Preventive treatment of hydrophobia and other diseases : a paper read before the Abernethian Society, Thursday, January 12th, 1888 / by T. Lauder Brunton.

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BY

T. LAUDER BRUNTON, M.D., D.Sc., F.R.S.

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A PAPER

READ BEFORE

THE ABERNETHIAN SOCIETY

THURSDAY, JANUARY 12TH, 1888.

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Gentlemen,—The subject of my paper to-night is one of enormous importance. It has been attracting a great amount of attention of late years, and very different views have been expressed regarding it. Our knowledge of infective diseases has greatly increased within the last few years, and we are beginning to regard them now as almost certainly due to low forms of plant life, so low as to be just on the verge of the vegetable and animal kingdoms. They are, however, usually classed at present amongst the plants, and it is probable that we may learn something regarding these low forms of plant life by consideration of some of the higher forms with which we have been long acquainted and whose habits of growth are well known to us. The attitude with which we are obliged to regard the growth of these low forms and that of the higher forms is very different. A luxuriant growth of the higher plants is frequently beneficial to man, and we are accustomed to rejoice in a good crop of wheat or of fruit, because good crops of such a kind are advantageous to us. The case is very different when we have to deal with the low organisms, for instead of man feeding upon them they are apt to feed upon man, and their luxuriant growth means his destruction. In regard to these organisms,

in fact, man's position is very much that of the earth in regard to the crops as sketched by Kingsley in 'Hypatia,' where Raphael regards the earth as a huge sensitive animal, which is irritated by man scratching its surface with ploughs, and wearying it with crops, until at last its anger finds vent in an explosion, as an earthquake or a volcanic eruption. The effect of crops upon the earth is to exhaust the portion of soil upon which they grow, and the more luxuriant they are the more rapidly do they exhaust it. In some years, from one circumstance or another, the crops are luxuriant, in others they are scanty. If looked at from man's point of view the scanty crops are disadvantageous, from the earth's point of view they are desirable. When bacilli or micrococci begin to grow in the human organism they exhaust and may destroy the organism, which on its part usually resents their intrusion by an explosion of heat, to which we give the name of fever. Just as the earthquake or volcanic eruption is hurtful to the earth as well as to its inhabitants, so this fever is hurtful both to the organism and to the microbes which have invaded it, but if it is only high enough to kill the microbe without killing the organism it is a most useful means of protection, freeing the organism from its invaders, and preserving its health and vitality. Now, just as there are good years and bad years for crops of wheat, so there are times at which microbes flourish luxuriantly and others at which they grow sparingly. These different times were recognised by the old physicians under the name of the "epidemic constitution," for they noticed that sometimes the disease flourished and the patients died, at other times the disease was of a mild form and the patients nearly all recovered. We now explain these different conditions by saying that at some times the microbes grew luxuriantly and destroyed the organisms which they attacked, but at other times the microbes grew sparingly and therefore did not destroy the organism in which they were growing. It is possible that the growth of microbes may be modified by many factors, but there

are two with which we are now becoming acquainted, namely, (*a*) alterations in the soil upon which they grow ; and (*b*) alterations in the microbes themselves ; or, as we may put it, by analogy with wheat (*a*) in the soil, and (*b*) in the seed sown upon it. It has long been known that certain crops are more exhausting than others, so that if they are sown in the same patch of ground year after year, the harvest becomes rapidly less plentiful, while others may be cultivated successively in the same soil for many years together. There is almost no crop, however, which will not grow more than once upon the same soil, but in the case of many of the infective diseases one attack renders the person insusceptible to another, and moreover even a mild attack is frequently sufficient to protect the person who has had it against any infection, however virulent it may be.

For this reason the practice of inoculation for smallpox was introduced, the infective matter being taken from a person who was having a mild attack of the disease. But unfortunately the disease germs thus inoculated sometimes throve too luxuriantly in the organism into which they had been transplanted, and greatly injured or destroyed it, so that the practice of inoculation for smallpox has now fallen completely into disuse.

When I had the honour of addressing you a year or two ago, I mentioned a fact that I believe has never been elsewhere published, which the late Dr. Charles Darwin asked me to mention whenever I was writing upon the subject of inoculation, viz. that Dr. Erasmus Darwin, struck by the success of inoculation for smallpox, tried to employ it for other diseases ; he chose scarlet fever, and with this he inoculated his son, Robert, but unfortunately the inoculation took to such an extent that the child barely escaped with his life.

Then came the plan of vaccination in place of inoculation. It is not regarded by everyone as certain that cow-pox is simply the smallpox of man weakened by its growth in the uncongenial soil of the cow's tissues, but

nevertheless it may be regarded as certain that the virus of smallpox, inoculated into the cow and re-inoculated back to man, is very much weakened, so as to produce only a slight disease, similar to that of ordinary cow-pox.

