[Front page]
Nineteenth Century
Pasteur – Article by **[Mrs P. Driesley]**
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Pasteur,

Although Pasteur's work has long been known and appreciated by the world of science, his name, on this side of the Channel, is mainly associated with the treatment of rabies, and he is considered to be unsuccessful.

Since the death of the regretted Lord Doneraile**,** who was misunderstood, it was thought that inoculations had been abandoned. However, according to certain people, Pasteur must have taken advantage; this scoundrel must have gotten rich with his dirty inoculations. Others think he is a charlatan, a fraud who keeps his secrets to himself; others still take him for a coldblooded murderer.

If Pasteur had wanted to keep his secrets and sold his scientific discoveries, he would today be one of the richest men in the world; but, after a long career, he is quite simply what he was at the beginning: a chemistry professor earning a professor's salary. He does not receive anything for the inoculations, and when we send our countryside postmen, our town sergeants to undertake his treatment, we ask the French government to grant us a favour that they refuse.

Pasteur himself rarely attends the inoculations; not being a doctor of medicine, he does not have the right to practice it nor to receive payment. Pasteur is quite simply a chemical scholar carrying out his microbiological research and living in the apartment which has been assigned to him at the Ecole Normale. "I could not work for money," he would say one day, "but I will work all my life for the love of Science."

When he was called to an unimportant position in this great school thirty years ago, he did not have his own laboratory. His enthusiasm was such that he had one installed at his own expense in the attic, and, although it was limited, this enabled him to complete some of the important research with which he had been preoccupied. He is currently the Head of the most comprehensive laboratory in the world and he will shortly become the Head of an even more extensive laboratory, which is being built thanks to a public subscription in recognition for the services he has given to Science and the entire human race. Luckily for the great Master and for Science, the State has been very generous to assist his work. The money, land and buildings have been put at his disposal for free, and his laboratory has tributaries in all the boards in Paris and elsewhere. Branches have grown from the tree, and have grown roots in Russia, in Austria, in Italy, in Spain, and in Rio de Janeiro, for the treatment of rabies.

One could not visit the laboratory on the Rue d'Ulm without being deeply impressed by the nature and the greatness of the work that is being carried out,

as all sorts of diseases are literally taken into one's hands, and every one is studied in each of its phases. We are so absorbed by the great and small issues of everyday life that we do not even think of the true cause of diseases; we do not consider what others do for us when we fall victim to something terrible, which could often be avoided and which we do not understand. We have been taught to consider diseases as the common lot, death as a mystery that must be accepted humbly and without any questions. However, in this laboratory at the Ecole Normale, death, or the poisons that live in tangible form and which produce death, are studied under the Master's direction, who controls everything and who has the power to open or close at will the door to the grave. He searched the invisible world for the secret to contagious diseases, which had for so long been hidden, and he made it appear in a visible form. Taking in his own hand the deathly microbe, he can make it live or die; he can force it to destroy life or to protect it against death. He weakens its terrible power, even destroys it; or, having weakened it to the point of annihilation, he can give it back all its virulence. He commands the awesome forces of the invisible world to obey his will.

Since Louis Pasteur founded this school by annihilating the theory of spontaneous generation, and by establishing the vitality of the ferments through observation, everything that was obscure has become clear; order has come out of the chaos. Such an interesting subject, so full of benefits for humankind, has attracted into the field of research physiologists, biologists and many more workers, who served to verify, to control and to confirm the discoveries of one and the other, by bringing together a concentration of the minds on these matters.

Visiting this disease factory, little can be seen on the surface. Here, in the Rue d'Ulm, professors, students, scholars from every country study in silence the living world of these microbes with powerful microscopes and a complicated biological method. Some are busy with dissections; others transplant the germs of the disease from the dead animal's body into the stocks in which they must live. Along the corridors, mysterious dark, heated cupboards can be seen, in which a hen's tuberculosis germs and many other diseases that can affect humans and animals are harvested and incubated at the temperature best suited to their existence. There are no mix-ups with diseases; each is maintained within its limits, imprisoned in glass tubes under a square cotton lid through which the air can penetrate without allowing the microbe to escape.

In this strange/curious collection, one can take a vase whose content is protected with cotton; it is dated and labelled "hen cholera." One can only see a slightly cloudy liquid; it looks like nothing, and yet it is full of life and the story of life. Only a few hours ago, the vase contained a clear and transparent chicken broth. It has been inoculated, as though injected, with the blood of a rabbit which had just succumbed to the disease, and you can see it: the microbe is alive; it prospers; it multiplies in the breeding stock until it fills it with its presence. It will only live there until it has exhausted the particular element upon which it feeds, and then, it shall die and sink to the bottom of the vase. In the rabbit's blood, the microbe can exist for years without losing its virulence, if one takes

care to enclose it into a glass tube sealed at both ends with a flame. Nearby, two preparatory assistants are studying the blood of a rabbit, which died of hen cholera, with a microscope. Between the blood cells, they can see very small bodies similar to dots, slightly squeezed in the middle; these are the subjects of their research, the microbes of hen cholera.

