REPORT

ON

M. PASTEUR'S RESEARCHES ON RABIES
AND THE TREATMENT OF HYDRO-
PHOBIA BY PREVENTIVE
INOCULATION.

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PART III.

INOCULATION WITH ATTENUATED RABID VIRUS AS A PROPHYLACTIC TREATMENT FOR THE HUMAN RACE.—*Inoculation with Rabid Virus especially prepared as a Prophylactic Measure for the Human Race.*—*Incubation-Period shortened by Successive Inoculation in the same Species.*—*Experiments with the same Virus carried on during Three Years.*—*Method of attenuating the Virus in Dry Air.*—*How to soon render a Dog Refractory to Hydrophobia.*—*First Inoculation of a Human Subject for Hydrophobia.*—*Order of Inoculations.*—*Virus in Rabid Spinal Cords prepared in Dry Air.*—*Micro-Organisms Secrete a Substance Hostile to their Development.*—*Interpretation of Phenomena Observed.*—*Details concerning Inoculation.*

Inoculation with Rabid Virus specially prepared as a Prophylactic Measure for the Human Race.—M. Pasteur continued to carry on his researches, when, as he said in a subsequent note (October 26th, 1885 to the Academy of Sciences, there arrived a moment when he was almost forced to apply his method to the human subject (July 4th, 1885). Before taking this momentous step, he perfected the method he had experimentally demonstrated before the Hydrophobia Commission already mentioned. As he admits himself, his method was more scientific than practical. "Its application to twenty dogs might have resulted in only rendering fifteen or sixteen refractory to hydrophobia." It was also necessary to keep the dogs under observation during three months, in order to be perfectly certain of the success of the inoculation. As some time is required for this method of preparing rabid virus, it evidently could not always be in readiness for inoculating after a bite from a mad dog. M. Pasteur perfected his experiments to such an extent, that they resulted in furnishing a prophylactic for hydrophobia, both prompt and practical, applied to a considerable number of dogs. Its success was highly satisfactory. This method, which M. Pasteur therefore thought capable of being applied to human subjects, was based on the following facts.

Incubation-Period shortened by Successive Inoculation in the same Species.—If a rabbit be, after trephining, inoculated under the dura mater with a fragment of a rabid spinal cord removed from a mad dog, hydrophobia always appears, after an incubation-period which, on an average, covers fifteen days. If this virus, by the same method of inoculation, be passed on to a second rabbit, from a second to a third, and so on through a successive series, it is soon observed that the incubation-period manifests a tendency to become shorter in the rabbits inoculated in succession. After from twenty to twenty-five successive inoculations, from rabbit to rabbit, the incubation-period is limited to eight days, and remains at this through a further series of from twenty to twenty-five successive inoculations, when the incubation-period is limited to seven days, which remains invariable until a further successive series of inoculations, amounting to ninety, has been effected. M. Pasteur had arrived at the ninetieth rabbit of the last series inoculated, when he made the communication we are now quoting, in which he further stated that there was, perhaps, a scarcely perceptible indication of an incubation-period a little shorter than seven days.

Experiments with the same Virus carried on without Interruption during Three Years.—These experiments were begun in November, 1882. A period of three years had elapsed between that time and the moment this communication was made, without the slightest interruption in their course. No other virus had been used than that removed from rabbits dead from hydrophobia after successive inoculations; therefore M. Pasteur had always at his command perfectly pure virus, always, or very nearly, identical. This, M. Pasteur de-

scribes as the essential condition of his method. The cords of these rabbits are virulent throughout their entire length, and equally so.

Method of Attenuating the Virus in Dry Air.—If a few centimètres be removed from the spinal cords of rabid animals, every antiseptic precaution being observed, and if they be suspended in dry air, the virulence slowly disappears, and finally becomes extinct. The time necessary to effect a thorough disappearance of the virulence depends somewhat on the thickness of the pieces of cord, and especially on the surrounding atmosphere. The lower the temperature, the more lasting is the virulence. These facts constitute the scientific features of the method.

