THE MEDICAL WORK OF PASTEUR

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(Translated from the French by Erwin F. Smith, U. S. Department of Agriculture, Washington, D. C.)

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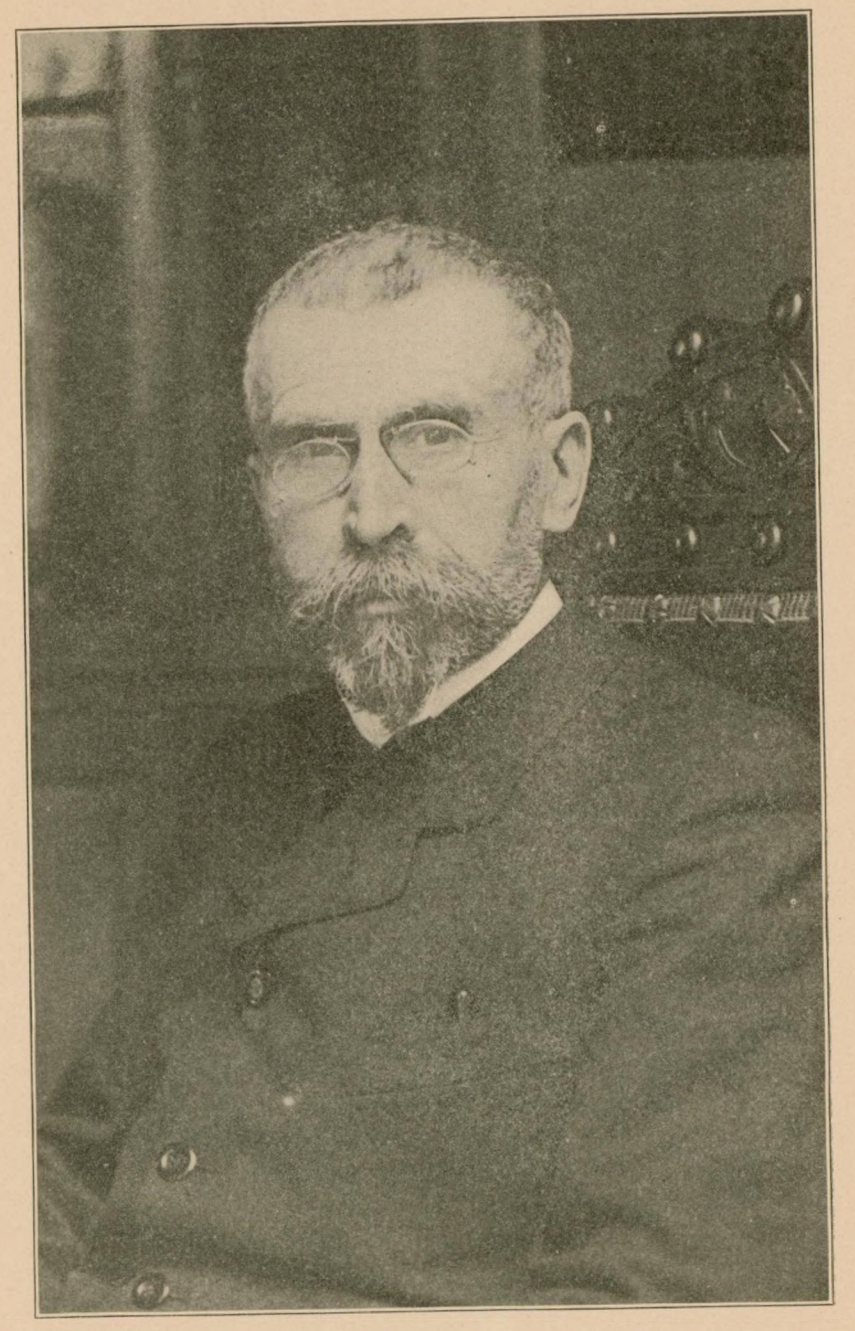

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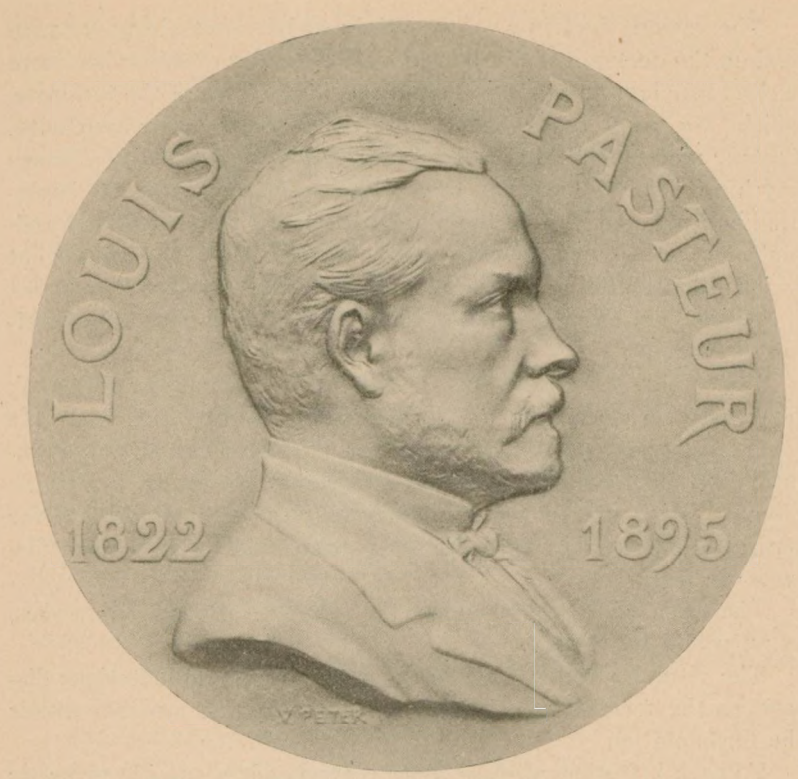

THE MEDICAL WORK OF PASTEUR[1]

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THE medical work of Pasteur begins with the study of fermentations. From the beginning men have associated fermentations with infectious diseases and regarded viruses and ferments as of the same nature. But between fermentation and disease there is this difference, that the fermentable medium is inert, that we can compound it as we please with definitely weighed-out materials while the body of the infected animal is living and of a complexity hitherto impossible to penetrate. Consequently, the study of fermentation is easier than that of infectious disease and naturally precedes it.