Until Pasteur discovered an artificial breeding ground that was suited to this microbe, it was impossible to study its habits. Having found out that it was able to live and prosper in chicken or rabbit stock, he is able to cultivate it through successive collections by transporting a small amount from stock to stock without having to use the animal's blood to obtain the living organism. During the course of his experiments, he finds that the microbe weakens when it is exposed to air and that it cannot withstand temperatures over 51 degrees Centigrade, even in an airtight tube. All these small facts were of great importance, as they inspired the hope – which has since come true – of providing a vaccine. To maintain all the virus's power, there should be no more than twenty-four hours between each culture. However, it can be passed on indefinitely from stock to stock without losing any of its virulence. To weaken it, it merely has to be left exposed to the air between cultures.

This discovery, this possession of the miracle, had as a consequence that a weakened infusion was sent to each infected barnyard in France, where it put an end to the epidemic by subjecting the surviving hens to a benign form of the disease. Although this disease is particular to poultry, it was accidentally discovered to also affect rabbits that had been placed in a cage in which hens had died from the disease. It even appeared that the rabbits were significantly more susceptible to contracting this illness than the hens, in that they showed signs of contagion after just one contaminated meal and died within twenty-four hours, whereas the hens usually succumbed only after several poisoned meals. This is, of course, a disease of the digestive system and despite its virulence and the rapidity of its course, it is devoid of pain, the intense torpor appearing very quickly and persisting until death. This is the disease with which we propose to exterminate the rabbits of Australia; it affects no other domestic animal, and – as we have seen – poultry can be protected from it. Horses, dogs, sheep and humans are all resistant. Only rabbits and hens, or the stock made from their flesh, can satisfy this microbe's appetite.

Passing, at a distance, the Asian cholera, and many other diseases, we stop by the anthrax bacillus. It is the specific fever of cattle, of wool sorters, the malign pustule of humans, a truly dreadful scourge. An innocent-looking jelly, about two inches thick, lies at the bottom of a glass tube and contains in its centre a singular vegetation spreading over its surface. It is the artificial culture of these deadly microbes. Upon inspecting blood from an animal that had died after having been inoculated with this culture, what we observe under the microscope is radically different from the little dots of the hen cholera. Here, we can see much larger bacillus; in some circumstances, they contain brilliant oval dots or spores, which look like peas in their pods. These spores are endowed with extraordinary vitality and intense virulence. They defy destruction methods through heat; however, Professor Tyndal found the means to kill them with intermittent

heating. During the heating intervals, the spores turn into bacteria that die during the first stock, not having had the time to make more spores. After three or four stocks, all vitality has been destroyed. The spores have such a tenacious vitality that they still exist in the air, multiply on any object upon which they land, and eternally maintain their virulence. Buried deep in a dead animal's body, worms bring them back to the surface, where they start their work of destruction all over again, impregnating the grass the cattle will eat, have to eat. This terrible organism resisted for a very long time all attempted effort at mastering it.

Finally, Pasteur, overcoming all the difficulties, made it repent for its crimes by becoming a prophylactic means of saving lives. Taking the bacteria, he maintained them at a temperature that was able to facilitate their life and even their multiplication through division, but not sufficient for the production and development of spores. At 42 or 43 degrees Celsius, the microbe does not produce spores. In contact with clean air, Pasteur maintained cultures devoid of spores. Within a few weeks, the culture dies, as it is deprived of spores with this method of forced development, and it is easily destroyed; but, before its extinction, all its virulence can be returned by putting it back in the appropriate conditions. Despite the very different characteristics of the hen cholera and anthrax, Pasteur managed to make a vaccine for each of them, by studying their capacities; he subjected them to his will. But, before bringing the anthrax bacillus to live and multiply without producing spores, he could be seen deeply absorbed and bearing on his face the expression of a great discovery. As soon as this great discovery was known, Pasteur was inundated with requests for vaccines; before the end of the year, 33,550 animals had been vaccinated. The following year, there were 399,102 and the following year (1883), 500,000 animals: sheep, cattle and horses.

During the course of this research on anthrax, he observed that poultry was resistant to it. When inoculated with the most virulent poison, they would remain unscathed. He wanted to penetrate this mystery and found that the temperature of the hens is too high for the microbe to live. He lowered this temperature by placing the hen's feet in a basin of cold water and made it ready to contract the disease. The hen suffered and died as the bacillus lived and prospered. Reversing the conditions, he warmed the hen in blankets; it healed and the microbe died. He was, therefore, able to make one or the other live or die at will.