Another plan of weakening the virus of infective diseases has been proposed by Pasteur, and consists in cultivating it artificially at a temperature somewhat higher than that which is most favorable to its growth. The effect of this upon the virus is like the effect of over-cultivation upon fruit trees, which run all to leaf and do not bear fruit, while the over-cultivated virus loses its energy when inoculated into an animal, grows but sparingly, and produces but slight disorder instead of severe disease and death. This plan has been used by M. Pasteur to preserve animals from anthrax. The anthrax virus is cultivated at a somewhat higher temperature in successive crops, each crop becoming weaker than the preceding. An animal is then inoculated with a weak virus which produces only slight symptoms. After these have passed off a stronger virus is used, and if necessary a stronger still, after which the animal is almost completely proof against any of the virus, however potent, and remains so for a certain length of time, which has not perhaps been as yet exactly determined.

His success with anthrax led M. Pasteur to attempt to discover a means to prevent death from other infective diseases, and his method of treating hydrophobia is the result of long study.

Hydrophobia in general, and M. Pasteur's treatment, has lately been largely discussed, and so much material is available for reading that it will be best for me not to attempt to go over the whole subject, but rather to deal with such points as have come under my own observation, and which have a certain amount of personal interest.

In the summer of 1886 I went over to Paris along with Dr. Burdon Sanderson, Sir Henry Roscoe, and Mr. Horsley, as a member of the Royal Commission, to investigate M. Pasteur's treatment and inoculations for the

purpose of preventing hydrophobia in persons who have been bitten by rabid animals. In pursuance of our mission we went to M. Pasteur's establishment in the Rue D'Ulm and saw there a very remarkable scene. Passing through a gateway in a narrow street, we found ourselves in a courtyard where people from all nations seemed assembled. Some of these were coming from a door in one corner and others were proceeding towards it. We saw there Polish Jews in long coats reaching down to their heels, with long curled locks hanging in front of their ears, side by side with Arabs from Algeria in their loose picturesque white robes and large white turbans, conspicuous amongst a crowd of persons with dress less distinctive to the eye, but whose various nationalities were at once apparent to the ear by the Babel formed by the different languages in which they were conversing. Following the stream and entering the door we passed into a small ante-room, where M. Pasteur met us and conducted us into the room where the inoculations were performed. There we saw one of his assistants sitting, with a small syringe in his hand and a row of glasses by his side. As each patient came near him preparations were made for the injection by the exposure of a small part of the skin of the abdomen, and as each patient's turn came a definite quantity of the liquid was injected subcutaneously, and he passed on. The syringe was then at once sterilised by dipping it into a bath of oil heated far above the temperature of boiling water. It was then refilled and the next patient was injected in turn ; each patient after receiving the operation adjusted his dress and passed out of the chamber in order to make room for others. It was a curious sight to a stranger to see this crowd of people of various nationalities and religions, speaking different languages, come from far-distant lands to have this operation performed, and to any chance observer the question would naturally arise, Why have these people all come here and what has been done to them ?

We will consider these questions separately, and take first the question, Why they had come there. It is easily answered. They had come because they had been bitten by rabid animals and were afraid of the dreaded disease, hydrophobia, coming upon them in consequence of the bite. But a stranger might next ask, and we often indeed do hear the question asked, What is rabies and what is hydrophobia? Are they the same disease or are they different, and what is the relation between them? The two diseases are the same, but the name of rabies is given to the disease when it appears in animals, and hydrophobia when it appears in man.

The disease may attack all animals, and it can be communicated from one to another, but as the virus by which inoculation occurs is contained in the saliva the danger of inoculation is much greater in the case of carnivora than herbivora, and it is more especially by the bite of dogs that the disease is propagated, although it is sometimes inoculated also by the bites of cats and wolves. As the herbivora are much less given to biting, they are not so likely to communicate the disease to other animals; but they may do this, as was shown in the recent epidemic of rabies amongst the deer in Richmond Park. If the animal which is bitten has a thick fur, a great deal or the whole of the virus may be wiped off the teeth of the animal which bites it, and it may therefore escape, but if it is bitten on a part not so protected, in all probability it will become inoculated with the disease.

There are few or no local symptoms, the wound usually heals quickly, and the animal remains apparently perfectly well for a certain length of time, which varies to a certain extent with the species of the animal and also with the virulence of the virus; then symptoms make their appearance which almost invariably end in death. The first symptom almost always indicates an affection of the brain, the mental character of the animal being altered; in the dog it not unfrequently happens that the first evidence of any alteration consists in an increased

display of affection towards its master or mistress, which it shows by attempts to lick their face or hands. The symptoms indeed are those of nervous excitement along with physical discomfort, which may possibly be due to the alteration in the digestive system, which is also an effect of the disease, the appetite being at first lost, and there being considerable thirst. The symptoms affecting both the nervous system and the digestive system gradually increase, the dog becomes more restless and escapes from its home, and is apt to rush wildly through the country, biting at any man or animal that may come in its way. It seems to have a certain amount of anæsthesia and not to feel either fatigue or blows in the same way that a healthy animal would do. The appetite, which was formerly lost, now becomes perverted, and the dog swallows bits of stick, hay, and other rubbish, the presence of which in the stomach is one of the characteristics of the disease. The want of food and the exhaustion tell upon the dog's appearance, so that it becomes lean and its coat staring, and symptoms of alteration in the throat now appear, the saliva running from the mouth, and the bark becoming altered in tone. The character of the saliva is an important diagnostic point between rabies and epilepsy, a disease which is often mistaken for rabies, many epileptic dogs being killed on the supposition that they are mad. The saliva in rabies is thick and viscid, hanging in long strings from the mouth, but in epilepsy it is thin and flows readily. The congestion of the throat interferes with swallowing, and this interference is aided by an alteration in the nervous supply, so that the dog, though apparently suffering from thirst, plunges its nose into water without being able to drink. These symptoms of nervous excitement are succeeded by paralysis, the muscles of the lower jaw, and those of the hinder extremities being affected, so that the jaw drops and the dog can only close it by an occasional spasm, and the paralysis of the hinder extremities renders it no longer able to run. The paralysis extends upwards, involving the