[1] A generation has passed since this paper was written (1896) but it is still as interesting as ever. It is, in fact, the best brief paper we have on the work of Pasteur and the writer of this note believes many will like to have it in an English dress.—E. F. S.

The various doctrines on the origin of life have always run up against the doctrine of fermentations. No other question has more excited religious and philosophic passions than that of the ferments, which, we must acknowledge, do not diminish their obscurity. Pasteur understood that on such a subject he ought not to advance anything which did not rest upon clear proofs and from the beginning he restricted himself to a scientific method which resolved each difficulty by an experiment, simple to interpret, an experiment which charmed the mind and at the same time was so decisive that it satisfied him like a geometric demonstration and gave him a feeling of security.

It was, therefore, from 1857 to 1865 that the great struggles took place over fermentations for the principles out of which has come forth triumphant the doctrine of germs. Pasteur had already revolutionized medicine before having undertaken the study of a single disease. Each one of the fundamental principles established for fermentations applies with the same exactitude to infectious diseases; in fact:

The virus is a living being like the ferment. Both are microbes, as we would say to-day.

The virus by multiplying in the body causes the infectious disease, as the ferment multiplying in a fermentable medium causes the fermentation.

To each infectious disease there corresponds a specific virus, as to each fermentation a special ferment.

The virulent disease is not spontaneous, any more than the fermentation. The virus comes from outside, and consequently contagion can be avoided.

The extension to diseases of notions acquired in the study of fermentations brought about unheard-of progress. Surgery, whose interventions so often provoked redoubtable infections, became henceforth beneficent. Enlightened by the experiments of Pasteur, Lister comprehends that the complications of wounds are due to microbial germs coming from outside and he invents antiseptic dressings. With antisepsis begins the new time in surgery. Thanks to an experiment on fermentations, well done, Pasteur, who had never touched a scalpel in his life, nor made a surgical dressing, has saved more wounded than all the masters of surgery.

These labors of Pasteur upon the fermentations have given to medicine not only a doctrine, but also a method of research and a technique of marvelous power.

In order to study fermentation, Pasteur prepared first of all a *pure* fermentable substance, that is to say, one which did not contain any living thing. He obtained it in these conditions by sterilizing it with heat. Thus heated, this nutrient medium preserves itself unchanged, indefinitely. Pasteur then sowed it with a trace of the ferment *in a state of purity,* that is to say, containing no other microscopic organism, which, developing along with it, might falsify the result of the experiment. This necessity for *pure cultures* imposed itself on Pasteur from the beginning of his experiments and led to the most ingenious inventions. To succeed in obtaining a pure culture how many difficulties had to be overcome! How could any one prepare sterile organic infusions if he did not know why they ended by changing under ordinary conditions? It is in the celebrated memoirs on organized corpuscles in the atmosphere and upon spontaneous generations that Pasteur has unraveled the causes of the alteration in organic infusions and laid the foundations of the fertile method of bacterial cultures.

We preserve piously in the Pasteur Institute some flasks containing fermentable liquids prepared by Pasteur himself in 1860 for the Commission of the Academy of Sciences before whom he had called his opponents. We may read still upon their yellowed labels the signature of the illustrious chemist Balard, reporter for the commission. After thirty-five years, these liquids are clear as on the first day and are witness of the certainty of the methods of Pasteur.

The culture of microbe-ferments led to the culture of microbe-viruses. The latter, it was thought, were formed only in living matter, proceeding from it by way of a chemical change. The new doctrine, on the contrary, regarded the viruses as parasites, developing in the body of the diseased animals, and capable without doubt of an independent life. The procedures which had succeeded with the ferments permitted also the culture of the viruses outside of the organism, in artificial media, where they multiply or swarm in successive generations, without ceasing to be deadly for man and animals. The culture of viruses in glass tubes, in a definite nutrient substratum, at the will of the experimenter, who becomes, so to speak, a gardener of microscopic pathogenic plants, constitutes the wonderful means of investigation which is to renew everything.

Thus prepared by the study of ferments, armed with a technique of incomparable surety, it would seem that Pasteur had only to attack contagious diseases. His thoughts, as a matter of fact, return without ceasing to this subject; but he was not a physician and he dared not advance upon a territory reserved to pathology. It was in spite of himself that he entered it in 1865. It required all the influence that Dumas had over him to decide him to do it; after much resistance, Pasteur, who had never dissected an invertebrate, never even touched a silkworm, set out accompanied by his faithful

assistants of the Normal School, Duclaux, Gernez, Raulin and Maillot, to study the disease which was destroying the silkworm industry of southern France and which extended into all the silk-growing countries. His hesitations once overcome, Pasteur set about the work with an ardor which finally ended in compromising his health.

Cornalia and other scientific men after him had found, long before, in diseased worms little oval corpuscles visible under the microscope. But from this observation nobody had drawn any conclusions by way of avoiding the disease or of curing it. Pasteur devotes himself to these corpuscles: they are for him the parasite, cause of the disease. He sees them in the diseased worm, follows them into the chrysalis, and into the winged insect and also into the eggs laid by the latter. It is therefore the direct transmission of the corpuscles from the perfect form of the insect to the egg which renders the disease hereditary. To obtain healthy eggs it sufficed to separate the layings of each female and to preserve only the eggs from the perfect insect exempt from corpuscles. The exact observation of the facts led necessarily to procedures which saved the industry of silk-growing.

But those worms hatched from healthy eggs may become diseased if they are raised in infected localities, for the disease is contagious. It is contagious because the corpuscles pass into the excretions of the sick worms and penetrate with the foods into the digestive tubes of the healthy worms or are introduced into their bodies by scratches on the skin. Pasteur, in many experiments, obtained the contagion by means of food artificially contaminated.

How many teachings there are for human medicine in this study on the disease of the silkworm! This disease was no less mysterious in its cause and in its extension than the infectious diseases of man; like several of the latter it is hereditary and to explain it observers had not failed to invoke the epidemic genius, idiosyncrasies of the subject, etc. Without knowing anything of all these doctrines, a chemist, who knows how to look through a microscope and make experiments, shows that all this is reduced to a parasite transmitted by the diseased to healthy subjects and by parents to their descendants. The mystery of the contagion and of the heredity is thus explained.