How to soon render a Dog Refractory to Hydrophobia.—These facts being established, M. Pasteur described in detail the method to be adopted, in order to render a dog refractory to hydrophobia, in a comparatively short time. In each a series of jars containing air dried by means of fragments of potash placed in them, a piece of fresh spinal cord, taken from a rabbit dead from hydrophobia after several days' incubation, is placed every day. Every day, a Pravaz's syringe full of sterilised broth, with which a fragment of one of these dried spinal cords has been mixed, is injected under the skin of a dog. The first injection is made with a fragment of cord prepared some days before, in order to be sure that it is not at all virulent. Previous experiments have demonstrated the degree of virulence of the cord. The following days portions of cord are used, which have been more recently prepared, and have remained two days less in the bottles. The last injection is made with virulent spinal cord, which has remained one or two days only in the bottles containing dry air. The dog thus treated is rendered refractory to hydrophobia. Virus may be inoculated under the skin, or on its cerebral surface after trephining; and rabies will not be contracted. By practising this method, M. Pasteur rendered fifty dogs, of all ages and races, refractory to hydrophobia, without one failure.

First Inoculation of a Human Subject for Hydrophobia.—M. Pasteur had so far succeeded in his experiments, when, on July 6th, 1885, Joseph Meister, sent by Dr. Weber, from Alsace, arrived at his laboratory in the Rue d'Ulm. This child had been bitten by a mad dog, in fourteen different places, on the hands, legs, and thighs. In the animal's stomach, straw, hay, and wood were found—the ordinary signs of canine madness. M. Pasteur consulted MM. Vulpian and Grancher. They considered Joseph Meister to be almost sure to die from hydrophobia. M. Pasteur, therefore, decided to apply to Meister the method of vaccination, which had often succeeded with dogs; but not without suffering acute anxiety. The fifty dogs rendered refractory to hydrophobia had not been, it is true, bitten by a mad dog before attaining that condition; but M. Pasteur knew, by previous experiments, that dogs previously bitten were easily made refractory to hydrophobia. The members of the Hydrophobia Commission had witnessed experiments demonstrating this.

On July 6th, 1885, M. Pasteur inoculated Joseph Meister, under the skin, with a Pravaz's syringe half full of sterilised broth, mixed with a fragment of rabid spinal cord, taken from a rabbit which had died on June 21st. The cord had, since that date, been kept in a jar containing dry air—that is, fifteen days. The subsequent days, Meister was inoculated according to the following table.

July 7 .. 9 A.M. ..	Marrow of 14 days	July 11 .. 11 A.M. ..	Marrow of 6 days
" 7 .. 6 P.M. ..	" 12 "	" 12 .. " ..	" 5 "
" 8 .. 9 A.M. ..	" 11 "	" 13 .. " ..	" 4 "
" 8 .. 6 P.M. ..	" 9 "	" 14 .. " ..	" 3 "
" 9 .. 11 A.M. ..	" 8 "	" 15 .. " ..	" 2 "
" 10 .. " ..	" 7 "	" 16 .. " ..	" 1 "

Thus Meister was inoculated thirteen times in ten days. At present, M. Pasteur only makes ten inoculations, one every day. He has suppressed the first three as useless; but it is easily conceived that, when treating Meister, he acted with excessive prudence. The fragments of cord used for the first inoculation were not virulent; this was ascertained by inoculating rabbits after trephining, with the same material as that used for the boy; all these animals escaped hydrophobia. The inoculation-fluid used on July 11th, 12th, 13th, 14th, 15th, and 16th, produced hydrophobia in rabbits. Each successive inoculation was made with a more virulent fluid than the preceding one. The last inoculations of Meister were made with a rabid virus taken from a mad dog, and rendered more virulent by being passed by inoculation from rabbit to rabbit. This virus produced hydrophobia in rabbits after seven days' incubation; and in a dog, not inoculated for hydrophobia, after an incubation-period of eight or ten days.

As Joseph Meister is in perfect health, and it is now more than nine months ago since he was bitten by a mad dog, and then inoculated by M. Pasteur, it may be concluded that he has escaped what appeared to be an imminent danger. The wounds were numerous

and serious; and the dog was proved to be mad. It is probable that the child would have died from hydrophobia forty to sixty days¹ after he was bitten. He has, therefore, been preserved from an almost certain death, and has, it may now be concluded, not suffered in any way from M. Pasteur's inoculations with rabid virus, as a preventive for hydrophobia. M. Pasteur admits that this method of inoculation as a preventive treatment for hydrophobia may be interpreted in many ways. At present, he abstains from formulating any interpretation of it. He only explains the aim of the experiments which he is carrying out, in order to arrive at a scientific explanation of certain phenomena.