In order to artificially cultivate the various microbes of the diseases, it is essential to isolate them completely and to protect them from the vibrio of putrefaction that fills the air. All the instruments must be sterilised with a flame, the students must blow the glass tubes themselves when they need them, and the air must be sterilised; all of this is carried out in an ordinary atmosphere. Losing sight even for one instant of the necessity of these precautions can make the experiment fail, compromise its success. One understands the difficulty of the operations when one thinks of the number and the diversity of the pathogenic and non-pathogenic microorganisms. We are dealing with the true and the false, and whilst some look similar, others are essentially different; they have features

that are as distinct, as characteristic as those of plants or trees in the superior vegetal realm. Pasteur has divided them into two main categories: the aerobic and the anaerobic, those that cannot live without oxygen and those that do not need oxygen or that oxygen could even kill. Each has its mission to fulfil, always working independently and yet in unison.

When the pathogenic parasite has massacred its victim, the vibrio of putrefaction begins its deed. In its role of sweeper of nature, it makes the dead disappear, or rather transforms it into other elements that are necessary to life.

Without stepping too far into the technique of ferments, we must go back to the beginning of microbiological research to understand the link connecting the yeasts of everyday life to the ferments of human disease. Yeast and ferment mean the same thing, and as zyme also signifies ferment, the name zymotic was given to certain types of diseases.

It was during the time of the first experiments in the attic, when the laboratories did not have the importance they have today, that the battle of the ferments was taking place in the brewer's vats. The chemical modifications of the wort under the ferments' action were known by those involved. It was obvious that carbonic acid was produced, that in the process of disappearing, sugar would leave its place to alcohol. Cagniard de La Tour was the first to explain that this alteration was due to the living vegetation of the yeasts. Liebig contradicted this explanation, but Pasteur appeared, and, knocking down Liebig's theory, he enforced La Tour's system with his experimental authority and opened the way to the future. Although, questions were asked, and it was Pasteur's remit to prove that ferments could be produced one over the other, that there was not just one ferment, but many ferments, some of which are invisible and fill the dust in the air.

Why does beer get corrupted? This was a great issue that Pasteur solved. He made the brewers understand that by observing their yeast with a microscope, they would find not only the necessary conditions for life, but also a variety of microorganisms, which are the beer's enemies.

By studying the wort cooled for some time under a microscope, it is found to be filled with an infinitude of mould, which would prevent the yeast from working. Moreover, even after the fermentation and the transformation of the wort into beer, it can still be corrupted, become cloudy and take on a bad smell. It was there again a disease, or putrefaction, caused by the bacterium spread around in the air and on the brewery's walls.

Having observed these facts, these mysteries having been penetrated, an intelligent brewer from Copenhagen understood that his brewery was nothing but a disease factory. He took it down and rebuilt it according to Pasteur's system. Beside his model brewery, he built a large laboratory, decorated with a bust of Pasteur, and he hired the services of an eminent chemist who was ready to defend the fortress, armed with an entire war arsenal.

The pure air that is crucial everywhere, was maintained at a temperature low enough so that no microbe was able to live amongst the blocks of ice spread everywhere. The wort could only be in contact with air that had been sterilised through heated pipes, and then cooled down over the ice. This machine to oxygenate the wort was established by Mr Vellen from Marseilles, another brewer who studied with Pasteur. With the old method, one would check the temperature of the wort by plunging a hand inside it. This custom was abolished, as it helped spread unhealthy germs. Everywhere people started using thermometers designed in such a way that the chemist in his office is able to record the temperature of the ovens and control it at any time.

Above each vat, there were meters recording the progress of the yeasts.
A room dedicated to physiological research, under the direction of a distinguished physiologist, was added to the chemistry laboratory. The physiologist was in charge of studying beer diseases. Thus, with a model brewery and an experimental brewery, Mr Jacobsen was able to take advantage of the enlightenment of science and to observe the mistakes of the past. His large laboratory soon became a centre for the scientific study of ferments. In the experimental brewery, the physiologist was able to artificially cultivate all the known diseases and make the worst beer in the world.

By adjusting the heat, he grew mycoderma and cryptogams, which he would study with his microscope, and the effects of which he was able to identify. Sometimes three different enemies would be at war, the strongest surviving after having annihilated the weakest.

This method of isolating, of classifying the saccharomyces cerevisiae, is due to the naturalist Dr Hansen, a dedicated worker at the laboratory. He discovered several varieties of yeasts and managed to cultivate a pure and healthy one, which would quickly multiply in the wort and which has supplanted in the whole of Europe the old impure yeast, which had been inherited from the Egyptians. Thus, the small experimental brewery of Pasteur's laboratory in his youth is the origin of the perfect brewery raised under the enlightened direction of Herr Jacobsen. Pasteur's objective was not only the production of a healthy beer, but the diffusion of scientific discoveries people had little time for in those days.