The disease of *pébrine* is not the only one which ravages silkworms: it is often confounded with another disease, *flacherie*. Pasteur discovers that this latter is due to fermentation of the leaves of the mulberry in the digestive tube of the worm. The agents of this fermentation are microbes, a vibrio and an organism of a rounded form united into chains. The excretions of the diseased worms transmit the malady, which has the greatest analogy with

certain contagious diseases of man that also have their seat in the intestine. This disease is not hereditary, but it persists in the silkworm nurseries from year to year, although the eggs from which the worms are hatched may be exempt from the germ of the disease. This means that the vibrios of flacherie remain alive in the dry dust. These vibrios produce in their interior shining corpuscles like those already seen by Pasteur, in 1860, in the butyric vibrio. These corpuscles are the eggs of the vibrio; of an incredible resistance to heat and drouth, they perpetuate the species; to-day we call them *spores*. It is the first example of a spore in a pathogenic microbe and the rôle of this very resistant production in the transmission of diseases that appear only after a long time has not escaped Pasteur.

The book on the diseases of silkworms is a veritable guide to whoever would study contagious diseases. Nevertheless how few physicians had read it in 1876! Pasteur did not fail to say to those who entered his laboratory and whom he took for collaborators: "Read the Studies on the silkworm; it will be, I believe, a good preparation for the labors you are to undertake."

The disasters of the war of 1870 were very grievous to Pasteur and it was with a patriotic thought that he busied himself with the beer industry, in which heretofore Germans had been without a rival. His "Studies upon Beer" made of brewing a scientific industry; but their reach exceeds by far what the title would lead one to suppose. The chapters on the origin of ferments, on life without air and fermentation, the diseases of beer, are filled with new general ideas, as suggestive for the biologist and the physician as they are useful to the brewer.[2] Nevertheless the doctrine of Pasteur penetrated little by little into medicine; the success of Lister and of his pupils carried conviction and, more and more, audacious persons described microbes in infectious diseases.

With what attention Pasteur followed these first labors! They rejoiced him and they vexed him at the same time: These experiments of physicians appeared to him often defective, the methods seemed to him insufficient and the proofs not rigorous, suitable rather to compromise the good cause than to serve it. Soon he could not endure it and resolutely he set himself also to the study of anthrax.

Rayer and Davaine had described in 1850 in the blood of sheep which died of anthrax little transparent motionless rods. After reading the memoir of Pasteur on butyric fermentation Davaine, in 1863, recognized that these little rods are parasitic microbes which constitute the inoculable virus of the disease; he gave to them

[2] Pasteur was aided in his studies on beer by Gayon, Grenet and Calmette.

the name of *bactéridie charbonneuse*. Then Dr. Koch (since become so celebrated) saw the bactéridie multiplying outside of the organism in drops of the aqueous humor obtained from the eyes of rabbits; he succeeded in obtaining as many as eight successive cultures. The bactéridie of this eighth generation, inoculated into animals, gave them fatal anthrax.

We do not very well understand to-day how after these experiments one could deny that the bactéridie were the cause of anthrax. But in 1876 the minds of men were not prepared for the idea that the viruses are parasitic microbes. For the greater number of medical men the bactéridie were only an accessory of the disease. "But in the blood of animals attacked by anthrax," they said, "the rods of Davaine do not exist alone; by the side of them there are globules and the blood plasma which contains the true amorphous virus; the cultures of Dr. Koch do not suffice any more to convince us. In the drop of aqueous humor which he sows with the blood from the animal, diseased by anthrax, M. Koch brings at the same time as the bactéridie the virus contained in the plasma; and the successive sowings which he makes in drops of the liquid simply lead to a dilution of this virus. Now do we not know that it is the property of viruses to act in infinitely small doses and that they may be diluted prodigiously without extinction of their activity?" At the time when they were made these objections appeared full of force.

Such was the state of the question at the time Pasteur attacked the problem. He also made cultures of the bactéridie; but instead of sowing the anthrax blood in a drop of nutrient media he introduced it into a flask which contained hundreds of cubic centimeters of an organic infusion where the bactéridie multiplied in some hours. With a trace of this first culture he sowed a second culture and in like manner up to the twentieth and even to the hundredth generation. A little drop of this hundredth culture gives anthrax as certainly as does the blood of an anthrax diseased sheep. Here one may not invoke dilution of the virus; the primitive droplet has been drowned in oceans; what does there remain of it in this hundredth culture, mortal, nevertheless, in the most minute doses? The virus, therefore, reproduces itself. It is, therefore, a living being; it can be only this bactéridium which exists alone in the culture flasks. It is indeed that which kills and not chemical substances which accompany it. Let us place, in fact, one of these flasks which contain it in a place at a rather low and constant temperature, in the cellars of the observatory as Pasteur has done; all the bacteria in suspension soon fall to the bottom of the flask. The clear supernatant liquid, injected into animals, even in large quantities does not make them sick, while a little of the bacterial deposit introduced into

their bodies destroys them with anthrax. These simple demonstrations were possible only on account of a perfect technique. Pasteur and his collaborator Joubert made use of that which had so well succeeded in the fermentations. It was no more difficult for them to prepare a hectoliter of sterile nutrient media than to obtain some cubic centimeters. Their procedures are so sure that in a long series of cultures the bactéridie remain pure without any error being able to cause the result to be suspicious.

If the bactéridium is the cause of anthrax, its properties should enable us to understand the etiology of the disease. Davaine had very well understood that the new notions would not be definitely victorious unless they explained how the animals took the anthrax in the fields, how they there came across the bactéridium, how it later penetrated into them and finally why certain fields were ravaged, while others, quite near, were spared by the disease. The preponderant rôle that Davaine attributed in the propagation of the disease to flies, which settle on the bodies of the dead animals, left without explanation the most characteristic circumstances of the epidemics. His adversaries very soon caused him to see clearly that: "this theory does not explain all, therefore it does not explain anything." Davaine did not have a certain bit of knowledge without which the etiology of anthrax remains incomprehensible; that of the anthrax spore. The spore of anthrax was discovered by Koch, who saw it form in the bacterial filaments cultivated in contact with the air. This spore resists drying and heat, and the greater number of agents which destroy the bactéridie when in the form of rods. It is the resistant form of the microbe and it perpetuates the species.

For Pasteur, it perpetuates also the disease in the anthrax country. Had he not already seen germ-corpuscles of the vibrio of flacherie preserve themselves in the dust of silkworm nurseries and carry over the disease from one year to another? First of all, by experiments in the laboratory he showed that sheep which ate the spores along with their food contracted anthrax and showed the symptoms and lesions of the natural disease.