muscles of the anterior part of the body, so that the animal lies perfectly inert, but even in this stage it may retain the tendency to snap at any object which is brought within reach of its mouth.

The symptoms just detailed are those of the ordinary form of rabies. In all cases there is a mixture of nervous excitement with nervous paralysis, the excitement gradually passing into paralysis in the ordinary form, or furious form, as it is sometimes called in order to distinguish it from the second or dumb form. In the dumb form the excitement is much less, the paralysis appears quickly and affects the muscles of the lower jaw rapidly, so that the animal does not howl. It also rarely bites. These two forms appear to depend upon the concentration of the virus, a concentrated virus tending to produce the rapid paralysis, evidencing itself in the dumb form, whereas a less active virus tends to exert a slower paralytic action and to produce the furious form.

In other animals the symptoms of rabies are evidenced also by excitement and paralysis, the amount of each varying in different cases. In rabbits tetanic spasms are occasionally noticed, combined with the paralysis ; and in horses a convulsion seems to come on whenever they attempt to run at anyone in order to bite. In consequence of this peculiarity horses are not liable to spread the disease.

The post-mortem appearances in cases of rabies are not well marked. They consist chiefly in congestion of the parts which I have already mentioned as being affected during life, namely, the brain, medulla, and spinal cord, the throat, and the stomach. The stomach is frequently found filled with sticks, stones, hay, straw, mud, and other foreign substances, and this is generally relied upon as being perhaps the most distinctive appearance in cases of rabies. The stomach itself is often very greatly ecchymosed, and microscopic examination has shown that in the medulla oblongata numbers of leucocytes have escaped from the blood-vessels into the surrounding

lymphatic spaces, but this is all, and one can hardly look upon this as distinctive.

The disease being so markedly infective is almost universally regarded by pathologists as due to a contagium vivum, but attempts to ascertain the nature of this have not been successful, although it seems not improbable that it is a very minute micrococcus. This opinion receives some confirmation from the fact that the virus does not retain its vitality long outside the body, while the virus of other infective diseases due to spore-forming bacilli may be maintained for a length of time outside the body, the spores long retaining their vitality.

In man the symptoms also point to an affection of the brain, spinal cord, and throat. In man, as in animals, the first symptom appears generally to be connected with the brain, and evidences itself in slight change of disposition; following on this we have an affection of the throat and spinal cord, so that after the change in disposition there occurs a difficulty of swallowing and a tendency to convulsive attacks when this is attempted which are very distressing to the patient, and which occur sometimes not only when they attempt to swallow but even at the very sight or sound of water.

Death may occur from exhaustion, but sometimes it may occur suddenly by syncope, and this is what one would expect from the fact that the medulla oblongata is involved in the disease.

Perhaps you will allow me to read a letter which I owe to the kindness of Mr. Whitehead, as it gives an admirable description of the symptoms in man, and afterwards to describe one or two cases that I have seen, although I have not been able to watch anyone during the whole course of the disease as in the case described in this letter.

"Huddersfield Infirmary; 11th Jan., 1888.

"I hasten to supply you as quickly as possible with some facts of the case you mentioned. Unfortunately these facts will have to be from memory, as the notes of the

case have either been lent out or been misplaced and I cannot put my hand on them now.

"The patient, a man (F. L—), æt. 27 or thereabouts, was a farm labourer, and was bitten by a strange dog on August 1st, 1887, along with his brother. They were driving the dog out of the farmyard when it turned on the younger lad. The elder one (our patient) went to his assistance and in pulling the dog off got bitten very badly on the right wrist. Within three days of this they were both off to Paris to see Pasteur, on the advice of their own doctor and of Dr. Hime, of Bradford. They both went through thirteen inoculations of the second grade. After returning from Paris all went well for six weeks, that was two months after the patient had been bitten.