Around the time when Jacobsen was reforming the beer-making processes according to Pasteur's system, another man, in another country, deeply impressed by the studies on beer, was trying to adapt his system to surgery. Sir Joseph Lister of Edinburgh was investigating the reasons why his patients were becoming prey to the septic bacteria in the air. An intact skin and a robust health are surely the best conditions for escaping disease, but after a surgical operation, the blood and the tissues are exposed to the air, and if this air is full of germs from diseases, which was unavoidable in the hospitals of the past, the breach had assured effects.

In the same way as the scientific brewer, he took no rest until he found a way of destroying the invisible enemy, and through the discovery of antiseptics, suited to local applications, he brought into the whole practice of medicine and surgery

an entire reform. His patients no longer succumbed to sepsis, nor to other subtle blood poisoning that all surgeons feared. Until then, he had ignored the cause of the disease. After even the most insignificant operation, the fever would come and all his efforts were in vain; the active, powerful ferment which would feed on blood cells would undermine the strength and bring on death. He understood that his hands, his instruments, even the air, were vehicles for the disease. The consequence of this discovery was a complete reform in the hospital, as well as in the brewery.

The air is no longer enclosed and fetid; it is pure and clean. All the instruments are sterilised, as well as the surgeon's hands, before the operation. All the items used for the dressings are also sterilised with antiseptics. In this manner, patients are Listerised according to the terms of the hospital, just like the beer and the wine are Pasteurised, which means that they are protected from the germs of the disease.

The doctor benefited from Pasteur's teachings, as well as the surgeon, and nowhere has the application of his method had better results than in maternity clinics, where the mortality rate was frightening. In Denmark, all the midwives are subjected to state control. They are obliged, on the most severe pains, to report all the cases of puerperal fever, and are suspended if they neglect taking the ordered necessary antiseptic precautions. The hospital founded and maintained by Catherine the Great in Saint Petersburg is perhaps one of the most remarkable. It is one of the best ordered; it is the worthy equivalent of the Copenhagen brewery.

The old buildings have been transformed and reorganized according to scientific progress, and since 1878 it has been considerably expanded. There is only one patient per room, and the sections have been separated and isolated so that no germ may be brought from one to the other. The communication keys do not come out of the Heads of Department's hands, and the domestic offices are also locked.

Heating and ventilation are operated with pipes. The greatest cleanliness reigns in the whole house. As soon as a room is vacated, the furniture is removed, and it is washed from top to bottom with hoses which are adapted to water columns found everywhere and which would be used in case of a fire. The rooms are covered, and paved with concrete with a slight slope, allowing the water to be rapidly evacuated.

The inspectors, the obstetricians, and the nurses are all wrapped in a stainless white apron. The doctors are also dressed in white jackets during their visits. The antiseptic system is applied in the smallest details so that no microbe can enter.

The employees' latrines are located in the garden, as well as the laundry rooms. All the dirty linen is firstly dipped into a disinfectant solution, and then washed, dried and folded in other rooms. Each washerwoman has her own duties and they are housed beside the laundry room. The result is most satisfying; I have

learnt that during the past three years, there has been only one death: that of a woman brought to the hospital having been already ill and who died there three days after the birth.

If there are few free hospitals that have reached this sanitary perfection, it can nonetheless be said that all the hospitals have taken advantage of the almost universal adoption of antiseptics. Death by pyohenin is hardly known, even in the busiest military hospitals in times of war. And the average number of deaths by puerperal fever and other blood poisonings has very significantly decreased.

Hydrophobia – Rabies

We have seen how Pasteur and his contemporaries have managed to isolate and cultivate the microbe of hen cholera, the bacillus of anthrax and the germs of many other diseases, in artificial food sources. We are going to see what he does with a disease in which he cannot find a specific microbe, and that is consequently impossible to cultivate in the same way as the others. Although the microbe of rabies has not been discovered, it is very probable that it exists. The presumption of its existence forms the basis of the entire method; indeed, according to Pasteur, it is such that we can say that the microbe of rabies exists as surely as the myriads of stars in the sky, which no-one has ever seen. Pasteur distinguishes easily with a microscope the brain of an animal that died of rabies from that of a healthy one. Both present an infinite number of molecular granulation, that of the rabid marrow being finer and more numerous, giving the idea of a microorganism of extreme tenacity, having the form neither of a bacillus nor of a diplodocus; these are just dots. To this day, they have defied all the efforts made to cultivate them outside of the living body; this is the fact that has made the study of rabies so terrible, so full of personal danger.