This anthrax spore should exist in the anthrax territories, it must be discovered there. It was not an easy enterprise, that of isolating some spores of anthrax from among the millions of microbes contained in each parcel of cultivated earth; it was successful, however, by putting to use the properties which the anthrax spores possess of enduring a temperature of 80° to 90°, which temperature kills the greater part of the microbes of the soil. Some of the soil of Beauce, classic land of anthrax, is put into suspension in water; the finest particles are gathered, heated to 80° and inocu-

lated into guinea pigs: some of which die of anthrax. It is, therefore, certain that the sheep in Beauce find the germs of anthrax in the pasture fields. But where do these germs come from? They come from the dead bodies of animals that the shepherds, following custom, bury in the open field where the beast has fallen dead. The filamentous bactéridie, innumerable in the blood, are carried with it into the aerated earth of the graves and thanks to the summer heat there rapidly form their spores.

From all these facts there results a very simple prophylaxis for anthrax. Do not bury the dead bodies of anthrax animals in the fields, but destroy them or bury them in restricted places. The soil of the pasture being no more provided with spores will cease to be dangerous.

This is what Pasteur never ceased to say to the farmers of Beauce, with whom he went to observe and to make experiments, for this etiology of anthrax has been established in the heart of the anthrax territory in the midst of shepherds and flocks. All this did not prevent contradictors from accusing Pasteur of being only a laboratory man, of seeing things over his retorts and his bouillons and not as they are in nature and in practice.

During several successive years, at the end of July, the laboratory of Ulm Street was abandoned for Chartres. Chamberland and I went there to live in company with a young veterinarian, Vinsot. We found there as guide M. Boutet, who knew his anthrax country better than anybody else, and we met there sometimes M. Toussaint, who studied the same subject we did. Every week Pasteur came to give directions and to follow the work. What pleasant remembrances these campaigns against anthrax in the land of Chartrain have left us! Beginning in the early morning, visits to the sheep pastures scattered over this vast plain of Beauce resplendent in the sun of August, autopsies performed in the knacker's yard in Sours, at M. Rabourdin's place or in the courtyard of the farms; after noon, drawing up of the experimental notes, letters to Pasteur, then the commencement of new experiments. The day was well filled and how interesting and salutary was this bacteriology in the open air!

The breakfast at the Hotel de France did not last very long the days when Pasteur came to Chartres; we were soon in the coach going to M. Maunoury's in Saint Germain, who had courteously put his farm and his flock at our disposal. During the journey we spoke of the experiments of the week and of those to be undertaken. Pasteur, as soon as he had set foot on the ground, full of haste, went to the sheepfolds; standing motionless close to the enclosures he gazed at the experimental groups with that sustained attention

which nothing escaped; for hours he followed with his eyes the sheep he thought diseased; we had to remind him of the hour and to show him that the spires of the cathedral of Chartres began to disappear in the night before he was willing to go. He questioned the farmer and the laboring men and always took into account the opinion of the shepherds who, on account of their solitary life, gave all their attention to their flock and often became very sagacious observers.

No fact appeared insignificant to Pasteur; from things slightest in appearance he knew how to draw unexpected indications. In course of a walk in a field on the farm at St. Germain was thus born the original idea of the rôle of the earthworms in the propagation of anthrax. The harvest was over, there remained only the stubble. The attention of Pasteur was drawn to a portion of a field on account of the different color of the earth; M. Maunoury explained that the preceding year they had buried in that place some sheep dead of anthrax. Pasteur, who always examined things very closely, noticed on the surface of the soil a multitude of little mounds of earth cast up by earthworms. The idea then occurred to him that in their continual journeys from the depths to the surface the worms would bring to the surface earth rich in humus which surrounds the dead body and with it the anthrax spores that it contains. This explains why the germs of the disease persist such a long time in the fields, although so many causes tend to make them disappear: they are brought to the surface of the graves by the incessant bringing up of deep earth. Pasteur never stopped with conceptions; he passed immediately to experiments. The latter justified his previsions. I remember, among others, demonstrations made before Villemin, Davaine and Bouley. The latter had brought worms that had fed on the earth of a grave where the bodies of animals dead of anthrax were buried several years before. The earth taken from the intestine of one of the worms when inoculated into guinea pigs gave them anthrax.

These researches on the etiology of anthrax will remain a model. Never hitherto had medicine known a like perfection in the experiments, a like rigor in the deductions and such a certainty in the applications. Pasteur knew very well that the decisive battle was on and he neglected nothing to make the victory certain. Not content with supporting all that he advanced with irresistible proofs, he desired to leave nothing obscure in the labors of others; he takes one by one the facts which seemed opposed to his doctrine and shows, sanely interpreted, that they confirm it and this work of control gives him the occasion for new discoveries.

It is thus that he goes over the experiments by which MM. Jaillard and Leplat had for a moment menaced the conclusions of

Davaine. Anxious to study anthrax, these experimenters had requested virus from Chartres. Blood of a cow diseased by anthrax was sent to them; they inoculated it into rabbits who died without showing bactéridie in the blood, and nevertheless this blood inoculated into other rabbits destroyed them. They conclude that the bactéridium is not the true virus of anthrax, since the disease may exist without it. Davaine examined these facts, recognized that the animals of Jaillard and Leplat had not succumbed to anthrax but to another disease. The conclusion of Davaine is perfectly correct; it does not dissipate all the obscurities, for it does not explain how anthrax blood inoculated has been able to cause a disease which is not anthrax. Pasteur, aided by MM. Joubert and Chamberland, is going to show us what takes place in the experiments of Jaillard and Leplat and at the same time disclose to us unexpected facts of the highest importance. When an animal, sheep or cow, is attacked by anthrax, its blood collected at the moment of death swarms with the bactéridie and gives with certainty anthrax to the animals into which it is inoculated. But already after some hours, especially in the heat of summer, putrefaction takes place, the microbes of the intestine invade the deep veins and then the other vessels. At this moment, the blood contains the bactéridie of anthrax no longer in a state of purity; with them is associated another microbe, a motile vibrio, which is always the first to pass from the intestine into the vessels. This vibrio is very deadly to rabbits; it kills them more quickly than the bactéridie. If, therefore, we inoculate a rabbit with blood taken from an anthrax cadaver some hours after death, the rabbit receives at the same time bactéridie and vibrios. It dies either of a mixed disease caused by the simultaneous development of the two microbes, or, more often, of a pure septicemia because the vibrio, multiplying more quickly than the bactéridium, eliminates it by a living competition. The septic vibrio swarms especially in the peritoneum and rarely invades the circulation until after death. These peculiarities explain to us how Jaillard and Leplat, having asked for anthrax blood from Chartres, have received septic blood and why in the blood of their animals they have not seen under the microscope the rods of Davaine any more than the septic vibrio which is found there only in small numbers.