Virus in Rabid Spinal Cords prepared in Dry Air.—M. Pasteur rejects the supposition that submitting the rabid spinal cords to the influence of dry air has the effect of gradually lessening their virulence, and finally entirely destroying it. He has ascertained certain facts which negative this belief, as he will later demonstrate. Experiments made on rabbits proved to M. Pasteur that the cords prepared in dry air were poorer in quantity of virus, but not in quality. Thence the following suggestion, contained in his communication: "Can it be admitted that inoculation with a virus of always the same degree of virulence probably produces a condition rendering the animal inoculated refractory to hydrophobia, if, at each daily inoculation, an increasing quantity of virus be used? This is an interpretation of the facts obtained by my experiments which I am now testing." (*Loc. cit.*, p. 711.)

Micro-organisms Secrete a Substance Hostile to their Development.—M. Pasteur appears more inclined to consider the bearing of the following facts. A great many microbes appear to produce certain substances which are hostile to their own development. In 1880, M. Pasteur had already indicated that the micro-organism of cholera in fowls secretes a poison dangerous to itself. The bacillus of measles in pigs presents the same phenomena. M. Reulin, in 1870, showed that the aspergillus niger secretes a substance which partially arrests its development, if its cultivation-fluid do not contain iron.

Interpretation of Phenomena Observed.—These phenomena led M. Pasteur to consider the probability of the constituent parts of rabid virus being composed of two distinct substances: one living, capable of developing in the nervous system; another, deprived of vitality, but, if present in a sufficiently large proportion, capable of arresting the development of the former.² Although a great deal has been written in the daily papers and elsewhere concerning the manner in which M. Pasteur inoculates for hydrophobia, we nevertheless believe that a clear and accurate account of these inoculations will not be misplaced here. A great many errors have slipped into the non-scientific descriptions.

When the patients arrive at the laboratory in the Rue d'Ulm, they are received either by M. Pasteur, or by one of his assistants; and their names and addresses are taken. A certificate from a veterinary surgeon or medical man is required, stating that the dog was mad. Their wounds are examined. If they have not been bitten on the face or hands, and their clothes be not lacerated by the animal's teeth, so that the virus has not passed into the wounds, they are sent back. Although M. Pasteur asks for a certificate, yet, when one is not forthcoming, and the dog has been lost sight of, and there is reason to believe that the dog is mad, he inoculates. For this, evidently, no voice can be lifted against him in blame: it is only humane to place these people beyond danger, especially as it is highly probable that the dog which inflicted the bite was mad.

The following incident is a proof that M. Pasteur acts wisely. A few days ago we were at his laboratory, when there arrived an elderly woman with a little boy. Both had been bitten, under the following circumstances. A collie dog, belonging to Colonel H., living forty miles from the village where the woman and the boy resided, rushed along the streets, in an excited condition, attacked the old lady, inflicting several deep wounds on her leg, then bit the boy, also badly. The animal was killed, after having also bitten a dog and a horse. The medical man who brought these patients to M. Pasteur, could not say whether the dog was mad or not; its dead body had been thrown he did not know where. He proposed writing to ask for more precise detail, directing that, if the animal's dead body could be found, a necropsy should be made. Had M. Pasteur refused to treat the woman and child, he would very probably have been blamed by the very same voices that now blame him for inoculating people, when he is not sure that they have been bitten by mad dogs. If a death occurred

among those who were bitten, and had not been able to produce a certificate, and therefore had not been inoculated, M. Pasteur would perhaps more bitterly reproach himself than could his present critics, who ask "if his patients are mad?" In order to have statistics absolutely accurate, a certain number of people would probably be doomed to a dreadful death, and certainly to undergo terrible anxiety. M. Pasteur humanely prevents this by inoculating, whenever it is probable but not certain that the dog is mad, and that the bite might therefore be dangerous.