For a long time, Pasteur and his devoted colleagues, Chamberlain, Roux, and others, continued their research under the inflamed eye, the dry bark and the fury of the rabid animal. They became encouraged when they thought they were approaching their goal, discouraged when it was escaping them. It was only after years of hard work, long sleepless nights, that the battle was finally won, that Pasteur obtained this happy result of saving animals as well as humans from the most frightful death.

At the beginning of his research, Pasteur conducted his experiments to protect dogs through the inoculation, and in this manner, indirectly save humans. Since then, the method used for dogs has also been applied to humans, and it will continue to save lives until the day when the ideal plan of destruction of the disease through prevention will have been accomplished.

In the course of his research, Pasteur discovered that the rabid animal's saliva does not necessarily give (communicate) rabies and that the most virulent matter resides in the bone marrow. Furious rabies, as well as dumb rabies, are both caused by the same virus; it is experimentally possible to produce furious rabies with dumb rabies and vice versa.

In the rabid animal's saliva, the virus is associated with various microorganisms; the inoculation of this saliva can bring death in three ways.
Firstly: through a new microbe described as the microbe of saliva.
Secondly: through an excessive production of pus.
Thirdly: through rabies.

The elongated marrow of humans, similar to that of animals, ensures that the rabies is always virulent.

Rabies communicated via a subcutaneous injection or virus presents very distinctive characteristics from those of furious rabies occurring after a bite or after a trepanation, and it is probable that many cases of dumb rabies have gone unnoticed.

In these cases of rabies that could be called spinal rage, paralysis is one of the first symptoms, whereas the fury and the rabid barks are rare or inexistent, but a singular phenomenon is sometimes observed: an intense itching of the skin. (Pasteur's communications)

After inoculation, the bone marrow is the first affected area. The virus settles there and multiplies before spreading elsewhere. On the 19th May 1884, Pasteur made the following announcement at the Académie des Sciences:

> The rabies virus transported from the dog to the monkey, then from the monkey to another monkey, weakens at each passage. After having diminished its virulence through several passages in monkeys, if the virus is brought back to the dog, the rabbit or the guinea pig, it remains attenuated. In other words, the virulence does not return at once to the degree it had in the ordinary street dog affected with rabies. On the other hand, successive passages from rabbit or guinea pig to guinea pig increase the virulence of the rabies virus. This virulence reaches its maximum in rabbits. Transported from the rabbit into the dog, the virus remains very violent and proves to be more virulent than that of street rabies. This acquired virulence is so intense that, if inoculated into a dog, the latter unfailingly dies. A logical application of the results we have indicated gives us the means to make dogs resistant to rabies, as we are currently able to prepare and keep at our disposal, a series of attenuated viruses of various strengths, some of them unable to cause death, preserving the animal economy from the effects of more active viruses and those from the effect of deadly viruses.

Pasteur was trying to determine the incubation period, which, in ordinary conditions, for the dog as for humans, is very uncertain. The world is full of traditions claiming that the illness has manifested itself months or even years after the bite. He soon ensured that there was no regular period of incubation when the rabid animal's saliva has penetrated the blood circulation through ordinary means. The incubation period is short when a strong dose of poison has penetrated; if there is a small quantity, it can be localised to the area of inoculation and be annihilated; or, if the ground is more favourable, it can do its

deed slowly but surely and rabies may incur after several months. It was, therefore, necessary to find the means of drawing an artificial certitude from the natural incertitude, and Pasteur achieved it. By inoculating the rabbit into the brain with the marrow of a rabid dog, the disease would usually bring on death on the fifteenth day. But, if another rabbit was inoculated with the marrow of the first rabbit, then a third with the marrow of the second, and so on, the incubation period would be greatly reduced as the poison would become more violent.

When the virus had gone through 25 rabbits, the incubation period would be reduced to eight days and remained the same for the next 25 rabbits, after which it became seven days. At the 90th passage, the maximum virulence was reached with a seven-day incubation period, with absolute certainty, using perfectly healthy rabbits aged six months.

The question being thus elucidated, in June 1884, Mr Fallières, Minister of Public Instruction, called for a commission in charge of making a report on the rabies research. This report was most satisfying. It observed that out of 23 vaccinated dogs having been bitten by rabid dogs, none of them had developed rabies, whereas within the space of two months, 66% of non-vaccinated dogs bitten in the same manner had become rabid.