This septic vibrio is an anaerobic organism like the butyric vibrio studied by Pasteur in 1861. It is killed by oxygen when it is in a filamentous state, but it produces spores which resist the air. It constitutes the first example of an anaerobic pathogenic microbe, and the procedures which have served for its cultivation will be later put to use in the study of other microbes living without air, such as those of tetanus and symptomatic anthrax.

This justly celebrated note by Pasteur, Joubert and Chamberland on septicemia and anthrax introduced into science the notion, since become very important, of microbial associations and also the idea of bacteriotherapy. We read in it, in effect, that when the anthrax bactéridie are inoculated along with certain other bacteria into animals, the latter may not take anthrax and that this observation will be perhaps the point of departure for therapeutic applications.

The experiments of Pasteur establish not only facts, they suggest especially ideas. Witness those of the chicken attacked by anthrax which caused such a great quarrel with M. Collin. Fowls are absolutely refractory to anthrax. Nevertheless, Pasteur, Joubert and Chamberland rendered them susceptible by lowering their temperature, which is 42° C., to 38° C. by immersion in water. It is the condition necessary and sufficient to enable the inoculated bactéridie to multiply in the body of the fowl. On the contrary, the fowl, chilled and inoculated, returns to health if it is again warmed. Is not this new receptivity, created by a simple chilling, an interesting fact? Does it not give the explanation of the rôle of circumstances, to all appearances harmless, in the appearance of a disease?

In spite of all these labors followed in the laboratory, Pasteur still finds time to go to the hospital to collect material for new researches. Chamberland and I assisted him in these studies. It was to the Hospital Cochin or to the Maternity that we went most often, transporting into the corridors or into the amphitheater our culture tubes and our sterilized pipettes. One can hardly imagine the repugnance Pasteur had to overcome in order to visit the sick and assist in autopsies. His sensibility was extreme and he suffered morally and physically the pains of others; the stroke of a bistory which opened an abscess made him tremble as if he had received it. The sight of dead bodies, the sad need of autopsies, caused in him a veritable disgust. How many times we have seen him come out of these hospital amphitheaters sick! But his love of science, his curiosity for the truth, were stronger; and he came back the next day.

In the pus of warm abscesses and in that of furuncles a little rounded organism was found arranged in heaps which was easily cultivated in bouillon. It was found in infectious osteomyelitis of children. Pasteur affirmed that the osteomyelitis and the boil are two forms of one disease and that the osteomyelitis is the boil of the bone. In 1878, this assertion caused many surgeons to laugh.

In the puerperal infections, the pus of the uterus, of the peritoneum, and the clots in the veins contain a microbe of rounded

elements arranged in chains. This appears in the form of a rosary, which is especially evident in the cultures. Pasteur did not hesitate to declare that this microscopic organism is the most frequent cause of the infections in lying-in women. One day, during a discussion on puerperal fever at the Academy of Medicine, one of his most distinguished colleagues held forth eloquently on the causes of epidemics in the maternity hospitals. Pasteur interrupted him from his place: "That which causes the epidemic is not at all what you have said; it is the physician and his assistants who carry the microbe from a sick woman to a healthy woman." And as the author replied that he very much feared this microbe would never be found, Pasteur hurried to the blackboard, drew the organism in the form of a chain and said, "That is the way it looks." His conviction was so strong that he could not prevent himself from expressing it forcibly. We can hardly understand to-day the surprise and even the stupefaction in which he put physicians and students when at the hospital, with a simplicity and an assurance which appeared disconcerting in a man who entered for the first time as an assistant at a labor, he criticized the methods of dressing and declared that all the linens ought to be put through the sterilizing oven. In addition to all this, he claimed that he was able to determine by examination of the lochia of the women which ones would have the fever, and he asserted that in the badly infected women he would demonstrate the microbe in blood taken from the finger. And Pasteur did as he said he would. In spite of the tyranny of medical education which then weighed heavily upon men, some pupils were attracted and came to the laboratory to see more closely those methods which resulted in diagnostics so precise and prognostics so certain.

Pasteur never gave botanical names to the microbes which he discovered: he designated them after some peculiarity of their form or of their manner of growth. Thus the microbe of the boil was for him the microbe of clumped grains, that of puerperal fever, the microbe of grains in the form of a rosary. It is these which, under the more regular names of Staphylococcus and of Streptococcus pyogenes, have made such a great highway in bacteriology, as we know it.

Pasteur is again a forerunner when he undertakes with M. Joubert the bacteriological examination of waters which since has led to the saving of so many human lives.

Generally, the infectious diseases do not occur a second time. Is it the same with anthrax? How shall one determine it since it appears certain that every attacked animal soon dies? Nevertheless, among the sheep inoculated in the course of the experiments made at Chartres, some had resisted, while their companions were dead. The idea came that perhaps in the fields of Beauce, so much exposed to anthrax, those sheep which survived had formerly contracted the disease and had recovered from it, this first attack having given them immunity. Some experiments, undertaken by Pasteur and Chamberland, with another purpose in view justified this hypothesis. A veterinarian of Jura had proposed a remedy against anthrax in cattle; to verify the efficacy of it the cattle were inoculated; one half were treated, the other half were kept as controls. In each one of the lots there were cattle which died and others which survived, although they became very ill. Having recovered, these last, without noteworthy disease, endured virulent anthrax inoculation which killed new cattle. The first attack had given them immunity; it is therefore possible to render cattle refractory to anthrax.

This question of immunity dominates the entire history of infectious diseases; Pasteur was led back to it without ceasing by his experiments. He thought of it all the time. The Jenner vaccination was especially the subject of his meditations. What relation is there between the vaccine and the smallpox? Why has Jenner's vaccination remained an isolated fact in medicine? We are ignorant of the nature of the virus of smallpox and of the vaccine virus. But there are viruses which we know better. Would it be possible to find vaccines against them? From our first entrance into his laboratory Pasteur said to us without ceasing, that is, to Chamberland and to me: "We ought to be able to immunize against the infectious diseases the viruses of which we can cultivate." Haunted by this idea, how many impossible experiments have we not gravely discussed, to laugh at them next day, during this laborious period which preceded the discovery of the attenuation of viruses!