"On September 29th (Saturday) our patient had been off at a local feast and whilst there he had been talked at a good deal about hydrophobia, and even before this his imagination had been worked on a good deal. However, on the Sunday he began to exhibit signs of the disease. He became very restless and excited with pain in his arm. On Monday his respiration began to be disturbed, and he exhibited the first spasm on trying to drink. This was towards evening. On Tuesday morning he was brought here and admitted under Dr. Cameron at 3.30 p.m. He walked into the hospital and showed no signs of illness beyond a certain wild, excited look and a nervous restlessness with sighing respirations occasionally. His pulse, I see from the temperature chart, was 88, his temperature 99·8° F., and respirations 28. When pressed to drink he made a great effort after some time and drank a small quantity, but it brought on a violent spasm, and the vessel from which he was drinking was thrown down, and he became very wild and excited. These spasms became towards evening very much more frequent, the slightest cause bringing them on, a draught from the door, or anyone coming near his bed being quite sufficient. During his spasms he was perfectly wild with regard to himself,

throwing himself about, banging his head on the pillows, and rolling on the floor, and all the time hawking and spitting mucus from his mouth. Towards 1 o'clock the spasms became so bad and so prolonged, and the patient was so violent and noisy, that chloroform was had recourse to. This to a great extent checked the spasms, but he rapidly got worse and died about 6 o'clock in the morning (October 4th). At 12 o'clock his temperature was 102°; at 2 a.m. it was the same; pulse 110, and respiration 32. At 5.30 a.m. his temperature was 104·4°, pulse 120, and respiration 40. He died from asphyxia brought on by the spasms.

"We held a post-mortem on the body the following evening, when nothing beyond the signs of asphyxia was found in the various organs until we came to the medulla and spinal cord, when on the floor and roof of the fourth ventricle distinct but small hæmorrhages were found. The whole of this was cut out and was sent off to Dr. Gowers, of London, for examination. We have not received a report of it yet.—Herbert Hirst, M.B.

"P.S.—I should state that the other brother, the youngest one, is still quite well."

Some years ago, when I was a member of the Committee of the British Medical Association for investigating Hydrophobia, I went to Bradford to see two cases which had occurred there. Six weeks before, a mad dog in rushing along the street bit a little girl, aged nine, and then crossing the street, bit a youth, aged nineteen. The youth was epileptic and to a certain extent idiotic. These two patients after the bite remained apart from one another, and knew nothing of what was happening to each other. On the same day six weeks afterwards they both evidenced signs of mental change, the little girl becoming troublesome in the playground, running after the other girls, pulling them about and annoying them, and would not desist when asked to do, although previously her behaviour had been exceedingly good. Next day

she had difficulty in swallowing, and some excitement. The difficulty of swallowing was, however, not great, she was put to bed, and in the afternoon the doctor came in to see her ; just as he entered the room she was sitting up in bed, she smiled at him, then suddenly fell back dead.

The youth, who knew nothing whatever about the girl, evidenced symptoms of mental change on the same day, but these were of a somewhat different character. He became somewhat sullen, and when I saw him just after the little girl's death, he was disinclined to speak and appeared to have illusions, apparently seeing dogs in the room, and calling them to him. The fauces were congested, but the only evidence of difficulty of swallowing was a slight twitching of the corners of the mouth accompanying deglutition, such as one often sees in cases of sore-throat. I recommended that he should be put on doses of quinine and bromide of potassium, giving the quinine with the idea of trying to prevent the issue of the white corpuscles from the vessels in the medulla. This youth's illness ran a curious course ; he continued in the same condition for some time, then some albumen appeared in the urine, but he ultimately got well. The fact that he recovered made some of the medical men who had seen the case with me doubt whether it was hydrophobia or not, but if it was not hydrophobia in a mild form, neither they nor I could say what it was. The mildness of the attack I attribute to the fact that the dog had wiped off nearly the whole of the virus on the little girl's clothes before it had attacked the youth, and as it rushed across the road straight from the girl to the youth, there would be no time for the further secretion of saliva.

In another case which I saw in the casualty ward of St. Bartholomew's Hospital the first symptom was also one of mental change. The patient, a labouring man, had been bitten by a dog, and remained perfectly well for some time afterwards, I am unable to state just now how long. One day he was sitting with his children on his knee according

to his custom, because he was very fond of playing with them. All at once he seemed to feel a sudden repulsion to them, and pushed them off his knees, saying, "I do not want you." Shortly afterwards, I think the same day, symptoms of difficulty of swallowing came on, and he was brought to the hospital. He presented, when I saw him, the well-marked symptoms of hydrophobia, the effort to swallow being ineffectual and bringing on a convulsive shudder throughout the whole body. He was at that time perfectly conscious; he knew what he was suffering from, and was greatly depressed on account of his wife and children, whom he was likely to leave behind with no provision.

Another case which I saw in Paris was that of a Russian woman who had been bitten by a mad dog, and who had been treated by M. Pasteur. When I saw her she simply presented the symptoms of nervous excitement, sitting up in bed, chatting and laughing continuously. There was a slightly fixed look in the eye, a good deal of thirst and some difficulty in swallowing; this gradually increased, and she died the next day. Had it not been for the fact that she had been bitten by a rabid dog one would have been inclined to look upon the case as one of hysteria, and I think between cases of hysteria and cases of hydrophobia there may be frequently considerable difficulty in arriving at a correct diagnosis, although the progress of the case would clear up all doubts in the course of a day or two. Two years ago I saw such a case at Leytonstone in a girl who died from hydrophobia.

