment; and that, therefore, the statistics brought forward by Dr. Ruffer might be taken as trustworthy and accurate in the highest degree. To conclude, he would say (1) that the number of Pasteur's friends and pupils who had inoculated themselves preventively, and sustained no damage whatsoever, showed how innocent the process was; and (2) that the physiological proof and the subsequent statistics had given all the data requisite for replying to the question "Should I send a patient bitten by a rabid dog to be submitted to Pasteur's inoculation?" in the affirmative, "Yes, and without an hour's unnecessary delay."—Brigade-Surgeon O'DWYER pointed out that the Government of Malta had prepared at a comparatively small cost a Pasteurean laboratory for protective inoculation against hydrophobia, and he urged that, instead of waiting for the creation of an elaborate building, we should start at once with a moderate institution on the Malta scale, which he thought could be effected at a cost of £200 for installation, and kept up for a sum of about £300 a year. He further added that, although hydrophobia was very prevalent in the Island of Mauritius, in the neighbouring Island of Bourbon, eighty-nine miles distant, a case of that disease was never known to have occurred. He complained of the unreliability of statistics concerning cures from hydrophobia from some foreign countries by protective inoculation, as the persons who formulated them were often peculiarly interested in the institutions where inoculation was performed. Although he had the highest opinion of veterinary science, he objected to consider a dog to have been mad on the certificate of a veterinary surgeon, except that gentleman found the animal to have been mad by the direct inoculation of a portion of the animal's nervous system into the body of another animal, and so producing the disease. If M. Pasteur told him an animal was undoubtedly hydrophobic, he had no hesitation in believing him, as he was not a *savant* who was led away by his enthusiasm.—Dr. SAUNDY said that, while they owed a great debt of gratitude to Dr. Ruffer for the admirable manner in which he had presented this subject, and to M. Pasteur for his splendid scientific services, they owed to themselves to discuss the matter critically, and apart from enthusiasm. As Dr. Ruffer had said, the basis for their judgment of the value of this treatment must be the estimate formed of the number of persons bitten who subsequently developed rabies. The last speaker had shown how difficult this was. Dr. Eddison had stated that until the recent epidemic, the disease had been unknown for forty years, although rabies in dogs had been continuous, and was so exceptionally severe twenty years ago, that a Local Government inquiry was held, and a large number of dogs were destroyed. In Birmingham no death from hydrophobia had occurred for forty years until the other day, when a young man who was bitten in Ceylon had died; yet rabies had not been extinct, and only a few months ago a reputed mad dog was destroyed in the middle of the city after having bitten twenty-two persons; yet no case of hydrophobia had happily occurred up till now. Dr. Drysdale had said that he attached less value to the statistics, being convinced by Pasteur's physiological proof, which he said was precisely the same as that by which Jenner proved the value of vaccination. But this was not the case. Had Jenner vaccinated everybody who had been exposed to the contagion of small-pox, and then attempted to show that because only a small percentage got small-pox his method had protected the remainder, people would at once have said, we do not know how many such people become infected ordinarily, and therefore we cannot judge of the value of the method. M. Pasteur might have inoculated a large series of animals by subdural injections, and given the world the result of his subsequent preventive treatment. This would afford at least a better test of his method than any yet put forward. With regard to the danger of the method, he admitted the value of the fact that a large number of laboratory assistants had been submitted to treatment without ill effect. But it must not be forgotten that Professor Peter, one of the leading physicians in Paris, believed that a case had died under his care from this cause. On the practical question he agreed with Dr. Ruffer, and would

himself submit to the treatment and recommend it to others, as the balance of evidence was in favour of the view that its dangers were not great, while its possible benefits were enormous.—Surgeon-General Sir WILLIAM MOORE drew attention to the statement made by the late Dr. Samuel Wright, of Birmingham, in his work on the saliva, that injections of healthy saliva into rabbits must, in the same manner as described by the lecturer, produce hydrophobic convulsions. He would not delay the meeting by remarking on how this bore on Pasteur's treatment, but he would ask if this had been reinvestigated. If not it was desirable it should be. Then, as regards the incubation, it was as difficult to explain incubation of three months as thirty-three months, or of three years as thirty years. They had a long incubation of syphilis. Cases of three, seven, even twenty-one months had been recorded, and he had himself seen a case which he believed to be over six. As regards fatality, several cases of recovery were recorded; one by himself in the Indian *Annals of Medicine*. It had been stated that the diagnosis was easy, but that did not accord with his experience. Shivering was sometimes a prominent early symptom. Before we could accept Pasteur's system the incubation of hydrophobia must be decided; and moreover, it must be shown that all persons bitten and taken to Pasteur would have got hydrophobia, which they certainly would not.—Dr. VAUGHAN HARLEY, having worked in Paris in the Pasteur Institute, supported the statements of Dr. Ruffer, as he well knew how carefully he had worked out the statistics while there.—Dr. DAVID W. TORRANCE, medical missionary from Palestine, said it might be interesting to notice in comparison a treatment pursued in Syria that he had seen. Women who had been bitten by wolves were put into a dark hovel and fed on bread saturated with the saliva of a religious Moslem sheikh, probably mad—a curious antidote, which never was successful.—Dr. GEORGE HARLEY said it was pleasing to see the unanimity of opinion existing in the meeting regarding the value of the facts that had just been laid before it. And, as no one expected that a great question like this would either be solved in a day or by one individual, it was the duty of everyone to add his quota to the general fund. He would therefore call attention to one or two errors which he thought were often overlooked in discussing the question of rabies: First, the term "mad dog," which had been used by one of the speakers, ought to be entirely abolished when speaking of rabies. Madness in the dog, or in the horse, or any other animal, meant insanity, just as it meant insanity in man, and that was an entirely different form of disease from rabies, which was a febrile disease associated with delirium, just in the same way as delirium was associated with scarlet or any other form of fever. Secondly, it was equally wrong to suppose that rabies was the product of the hot weather, for rabies occurred in the Arctic circle as well as in the torrid zone. Dr. Kane, in his Arctic voyages, told how sixty-five of his sledge dogs died from rabies. Consequently it was an absurdity to speak of the "dog days." Thirdly, he believed it was as wrong to suppose that it was the germ, constituting the *fons et origo* of the disease, which either induced the symptoms or killed the patient, for, as he had shown (on the previous day), it was an error to imagine that it was the loss of the albumen that caused death in Bright's disease. So, in rabies it was not the germs themselves, but the poisonous products they developed in the victim's system that were the true agents of death. Fourthly, although the virus of hydrophobia could not be said to act as a chemical agent, he thought that the poisoning substances it developed in the animal body were as truly chemical agents as strychnine, which had an equally powerful effect on the nervous system, though giving rise to a different chain of symptoms.

M. PASTEUR AT HOME.—The members of the Société de Médecine Pratique, of Paris, recently visited the Pasteur Institute, where they were received by M. Pasteur himself. The distinguished biologist delivered a short address, in which he spoke of the danger of placing dogs that had been bitten in quarantine for a short time, and then releasing them, instead of having them at once destroyed. This culpable negligence often led to disastrous results. M. Pasteur was particularly emphatic in affirming that rabies is never spontaneous.

MR. ROBERT MUSGRAVE CRAVEN, D.P.H.Camb., and assistant medical officer of health for the borough of Southport, has been appointed medical officer of health to the combined sanitary authorities of the county of Westmorland, in succession to Dr. C. E. Paget, who a few months ago was appointed medical officer of health for the county borough of Salford.