The latter was realized in a disease of fowls, the chicken cholera. The microbe of this disease multiplies readily in bouillon made from the muscles of fowls. A young culture is extremely deadly: it kills all the fowls which receive even the least quantity of it under the skin. Kept in a thermostat at 37° C. in contact with the air, this culture loses little by little its activity. After a certain time, inoculated into chickens, it only kills now and then one; at the end of a longer time, it no longer kills them but it makes them ill; finally, it becomes so inoffensive that it produces in them only a slight fever. These fowls, once recovered, will then endure the inoculation of the most virulent virus, mortal for new fowls. It does not kill them, they have acquired immunity.

This experiment therefore realized the artificial attenuation of a virus and preventive vaccination by means of this attenuated virus.

The cause of the attenuation is the prolonged action of air upon the virus, at a suitable temperature. In fact, the same culture which becomes attenuated in the air keeps its virulence in a sealed tube to which air does not have access.

The attenuated viruses, thus prepared, may reproduce themselves for successive generations, transmitting their qualities to their descendants. Attenuation is *hereditary*. The viruses are microscopic plants; they may be modified by culture just like the higher plants. Pasteur has obtained races of virus, as the gardeners obtain races of plants. The methods which gave the vaccine for cholera of chickens have furnished those for anthrax, for rouget of hogs and for still other diseases.

In the preparation of the anthrax vaccine, in the very beginning, difficulty was encountered. The attenuation of the virulence is produced by prolonged action of the air upon the microbial cell. But this cell is modified only so long as it remains in a vegetative state; in this form it is more sensitive to the diverse influences which act upon it. It is not at all the same when the cell forms spores. The agents which modify the vegetative cells have no influence upon the spores, which are much more resistant. The cultures of chicken cholera never give spores; consequently they become attenuated easily. Those of anthrax, which produce spores, remain indefinitely virulent. To attenuate the anthrax bactéridie, it is therefore necessary to prevent them from forming spores. This end was reached by cultivating them at the temperature of 42½ to 43° C.; at this temperature, after the action of oxygen, the attenuation takes place little by little, so that we obtain a series of viruses of diminishing activity by drawing at various times from the culture originally kept at 37° C. These attenuated bactéridie preserve their weakened virulence through successive generations cultivated at 30° to 40° C.; and at this temperature they give once more spores, which fix this virulence. We have thus a whole scale of virus more and more feeble, and which can be reproduced at will. There remains only to choose in this series a culture which, inoculated into animals, gives a slight disease, but one which is sufficient to confer upon them immunity.

The individuals of the same species present very great differences with respect to their resistance to anthrax; consequently, in practice, we make two vaccinations with a twelve days' interval, the first with a feeble virus, the second with a stronger virus, which completes the immunity.

Preventive vaccination against anthrax entered at a bound into practice. The Society of Agriculture of Melun proposed to Pasteur a public trial of the new method. The program was ar-

ranged for the 28th of April, 1881. Chamberland and myself were on our vacations; Pasteur wrote to us to return at once, and when we were together in the laboratory, he told us what had been agreed upon. Twenty-five sheep were to be vaccinated and then inoculated with anthrax at the same time as twenty-five control sheep; the first would resist the disease, the second would die of anthrax. The terms were precise, no place was left for the unexpected. When we remarked that the program was severe, but that nothing more remained than to carry it out as agreed upon, Pasteur added, "What succeeded in fourteen sheep in the laboratory will succeed just as well in fifty at Melun."

The animals were herded at Pouilly-le-Fort, near Melun, on a farm of M. Rossignol, veterinarian, who had proposed the experiment and who was to supervise it. "Especially do not make any mistake in the flasks," said Pasteur gayly, when on the fifth of May we left the laboratory to make the inoculation with the first vaccine.

The second vaccination was performed the seventeenth of May, and each day Chamberland and I went to visit the animals. In these repeated trips from Melun to Pouilly-le-Fort, many observations reached our ears, which showed that the multitude did not believe in our success. Farmers, veterinarians, physicians followed the experiment with a lively interest, some even with passion. In 1881 the science of microbes had very few partisans; many thought that the new doctrines were baleful and regarded it as an unexpected opportunity that they had been able to draw Pasteur and his assistants out of the laboratory to confound them in the open air, in a public experiment. Here was a chance to be done with these compromising novelties in medicine and by a knock-out blow to find again security in the same traditions and the ancient practices menaced for a moment.

In spite of all the passions which arose around them the experiment followed its due course. The trial inoculation was made the thirty-first of May and the second of June was the date set for the return to determine the results. Twenty-four hours before the decisive time, Pasteur, who had gone on with such perfect confidence in the beginning of the public experiment, began to regret his audacity. For some moments his faith was shaken, as if the experimental method might betray him. A too continuous tension of his mind had led to this reaction, which moreover lasted but a short time. The next day, more certain than ever, Pasteur went to confirm the striking success which he had predicted. In the crowd which thronged about him that day at Pouilly-le-Fort, there were no longer any incredulous persons, but only admirers.[3]

[3] The results were perfectly clear-cut; all the vaccinated sheep lived, all the unvaccinated ones died.—E. F. S.

It is now fourteen years since anthrax vaccination has been subjected to practical tests: wherever it has been applied the losses from anthrax have become insignificant. It was followed by a vaccination against measles in swine, in which our poor comrade Thuillier has particularly labored.[3a] But these immediate results are the least merit of the Pasteurian vaccination; they have given an immense confidence in a science which obtained such a success and provoked such an irresistible movement. Especially they have inaugurated that series of researches upon immunity which must finally lead us to an efficacious treatment of infectious diseases.

Virulence is a quality that microbes may lose. They may also acquire it. If we met in nature this anthrax organism attenuated to the point that it would no longer kill any animal, certainly we should not recognize it for the virus of anthrax. It would appear to us to be a saprophytic microbe. One must have assisted in all the phases of its attenuation to know that this inoffensive bacillus is the descendant of a redoubtable virus. We may nevertheless restore to it the virulence which it has lost by inoculating it first into an extremely susceptible being, a mouse only one day old. Cultivated in the body of this very young mouse, the bacteridium recovers its parasitic aptitude. If with the blood of this mouse we inoculate another a little older it will perish. By passing thus from younger to older mice, we finally succeed in killing adult mice, guinea pigs, then rabbits, then sheep, etc.