The fatality of the disease is so great and recoveries are so rare, if they exist at all, that many doctors, like my friends in Bradford, look upon the fact of recovery as disproving the existence of hydrophobia in the case, but it is quite certain that animals may have a very slight attack of rabies and recover, and I see no reason why the same should not occur in man. Yet the almost certain death of persons affected with the disease has caused it to be regarded with horror, and this horror is,

I think, intensified by the fact that during the incubation period the patient appears perfectly well, so that people who have been bitten do not know for a long time afterwards whether they are going to have the disease or not. The usual period of incubation in the cases that I have seen has been six weeks, but in the one that I saw at Leytonstone it was only three weeks. It is said, however, that the incubation period may be as much as one or even two years, so that during a long period persons who have been bitten are going on with the sword of Damocles over their heads. Last year Lord Doneraile was bitten in January by a pet fox ; for this he was treated by M. Pasteur, and he remained free from all symptoms till the end of September, when he was attacked with hydrophobia and died in a day or two. Here the latent period was eight months.

The disease has been known since the time of Hippocrates, 2000 years ago, and probably for a long time anterior, but the frequency with which cases occur varies very considerably. I do not think that this can be illustrated more strikingly than by the fact that in St. Bartholomew's Hospital during all his long experience, Sir William Lawrence only saw three cases, Sir James Paget saw no more than three, and one of these was the same as one of the cases seen by Sir William Lawrence, so that the whole experience of these two distinguished surgeons only included five cases. Mr. Stephen Paget informs me that he has already seen four cases, I think in the course of little more than a year, in the hospital. The terror which the disease inspires makes people willing to do almost anything to escape it, and many plans of treatment, both local and general, have been used. The most important local measure is immediate cauterisation or excision of the bitten part. Should no cautery be at hand it is no doubt advisable to treat the wound as one would a snake-bite by tying a ligature above the bitten part, so as to prevent any absorption of the virus. Such measures as washing with vinegar are of little use, and even stronger caustics should not be depended upon. I saw

one case of a boy who had been bitten in the face by a dog, who only lived about a hundred yards from the house of Dr. Dobie in Keighley, who is an exceedingly able man, and one on whose skill every reliance might be placed. The boy was taken at once after the bite to Dr. Dobie's house, and was thoroughly cauterised with nitrate of silver within five minutes, yet six weeks afterwards I saw that boy dying of hydrophobia.

In the course of my observations on hydrophobia when I was on the committee of the British Medical Association, I unfortunately punctured my finger while making a post-mortem. I did not notice it at all till several hours afterwards, when I felt upon the finger something like a sting of a fly, and on pressing it a drop of clear serum exuded. I made a small incision into it, and applied first some carbolic acid and afterwards some permanganate of potash, but as a small hard tubercle formed over the part. I thought it advisable to use a stronger caustic, and therefore used caustic potash, but there is a difficulty in regulating the action of this substance, so that instead of simply destroying, as I had intended, the tubercle and the parts around it, the potash destroyed the matrix of the nail and the greater part of the extensor tendon of the last phalanx of the index finger, and caused the remaining part to slough away. The actual cautery would not have caused so much pain, and one would have been able to limit its action very much better.

The bites of cats are said to be more dangerous than those of dogs, one reason of this probably being that the cat's tooth makes a deep narrow puncture, admirably adapted for inserting the virus and preventing its removal. In the case of a bite from a cat the excision would require to be carried as deeply as the point had penetrated, and cautery might be applied afterwards, or else a long steel point might be heated and pushed down in the track of the tooth. After the outbreak of the symptoms remedies of all sorts have been tried, and cures have occasionally been reported, one under the influence of

anæsthetics, another by curara, &c. There are also a number of secret remedies which have been vaunted as specifics, but when actually put to the test, like the so-called specifics for snake-bites, prove to be of no use at all. One method of treatment has attracted a good deal of attention ; it is the so-called Buisson method, which consists in putting the patient into a vapour bath, so as to induce profuse sweating. Dr. Buisson states that he cured himself in this way after the symptoms of hydrophobia had already come on.

All treatment appears very nearly useless when the symptoms have once appeared, though one would naturally try anything that was likely to give a chance. The hopelessness of the treatment induced M. Pasteur to try whether it was possible to find a method of preventing the disease by inoculation, as he had already succeeded in doing in the case of anthrax. It seemed probable that this might be done, inasmuch as dogs which have been slightly bitten have recovered, and have afterwards been found to be proof against the disease. Numerous experiments showed that subcutaneous injection of the virus was not a perfectly certain method of inducing the disease, and as the symptoms pointed to an affection of the central nervous system, he determined to inoculate the virus by trephining and then injecting it under the dura mater. This method of inoculation he found produced the disease with almost invariable certainty. The incubation period which elapsed between the inoculation and the appearance of the symptoms he found to vary with the intensity of the virus. When the virus taken from a rabid dog in the streets was injected subdurally into a rabbit the injection was followed after fourteen to twenty-one days by the appearance of the first symptoms. When part of the nervous system of this rabbit, say part of the medulla oblongata, was inoculated into a second rabbit in a similar manner, the incubation period became shorter, and by a continuous series of inoculations the virus acquired a greater and greater intensity, so that the