At the beginning, in June 1885, Pasteur was finally due to test his treatment on a human being for the first time. Three Alsatians came to him from their remote countryside. Théodore Vone had had his arm bitten by his dog that was rabid. Joseph Meister, a child of nine, had received fourteen bites from the same dog on his hands, his legs, and his thighs. His mother, who was with him, had not been bitten. They had faith, a perfect faith, simple and reasonable. Pasteur could cure dogs; why couldn't he also cure humans? Science did not know of any reason why the method could not be applied to humans. Doctors were called to deliberate over the case. They all decided that the man was not in any danger, as his injuries were only contusions, and the skin had not been broken. He was sent home, reassured. However, the child was certainly condemned to die of rabies. The mother begged, and the doctors carried out the operation under Pasteur's direction. On the 6th July at 8 o'clock in the evening, the child was inoculated for the first time into the right hypochondrium with a liquid containing the marrow of a rabbit that had died of rabies a fortnight before. The virus of this marrow had weakened by drying out in the air's oxygen for a fortnight. It never remains exposed to the open air, in which it would decay, but it is suspended in a vase sealed with cotton at both ends, which allows the air to penetrate, pure and filtered. In order for this air to always remain dry, caustic potassium is placed at the bottom of the vase.

The following chart enables us to follow the progress of the virus from the weakest to the most violent, each inoculation getting closer to that of the rabid dog, and overtaking it to reach the most intense virulence of the rabid rabbit.
Joseph Meister was inoculated on

July 6th	at 8am	with a marrow dated	June 24th	15 days
July 7th	at 9am		June 23rd	14 days
July 7th	at 6pm		June 25th	12 days

July 8th	at 9am	June 27th	11 days
July 8th	at 6pm	June 29th	9 days
July 9th	at 11am	July 1st	8 days
July 10th	at 11 am	July 3rd	7 days
July 11th	at 11am	July 5th	6 days
July 12th	at 11am	July 7th	5 days
July 13th	at 11am	July 9th	4 days
July 14th	at 11am	July 11th	3 days
July 15th	at 11am	July 13th	2 days
July 16th	at 11am	July 15th	1 day

In order to control the degree of virulence of each of these operations, two rabbits were inoculated at the same time as the child. The marrows that were used for the inoculations of the 6th, 7th, 8th, 9th and 10th were not very virulent; the rabbits did not become rabid. The marrows which were used on the 11th, 12th, 14th, 15th and 16th of July were more and more virulent. The rabbits that were inoculated on July 15th and 16th contracted rabies after a seven-day incubation; those inoculated with the marrow on the 12th and 14th, after eight days, and those of the 11th, after 15 days.

Joseph Meister had thus received the most violent rabies virus, that of the dog, after several passages through rabbits, a virus determining rabies in the rabbit after seven days and in the dog after eight to ten days.

Pasteur considers that when the level of immunity is reached, there is no danger in inoculating whatever quantity of the most powerful virus. The only consequence is to consolidate the resistant status. The little Meister boy underwent this treatment three years ago and he is in perfectly good health. After this first experiment, people came in numbers from across the world to get treatment. The aisles were full of picturesque groups, people looking solemn, worried, happy, reassured would wait their turn. In the month of April that year, Pasteur had seen 688 people who had been bitten by dogs, and another 38 by rabid wolves, being inoculated. All of the former were preserved, except for little Louise Pelletier, aged ten. She had been horribly bitten, torn to the head, and she came too late, 37 days after the accident. Her wounds were purulent and there was never any hope of saving her. Out of the 38 Russians who had been bitten by wolves, only three succumbed. The inoculation is not as prolonged after a wolf bite as after a dog bite, and the average rate of deaths is higher. When, after the death of one of the Russians, Pasteur was able to research the virulence of his brains, he found it to be the same as that of the dog, the only difference being in the nature of the bites. According to the Police authorities' statistics, the ratio of deaths caused by rabies in the Seine Department was one in six. At the end of October 1886, 2,490 people had been treated in Rue D'Ulm – 1,726 French people, among whom there had been ten deaths, which means one death for every 170 people bitten. When the Russian died during the treatment, followed by a further two, Pasteur and Dr Graucher feared they would see all 16 succumb. They decided to repeat the treatment, and even make them undergo the treatment three times, ever increasing the violence of the virus. This has since been called intensive treatment, and it worked perfectly for the 16 Russians.

Since then, the scene of the operations has been transported to Rue Vauquelin**,** where buildings have, for the time being, been put at Mr Pasteur's disposal. Instead of the small personal laboratory of the Rue d'Ulm, a series of rooms is dedicated to the use of men, women, children who would come each day from 10 to 1 o'clock to be inoculated. Here, nothing is asked, everything is given, and with the most affectionate care and attention. In summer, a basket of cherries is always at the disposal of children, who are terrified and crying. In winter, they are given sweets. The wounds are dressed by skilful men. It is very interesting to follow all these operations; everything is done with mathematical precision. Patients are required to bring in a doctor's or veterinarian's letter ascertaining that the dog by which they were bitten was rabid. The wounds are examined, and if they are mere contusions, if the skin has not been broken, they are sent home.