During these passages the virulence has gone on increasing. This increase of virulence, which we obtain experimentally, takes place without doubt in nature and we can imagine very well that an ordinary microbe harmless for an animal species may become deadly to it. Is it not in this manner that in the course of the ages the infectious diseases have appeared?

From these modifiable viruses which are so plastic that the experimenter, so to speak, shapes them to his will, it is a far cry to the ancient conception of virulent entities! Pasteur's note on the attenuation of the viruses and the return to virulence was presented to the Academy of Sciences the twenty-eighth of February, 1881. Better than any other it gives the measure of Pasteur and makes us understand the extraordinary penetration of his mind.

The researches on anthrax did not occupy all Pasteur's time. During the same period he began studies upon rabies. This disease is one of those which take the fewest victims among men; if Pasteur chose it as the subject of studies it was because the virus of rabies has always been regarded as the most subtle and the most mysterious of viruses, and also because hydrophobia is for every-

[3a] T. lost his life studying cholera in Egypt.—E. F. S.

body the most dreaded and frightful disease. Pasteur shared the common horror; and believed that to solve the question of rabies would be a benefit to humanity and a striking triumph for his doctrines.

In 1880 the first experiments were undertaken. Rabies is inoculable into animals, it is therefore accessible to experimentation; no doubt it is caused by a microbe, and he did not question that the methods which had led to the discovery of so many other viruses would succeed also in demonstrating that of rabies. But it was not so: not only have we never been able to cultivate the microbe of rabies, but no one has succeeded in seeing it. The most patient investigations with the microscope, the most advanced methods of staining have miscarried up to this time.[4] It was necessary to work upon a virus which could not be cultivated and was invisible, and nevertheless we have succeeded in establishing a prophylaxy for rabies, after the bite, the results of which exceed by far the most successful that have ever been obtained in medicine. Is there a more striking example of the power of the experimental method applied to things medical? Rabies is transmitted by the bite of a mad animal, because the virus is contained in the saliva. But inoculations made with the saliva do not give the disease with any certainty; even when they succeed, the latter appears only after an incubation period which is often prolonged during several months. The first step was to learn how to give rabies with certainty; in order to do that it was necessary to give up inoculation with saliva, which, in addition to the rabic virus, contains a large number of common microbes, sometimes hindering its action. Where then should one find in a rabic animal the virus in a state of purity? Rabies is manifestly a disease of the nervous system; perhaps the virus is in the nervous centers. In fact, experiment shows that the true seat of the rabic virus is the brain and the spinal cord. The inoculation of the substance of these organs, taken from a rabid animal, gives the disease with more certainty than the saliva, because the virus is there more abundant, and especially because it exists there in a state of purity. Nevertheless, it is not sufficient to have a pure rabic virus in order to give the disease immediately. The inoculation of the substance of the rabic brain under the skin is not always followed by rabies, and when the latter does occur, it appears most often only after a long incubation period. Subcutaneous inoculation therefore is not to be trusted. Then the idea came that to transmit rabies with certainty the virus should be deposited in the nervous centers, since it is there that it grows best. It was therefore decided that a dog should be inoculated under the dura mater by trepanning the skull.

[4] Rabies is now generally believed to be due to the Negri bodies.—E. F. S.

Ordinarily as soon as an experiment was conceived and discussed it was set in operation without delay. This one, upon which we nevertheless counted so much, was not at once executed; Pasteur, who must sacrifice so many animals in the course of his beneficent studies, experienced a strong repugnance to vivisection. He assisted without too much squeamishness at a simple operation like a subcutaneous inoculation, and yet, if the animal cried a little, Pasteur was immediately full of pity and gave to the victim consolations and encouragements which would have appeared comic if they had not been touching.

The thought that it was necessary to bore through the skull of a dog was disagreeable to him. He earnestly wished that the experiment might be realized, but he feared to see it undertaken. I did it one day when he was absent. The following day, when I reported to him that the intracranial inoculation did not offer any difficulty, he was full of pity for the dog: "Poor beast, its brain without doubt is injured, it must be paralyzed." Without replying I descended to the basement to find the animal and brought it into the laboratory. Pasteur did not love dogs; but when he saw this one full of vivacity nosing about curiously he expressed the liveliest satisfaction and lavished upon it the most amiable words. Pasteur felt a great tenderness for this dog who had so well endured trepanation and had thus removed all his scruples against future trepanations.

This first trepanned dog took rabies characteristically in fourteen days. The experiment, repeated a great many times, gave the same result; it was possible therefore to give rabies with certainty and in a relatively short time; consequently it was easy to experiment with it.

The inoculation of rabic virus by trepanation succeeded also in the rabbit, and it is easy to transmit rabies in this manner from rabbit to rabbit. During these successive passages the virus is strengthened and the duration of the incubation diminished to a period of only six days. In this way we obtain veritable intracranial cultures of the rabic virus. Instead of making the culture in artificial media, as in case of other viruses, we make that of the rabic virus in living material. These cultures in the substance of the nerves may be modified like the cultures of anthrax or of the chicken cholera.

The rabic spinal columns, exposed to the action of the air, in an atmosphere deprived of moisture, dry out and lose their activity. After fourteen days the virus is weakened to that degree that it is inoffensive even in the strongest doses.

A dog which receives this spinal cord fourteen days old, then on the next day a cord thirteen days old, then that twelve days old, and so on till he receives a fresh cord, does not contract rabies, but he has become refractory to it. Inoculated in the eye or in the brain with the strongest virus he remains well. It is therefore possible, in fifteen days, to give immunity to an animal against rabies. Now men bitten by mad dogs do not ordinarily contract rabies sooner than a month and often more after the bite. This incubation period may be utilized to render the bitten person refractory to the disease.

Experiments made upon bitten dogs or inoculated ones succeeded beyond expectation. You will remember how, with the aid of MM. Vulpian and Grancher, it was extended to man. More than sixteen thousand persons have undergone to-day antirabic treatment and the mortality of these treated persons has been less than one half of one per cent.

The discovery of the prophylaxy of rabies brought about everywhere a veritable enthusiasm. It did more for the popularity of Pasteur than all his previous labors. In return for such a benefit, the great public wished to manifest its gratitude in a fashion worthy of itself and of him who was the object of it; it was then that a subscription was opened which laid the foundations of the Pasteur Institute.