Details concerning Inoculation.—The inoculations are made at 11 o'clock A.M., at M. Pasteur's laboratory in the Rue d'Ulm, by Dr. Grancher. M. Pasteur calls in the patients one after the other, and not haphazard, as has been asserted. When an entire series is assembled, Dr. Grancher makes the inoculations, one day in the right hypochondriac region, another in the left, and so on alternately. This precaution is observed to prevent irritation or inflammation consequent on the introduction of the virus. The last inoculations are sometimes followed by a slight cedematous redness; but a phlegmonous condition has never resulted, nor have abscesses ever appeared. The dose for adults is a Pravaz's syringe (about a cubic centimetre) of virulent mixture; for children, the syringe about half or three-quarters full, according to their age. In a room close to the one where M. Grancher inoculates, M. Terrillon dresses the wounds resulting from the bites. When the wounds are of so serious a nature that the sufferers are obliged to be treated at a hospital or in their own lodgings, M. Pasteur, or one of his assistants, goes to make the inoculations. The treatment covers a period of ten days. Every day, an injection is made with rabid spinal cord of increasing virulence. For the first injection, a spinal cord which has been preserved in dry air during ten days is used; for the second, one that has been so prepared during nine days; and so on until, for the last inoculation, one that has been so prepared during one day is used. In effecting the inoculations, everyone has his separate duty. An assistant, who prepares the inoculation-fluid, fills the syringes according to series, and gives them to Dr. Grancher. Thus his duties are limited to filling the syringes with fluid of the requisite virulence—a duty requiring his entire attention.

ERRATUM.—At page 673, column 1, lines 9 to 11, for "one cubic centimetre of rabid medulla was mixed with sterilised broth, and injected into the veins of a dog," read "a cubic centimetre of a mixture composed of sterilised broth and rabid medulla oblongata was injected into the veins of a dog."

LOST AND STARVING DOGS.—The number of dogs admitted to the Temporary Home for Lost and Starving Dogs, Battersea, during the past year, was 25,578, being an increase of 10,806 as compared with 1884. This increase, says the annual report of the institution, was due mainly to the police-order for the seizure of all dogs not under control. The lethal chamber had admirably fulfilled all the predictions made in its favour. The outbreak of rabies, which occurred during last year, extended to a degree never before reached in the experience at the Home. As large a number as sixty dogs, suffering from that terrible disease, were killed during 1885, which was just four times the number of cases discovered there in 1884. Of these, fifty-four were males, and six females. Upon the suggestion of the Queen, the committee had decided to keep the dogs brought to them for five days instead of three, as provided by the Act, which would bring up the average number kept from 500 to about 800. A resolution, moved by Professor Corfield, approving of the means of death afforded by the lethal chamber, was agreed to.

POLLUTION OF THE RIVER LEA.—Mr. Abel Smith, M.P., presided at the sitting of the Select Committee on April 10th. Mr. G. A. Eachus, engineer to the Edmonton Local Board of Health, gave evidence. He had noticed an increased pollution of the river during the past few years. He did not recommend the use of filter presses, as suggested by the Metropolitan Board, because they were expensive, and the sludge left a deposit behind it, which was almost certain to find its way into the filters, notwithstanding all care. The main want of the entire district was, in his view, an improvement of the subsoil drainage, and the widening and deepening of the New Cut. As an immediate and temporary remedy for the existing pollution of the Lea, witness would suggest a thorough flushing of the river. The pollution of the river increased from and after 1867, when the water companies began to draw larger supplies of water; and he believed the pollution was consequent upon this action of the companies. The right thing to be done was, that the water companies should largely increase their reservoir storage capacity. Mr. William Croft, surveyor to the Tottenham Board of Health, gave evidence, and the Committee adjourned to May 14th.

¹ According to statistics, forty to sixty days is the length of the incubation-period in hydrophobia. A longer period is excessively rare.

² Il se pourrait que ce qui constitue le virus rabique soit formé de deux substances distinctes, et qu'à côté de celle qui est vivante capable de pulluler dans le système nerveux, il y en ait une autre non vivante, ayant la faculté, quand elle est en proportion convenable d'animer, le développement de la première." (*Loc. cit.*, p. 771.)