incubation period became shorter and shorter until it reached seven days, at which it appeared to be constant. The virus is not contained only in the brain, medulla, and spinal cord, it is contained also in the peripheral nerves and in the saliva, but the spinal cord and medulla are the most convenient parts to use. Spinal cords of rabbits dying of rabies produced by a subdural injection of the virus, which is thus obtained at its highest intensity, are what M. Pasteur uses for his preventive inoculations. The first idea that occurs to one is, Why should M. Pasteur have thus completely changed his mode of inoculating and use an intensely virulent form of the virus instead of attenuating it by cultivation as he does in that of the anthrax? For in his method of protecting from anthrax M. Pasteur gradually weakens the virulence of the bacillus which causes the disease by successive cultivation at a high temperature, and Prof. Roy has done the same by transmitting the poison of anthrax through the prairie dog. When this weakened cultivation of anthrax is injected into the cow slight symptoms occur, which pass off. A stronger cultivation may then be injected; this will again produce some slight symptoms, and after these pass off the strongest possible virus, one that would have produced death with absolute certainty in an unprotected animal, may be injected without producing almost any result at all. But in the case of hydrophobia, M. Pasteur has not weakened the virus either by cultivating it or by passing it through an animal in which its deadly power is lessened. On the contrary, he has cultivated it through a series of rabbits until it seems to have attained its maximum power. The idea upon which M. Pasteur proceeds is that the organisms which cause disease in animal bodies produce during their growth certain chemical substances which are injurious to them, just as the yeast plant when grown in a solution of sugar produces alcohol, which by-and-by, when it becomes strong enough, will check the growth of the yeast plant itself. During its growth, then, in the organism the disease germ produces

its own antidote, and M. Pasteur thinks that probably it is by the production of some chemical substance that the immunity to subsequent attacks of the same disease is produced. By increasing the virulence of the virus he supposed that he had increased at the same time the amount of this antidotal substance, and that therefore the spinal cord or medulla of a rabbit poisoned by an intense form of rabies would contain more of the antidote than that of an animal dying of a slight form of rabies.

It is obvious that no good could be gained, but rather harm would be done by the injection of such a spinal cord unless the portions contained in it could be weakened while the antidote was left. M. Pasteur found that by drying the spinal cord in a glass vessel exposed to the air, the virus was much weakened, the weakening increasing with the length of time of the exposure, so that while a spinal cord exposed one day would certainly produce rabies when inoculated subdurally, one exposed for more than fifteen days would not do so. His idea is that by this process the power of the antidotal substance is weakened as well as that of the virus, but not to the same extent, so that although a fresh cord contains more of the antidotal substance than one fifteen days old, yet the proportion of the antidote to the poison is greater in one fifteen days old, so that it may be injected without the least danger, while a cord only one day old would produce the disease.

The crowd of people that I saw in the Rue d'Ulm had come from various parts of the world in order to have the inoculations performed which were likely to prevent the development of the symptoms of hydrophobia in them after they had been bitten by rabid animals. I have already described the method of inoculation, and the fact that local symptoms of inflammation very rarely, indeed almost never, followed the inoculations, shows that the antiseptic measure of dipping the point of the syringe in heated oil each time was an efficient precaution against sepsis. At the time of our visit the inocu-

lations employed by M. Pasteur extended over ten days, one injection being made every day. On the first day an extract from a cord dried 14 days was injected, on the second one dried 13 days, on the third 12 days, and so on to the tenth day, when an extract of a cord dried for 5 days was injected. At that time M. Pasteur was unwilling to inject extracts from cords which had been dried for fewer than five days lest he should actually induce the disease. The death of the Russian woman whose case I have described affected M. Pasteur very much, because that was the first case of death from the bite of a dog which had occurred after his treatment had been adopted; all the deaths previously had been due to bites from rabid wolves. Other deaths occurring afterwards, M. Pasteur adopted what is termed the intensive method, which he employed in cases of severe bites, or of persons bitten long before his treatment could be commenced. This intensive method consisted in using the injections for eleven days instead of ten, in repeating the injections three times a day on the first and second days; twice on the third, fourth, fifth, eighth, and ninth days; and in using at the last cords which had been dried only for one day. On the first day he used cords dried 14, 13, and 12 days, on the second 10 and 9; on the third 6 and 7; on the fourth 6 and 5, so that at the end of the fourth day by this method he had got to as powerful an injection as he had at the end of the whole treatment in the first plan; but under this treatment a case occurred, that of the assistant at the Brown Institute, in which it appeared quite possible that death was due rather to the treatment than to the original bite, although this could not be determined with certainty. The reasons for supposing that it was due to the treatment were that the man died with symptoms of paralysis proceeding from below upwards instead of the ordinary symptoms of hydrophobia, and that an extract from his spinal cord produced rabies when inoculated into a rabbit with a shorter incubation period than the usual one of rabid

dogs taken from the streets, although in certain cases of street rabies the incubation period was just as short, so that the question could not be settled quite definitely. M. Pasteur, however, being afraid of doing harm, changed his plan ; he now carries his treatment over fifteen days, getting by successive inoculations on the fifth day down to a cord which has been dried nine days, and then slowly down to one which has been dried five days.