The name of the dead is inscribed in a register with a list of all the particulars/details of their cases. The newcomers are introduced by the assistant, who has to sort them. He keeps a list of their names and calls them in turn. The doctor in charge of inoculations is seated behind a screen in a spacious room; beside him is an assistant standing in front of a high table on which a series of glasses containing a greyish liquid, which is to be used for the inoculations. The glasses are covered with filter paper, in order to protect the liquid from the bacteria suspended in the air, each bearing on a label the date of the marrow. This assistant has himself a list of the names, which serves as control.

When everything has been prepared, the patients are called in and they come to the operator baring the area of skin which is to receive the injection. Having rubbed the skin with a disinfectant, the doctor presses it between his fingers and introduces the needle of the Pravaz syringe handed by the assistant. Two syringes are enough, except in exceptional cases. The needle is sterilised after each operation, by being passed through the flame of a wine spirit lamp, and dipped into the liquid through the filter paper and finally, into boiling oil. We necessarily begin with the weakest viruses to arrive successively to the most violent, so that no one receives even one fraction of virus that is stronger than required. The individuals whose conditions require the intensive treatment come back in the afternoon. Since this doubly intensive treatment has been applied to the Russians bitten by wolves, Pasteur has made it quicker still for extreme cases, with constant success.

As soon as the patients have gone, the scene changes. The assistants all carry out the preparations required for the following day's operations. A man takes apart the syringes, brings the pistons and the other parts to boiling point, disinfects the metal and sends them to the instrument manufacturer to rebuild them. All the bandages, all the linen that has been used, are dipped into an antiseptic solution; the instruments are cleaned, disinfected and sterilised. Meanwhile, the assistants prepare the rabbits for future requirements. Each day, two rabbits are anesthetised with chloroform and inoculated under the skull with the marrow of a rabbit that died the same day. On the seventh day, these rabbits will have all the signs of the disease and they will die paralysed on the tenth day. One rabbit would suffice to the needs, but two have to be sacrificed, in case one would die of

another illness. This is why two rabbits die each day, while two others are inoculated.

As soon as they are inoculated, the rest of the marrow is cut into three pieces and suspended into three vases, dated and labelled. Then, they are placed into a certain laboratory, in which an even temperature is maintained day and night with a heater. Beside this chamber of viruses is another room, the entry to which is forbidden to all but the preparation assistants who mix the marrow to the sterilised stocks each day. It is so important to let no dust into this room that the door is opened just enough to let the preparation assistant slip inside. He takes the stock out of the pipette tube (a vase sealed against the bacteria in the air) and the marrow out of the tube in which it has dried out; he crushes them together and passes from time to time his glass pestle, sterilising everything he uses. The glasses in which all the various liquids are placed are all marked and arranged in the desired order at the very moment when all the patients are already assembled.

Since the first human inoculation, carried out with such complete success on Joseph Meister, several rabies treatment stations have been established; the statistics of all these establishments provide the following results up to 28th February 1887.

	Cities	Number of inoculated	Dead	Per cent
Mr Pasteur	Paris	3,020	34	1.15
Dr Budjivid	Warsaw	84	-	-
Prince d'Oldenbourg	St Petersburg	140	3	2.14
Dr Petermann	Moscow	112	4	3.57
Dr Gamaléia Dr Burdach	Odessa	325	12	3.69
Dr Catani Dr Vestea	Naples	28	-	-
Dr Ullmann	Vienna	96	-	-
Dr Parschensky	Samara	47	1	2.14

Therefore, by gathering all the cases, even those of bites received from wolves and the deaths of patients who have died during treatment, we find 1.40% of deaths.

On the Chief of Police's order, a report is made each year to the hygiene council of the Seine Department on all the cases of rabies that have occurred during the year. We read in Dr Dujardin Beaunet's report, who is in charge of it, the following facts:

In 1887, 306 people were bitten by dogs identified as rabid and have undergone Mr Pasteur's treatment. Another 44 bitten individuals refused to be treated. On the first 306, there were only two deaths, whereas on the 44 others, seven died

of rabies; the proportion is, therefore, thirty times greater. Dr Dujardin adds that the two deaths which have occurred amongst the 306 inoculated people are due to the fact that they had not regularly followed the treatment, one because she was constantly drunk, the other because she could not leave her children.