It may be interesting to describe the way in which the material for injection is prepared. A rabbit is anæsthetised very quickly by means of chloroform, and anæsthetised in a somewhat peculiar way. A quantity of chloroform is poured upon a towel, and this is wrapped round the animal's nose ; it immediately ceases to breathe, and remains without breathing until you think the animal is dead. It then takes one or two deep inspirations, and is found to be completely anæsthetised. The head having been previously shaved the skull is removed with a small trephine and the virus injected. The wound is then dressed antiseptically, and the operation is conducted with strict antiseptic precautions. Two animals are inoculated at the same time in order to prevent any risk of one of them failing, and thus of losing the supply of virus. Just after death the cord is removed, and is then suspended by a thread in a large glass flask with an opening above and below, so that a current of air can pass through it, and is allowed to dry there for the proper number of days. It is then taken out, and broken up in a mortar with some sterilised veal bouillon and filtered. The veal broth is to show whether the cord is free from any ordinary septic germs, and contains only the virus of rabies. Should any other germs be present they cause the veal broth to become turbid, whereas it ought to remain bright and clear. It is this broth which is used as a material for inoculation.

We may now consider the success which has attended M. Pasteur's method of treatment. In estimating this there are certain difficulties, inasmuch as we have no perfectly definite standard of comparison to go upon in

comparing his results with those of patients who have not been treated at all, yet the statistics, both of patients who have never been subjected to treatment and of those who have been treated by M. Pasteur, give us such approximate results as will enable us to judge quite easily whether his treatment has been useful or not. In persons bitten by dogs alleged to be mad, there is first of all the difficulty of ascertaining whether the dog was mad or not; thus in the case that I saw at Leytonstone, a girl was bitten in the face by a dog which was rushing along the road, and no one knew whence it had come or whither it went. Its peculiar behaviour, and perhaps its appearance, were the only evidence of madness. The proof that it was mad was afforded by the poor patient dying of hydrophobia. The madness of this dog might quite reasonably have been denied until the proof was afforded by the symptoms breaking out in the person bitten. On the other hand, people are sometimes bitten and the dog is supposed to be mad when it is not really so. A second difficulty arises from the position of the bite and the amount of clothing. When people are bitten through thick clothes most of the virus is wiped off and little harm is done; a large proportion of the cases bitten in this way present no symptoms whatever, but when people are bitten in unprotected parts, and especially on the face, the mortality is very great, and as nearly as can be estimated amounts to 60 or 70 per cent. We may take as an average for all cases bitten on any part of the body by dogs alleged to be mad a mortality of 5 per cent., this figure being purposely fixed low. M. Pasteur, in admitting cases for inoculation, registers each of them and divides them into three classes.

Class A contains those persons who have been bitten by dogs proved to be rabid, either by rabies having been produced by inoculation from their spinal cords, or by animals bitten by them afterwards becoming rabid.

Class B contains dogs regarded as mad by competent veterinary surgeons, who have based their diagnosis on

the symptoms of the animal during life and from the post-mortem appearances.

Class C contains those persons who have been bitten by dogs where there was no distinctive trustworthy evidence of madness. The objection has been raised that a great number of the persons treated by M. Pasteur have been persons who have been bitten by dogs which were not rabid. It is quite possible that this is true, but M. Pasteur has not felt himself justified in refusing treatment, although there was no evidence of rabies; and the correctness of his conduct in this respect is shown by the case, which I have mentioned as occurring at Leytonstone, where the dog was rabid, and the patient died, although no evidence whatever could have been afforded of the dog's condition till the symptoms appeared in the patient, and when of course any treatment by inoculation would have been in vain.

But for the purpose of judging of M. Pasteur's results it is best to disregard this Class C, and to take the cases of persons bitten by dogs either proved conclusively to be rabid by the method of inoculation or by having produced rabies by biting, or else have been certified as rabid from their symptoms and post-mortem appearances. Up to October last year, these two classes included 1297 patients, and out of these only twenty-five deaths had occurred, a proportion of 1·6 per cent.; even of these twenty-five deaths, four might properly be excluded as the symptoms began during the treatment. This average is so much lower than any other of untreated patients that I think no unbiassed mind can refuse to believe that M. Pasteur's treatment has been of enormous benefit. The most conclusive experimental proof of the advantage of his treatment would be no doubt afforded by the inoculation of dogs subdurally by rabid virus, and then subjecting them to inoculations. This method has been tried by two men with very different results; the one man was Prof. Frisch, of Vienna, who obtained negative results, but this is attributed by Prof. Horsley to the fact that

Frisch had not sufficiently dried his cords at the requisite temperature. The other series of experiments were made by Dr. Bardoch, of Odessa, who inoculated dogs subdurally and then treated them by rapid inoculations from the spinal cord, inoculating every two hours for the first day, and four times a day afterwards. The result of this was that, while every animal inoculated subdurally and not treated died, 60 per cent. of those which were treated survived.

We now come to the last point which I can take up to-night, although the subject is a very extensive one and would admit of much fuller treatment if time permitted,—it is the theory upon which M. Pasteur has based his treatment. It is an interesting fact, which M. Pasteur himself told to my wife, that he does not himself know how he came to devise this plan; it simply occurred to him. It was no doubt the result of long-continued thought; but it struck him in its complete form all at once, just as the notion of universal gravitation struck Newton on seeing the fall of an apple. Various attempts have been made to produce protection against infective diseases by the injection of chemical substances. Some time ago Koch tried to render animals resistant to the virus of anthrax by injecting corrosive sublimate subcutaneously. He began the injections of sublimate after the inoculation and his experiments all failed; a similar series of experiments was undertaken by Dr. Cash, who commenced the administration of the sublimate before the inoculation of anthrax and he succeeded. A little while ago I saw at the Brown Institute one of the animals thus protected alive and well a year after the operation, although the unprotected animals all died. Since then some very interesting experiments indeed have been made by Dr. Wooldridge, which go far to support M. Pasteur's theory. Dr. Wooldridge cultivated the anthrax bacillus in an infusion of the thymus gland. In this infusion the bacillus grew rather sparingly; it was removed by filtration and the liquid injected into an animal; this animal, which

had thus received the products of the growth of the *Bacillus anthracis* in an albuminous fluid, was found to be protected from subsequent inoculation and remained alive just as it would have been if the anthrax bacillus had been weakened by cultivations and injected previously into its own body.

These experiments open up a new field of research, and we can hope that we shall by-and-by be able to protect against attacks of infective diseases by means of chemical substances much more thoroughly than we have yet been able to do, and that we shall be able to afford efficient help and save life in cases where at present we are obliged to stand by well-nigh helpless.

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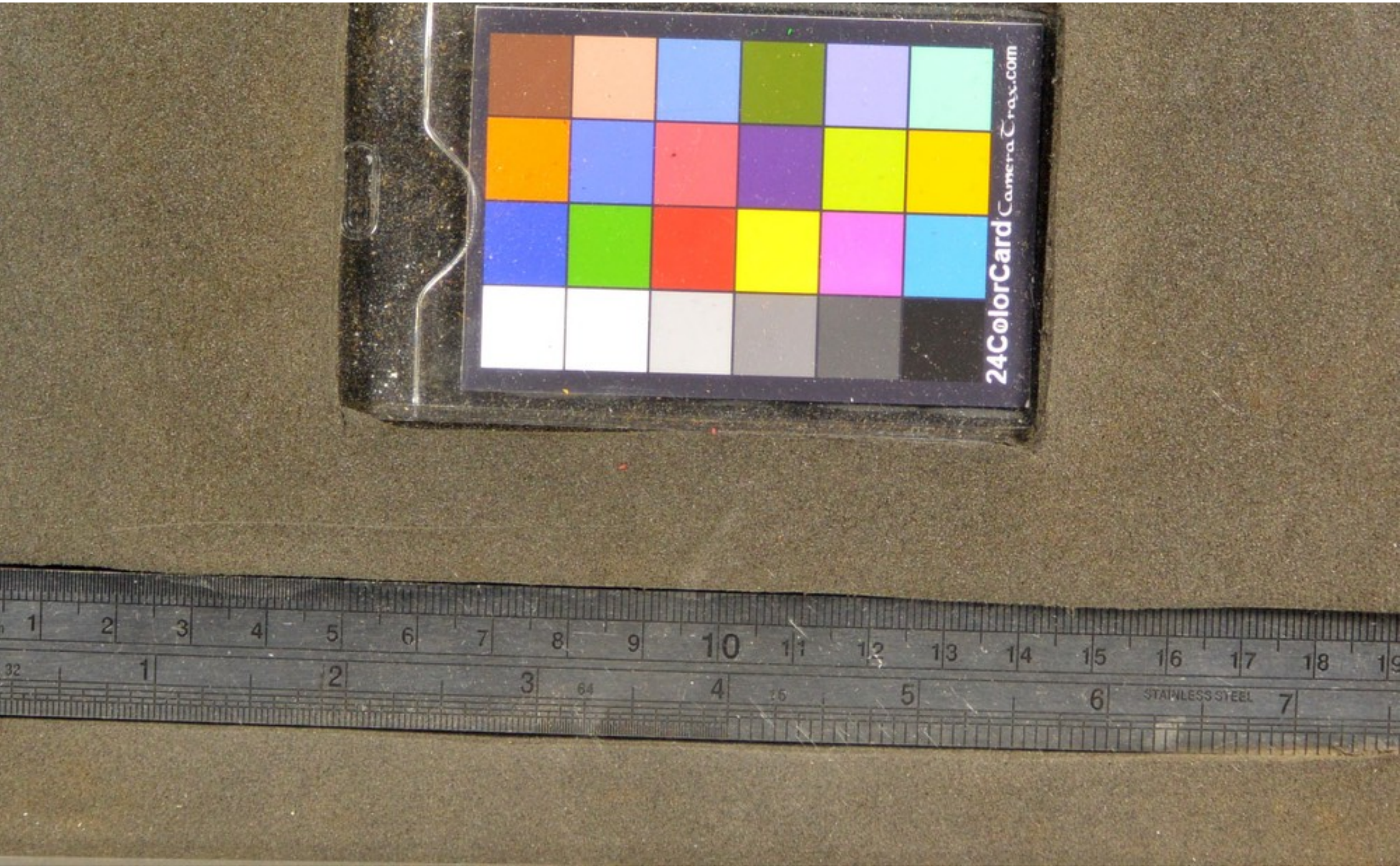
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