The facts appeared so remarkable to the hygiene council that it communicated the report to all the newspapers, in order to encourage people who got bitten to get treated at Pasteur's laboratory. The question being asked is this one. What happens when the virus is introduced into the body? The answer is still only based on a hypothesis. It is not that our knowledge is too limited, but the research has expanded in several directions, and the explanation can be given to us by the physiologists, the biologists, the naturalists. As far as the vegetal yeast is concerned, we know that it feeds on the sugar contained in the barley, that the absorption of this sugar produces a chemical operation favourable to beer, but contrary to the life of the organism that dies, not only because it no longer finds any sugar, but because there is alcohol. By feeding on the sugar, it produces the alcohol that kills it. Adding new yeast after the fermentation would be absolutely useless; there is nothing left to feed the organism with, which, consequently, can no longer develop. When a man is vaccinated with smallpox, one supposes that the living organism will find in the blood some elements that can facilitate the stronger smallpox microbe and it will exhaust them. Consequently, if it does not find its food, it dies. Beside this explanation, there is also this one: the blood cells are given the strength to resist against the invasions of microbes by getting them used to its presence.

De Quincey slowly managed to withstand 8,000 drops of laudanum a day, and, after having used it moderately for 17 years and having abused it for eight years, he once again got used to making do with 12 drops, not without having suffered a lot from this privation. He would complain of being agitated, writhing, having convulsive sobs and remaining very upset. One day he offered a wandering Malaysian a dose of opium, which was enough to kill three dragons and their horses. To his great surprise, the Malaysian swallowed it in one gulp, and as no Malaysian was found dead in the vicinity, he concluded that this man was used to opium. Dr Dallinger progressively brought some microorganisms, the saprophytes, to tolerate a temperature which would be fatal to them if they were subjected to it at once. From their natural temperature of 60 degree Fahrenheit, he made them withstand 158 degrees Fahrenheit by gradually increasing the heat, decreasing it slightly if they were about to die, only to raise it again later; he made them live in very different conditions. Within several months, they become larger, were covered in pustules, or looked like pustules, and their shape was altered, but they were resistant. In the same way, sea jellyfish can be made to tolerate fresh water, which would kill them if they were suddenly placed in it. These interesting facts help shed light when we are trying to elucidate the mysteries of Pasteur's method of gradually introducing more violent viruses into veins.

A few years ago, when Mr Dumas of the Académie des Sciences was responsible for bestowing the medal of honour to Pasteur, his former student, he was able to tell him in a flattering speech:

In the infinitely small universe of life, you discovered a third realm, that to which these beings belong, which with all the prerogatives of animal life, do not need air to live and find the heat they need in the chemical decay they provoke around them. The in-depth study of the ferments gave you the comprehensive explanation for the alterations that organic substances undergo: wine, beer, fruit, animal matter of all kinds; you explained the preservative role of heat applied to their conservation and you learnt to control its effects according to the necessary temperature to determine the death of the ferments… Applying this thought to the alterations – so often deadly – that wounds and injuries undergo when the patients live in contaminated places, you learnt how to protect them from this danger by the simple application of filtered air, and your precepts, adopted by surgical practice, assure each day the success it ignored and give its operations a success our predecessors did not have**.**

The vaccine was a beneficial practice. You have discovered the theory behind it and clarified its applications. You learnt how to make a vaccine out of a virus, how a mortal poison becomes an innocent preservative…

Your life has only known success. The scientific method you make such assured use of owes you its best triumphs. The Ecole Normale is proud to have you amongst its pupils; the Académie des Sciences prides itself on your work; France sees you as one of its glories…

List of the honours conferred to the one to whom humankind owes so many benefits, and who is still so unknown on our island.

1. Grand Cross of the Légion d'honneur
2. Grand Cross of Saint Anna of Russia. Cross and diamond insignia
3. Grand Cross of Saints Maurice and Lazarus – Italy
4. Grand Cross of Isabella the Catholic – Spain
5. Grand Cross of the Rose of Brazil with necklace
6. Grand Cross of the Medjidie of Turkey
7. Grand Cross of Saint John of Portugal
8. Grand Cross of the Polar Star of Sweden
9. Grand Cross of St Sana – Serbia
10. Grand Cross of the Iron Crown – Austria Hungary
11. Grand Cross of Romania
12. Grand Cross of Tunis
13. Officer of the order of agricultural merit – France
14. Commander of the Crown of Italy

In the same display, another 16 gold medals can be seen, including the Copley medal of the Royal Society of England and the Albert medal.
Three golden anchors, a gold laurel crown from the city of Clichy.
A charming group of gem and gold fruit from the Emperor of Russia.
A coffer of Byzantine enamels from the Duke of Oldenbourg.
Several silver medal from Barcelona representing a dog in the typical attitude of rabies, torn clothes under its feet, in front of it, a naked child, smiling, without

fear, holding a branch of laurel. This is as interesting to Pasteur as the Emperor of Russia's diamonds and all the Grand Crosses.

One would need more pages to list all the honours, all the works of art which have been given to the scholar by the whole world. But, in the midst all of this, this honorary doctor of all the great universities in Europe, the member of 83 societies of scholars, lives in the noise amongst his own. He is too simple to be spoilt.

Elyra Priestley