It seems that those results acquired in the study of rabies might have presented themselves naturally to the experimenter and in a logical order. One must have participated in this study to know what stubborn labor it necessitated during more than five years. Pasteur displayed therein that tenacity of purpose which leads to success. How many times, in the presence of unexpected difficulties when we could not imagine any way out, I have heard Pasteur say: "Let us do over the experiment, the essential thing is not to be discouraged."

After the studies on rabies, the health of Pasteur continued to decline. He supported better the obstinate labor of the period of researches than the emotions of the triumph. Pasteur welcomed gladly the demonstrations and the universal gratitude lavished on him, not through a vain love of praise, but on account of the honor which accrued from them to his country, to science and to his loved ones.

The numberless manifestations of which he was the object at this period excited his sensibility even to tears. As soon as the preventive inoculations were applied to man all repose was lost for him. Every bitten person brought him a new preoccupation. The sight of wounded children especially caused him emotions which he could not control. When desperate cases supervened against which no method was of any avail, Pasteur suffered all the torments of

these diseased ones. Every visit he made to them was for him a torture, and he could not help visiting them. It was necessary to get him away from Paris. He was in Italy when those attacks appeared against the antirabic method which made so much noise at the epoch and which are so thoroughly forgotten to-day. He felt them at a distance and was keenly afflicted by them. From this time, Pasteur had to renounce the life of the laboratory; for such a worker as he was, the inaction was a sorrow. Only the visits of his collaborators and the company of his grandchildren were capable of restoring to him a little gaiety. The never-to-be-forgotten ceremony of his Jubilee, in December, 1892, by showing him what a place he held in the esteem of scientific men and in the veneration of peoples, caused him to experience a profound emotion. From that time on Pasteur lived only in the love of his own people; all the care and all the affection with which he was surrounded was necessary to keep him alive, he was so feeble. But even to the end, his thought was in the laboratories, with those who labored strenuously in order that the foundation which bears his name might remain worthy of him. These labors on anthrax, the attenuation of virus, the swine fever, rabies, Pasteur accomplished them in less than ten years, from 1876 to 1885, with the aid of only a few collaborators, M. Joubert at first, and then MM. Chamberland, Thuillier and Roux. Those years passed in the laboratory of rue d'Ulm during this period of discoveries remain present in my mind as the best ones of my life. In order to be nearer the work, master and disciples lived in l'École Normale. Pasteur was always the first to arrive; every morning, at 8 o'clock, I heard his hasty step, a little trailing [on account of his paralysis] over the loose pavement in front of the room which I occupied at the extremity of the laboratory. As soon as he had entered, a bit of paper and a pencil in his hand, he went to the thermostat to take note of the state of the cultures and descended to the basement to see the experimental animals. Then we made autopsies, cultures and the microscopic examinations. One must have seen Pasteur at his microscope to have an idea of the patience with which he examined a preparation. Moreover, he looked at everything with the same minute care; nothing escaped his myopic eye, and we said jokingly that he saw the microbes growing in the bouillons. Then Pasteur wrote out what had just been observed. He left to no one the care of keeping the experimental records; he set down most of the data which we gave him in all its details. How many pages he has thus covered, with his little, irregular, close-pressed handwriting, with drawings on the margin and references, all mixed up, difficult to read for those not accustomed to it, but kept nevertheless with extreme care. Nothing was

set down which had not been established; once things were written, they became for Pasteur incontestable verities. When, in our discussions, this argument resounded, "It is in the record book," none of us dared to reply. The notes being taken, we agreed upon the experiments to be made; Pasteur stood at his desk ready to write what should be decided upon, Chamberland and I facing him, with our backs to a show-case (vitrine). It was the important moment of the day; each one gave his opinion, and often an idea, confused at first, became clear in the course of the discussion and ended by leading to one of those experiments which dissipated doubts. Sometimes we were not in agreement and the discussion was heated, but, with Pasteur, who passed nevertheless for the authority, one could say freely all his thought; I have never known him to resist a good reason.

A little before noon, they came to call Pasteur for the midday meal; from noon till two o'clock he came into the laboratory and the most often, on our return, we would find him motionless in front of a cage, never wearying of observing a guinea pig or an interesting rabbit. About two o'clock Madame Pasteur sent for him, else he would have forgotten to go to the Ácademy and to the committees of which he was a member. Then we spent the afternoon in making the experiments agreed upon, interrupting ourselves only in order to allow Chamberland to smoke a pipe. The master had a horror of tobacco and we smoked only in his absence. Pasteur returned toward five o'clock. He informed himself immediately of all that had been done and took notes; his notebook in hand, he went to verify the tickets fastened on the cages, then he told us the interesting communications heard at the academy and talked of the experiments in progress. It was at this moment that Pasteur revealed his thought most willingly, especially if we provoked him by objections; then his clear eye flashed more vividly; his speech, a little thick in the beginning, became more and more animated and persuasive. He developed the most profound and the most unexpected ideas, he proposed the most audacious experiments. This rigorous experimenter had a powerful imagination; for him *a priori* there was nothing absurd. But his most enthusiastic flights always led him to an experiment to be made and he retained only that which could be demonstrated. His ardor was so communicative that after having heard him the experimental projects filled the mind. When we got him going on the subject of his first labors, he expressed himself like a poet on molecular dissymmetry and its relation to the dissymmetric forces of nature. Those days, Pasteur forgot the dinner hour; and Madame Pasteur had to send for him two or three times, or come to find him herself; then he went away smiling and saying to us, "You are to blame, I shall be scolded."

The laboratory was always shut up; one was able to enter it only after having sounded at the great door, constantly closed. Visitors rarely got past the antechamber; when Pasteur was at work he was not receptive, even to his friends; to interrupt him was to make him unhappy. I see him turning toward the intruder, waving his hand as if to send him away, and saying in a supplicating and desperate tone: "No, not now, I am too busy." He was nevertheless the most simple and the most approachable of men, but he did not understand how any one could disturb a scientific man who is occupied in making laboratory notes. When Chamberland and I were pursuing an interesting experiment, he stood guard over us. Seeing at a distance, through the glass windows, the comrades who came to ask for us, he went himself to receive them and to turn them away. These whims of Pasteur showed so naïvely his sole preoccupation in the work that they never vexed anybody.

Pasteur has been reproached for not having opened widely his laboratory to students who might have spread his ideas and his methods; it has even been said that he loved to keep secret his methods of research. Nothing is more unjust; in his communications, Pasteur sowed with an open hand new ideas and every one has been able to profit by them. He was therefore an incomparable teacher; he has not advanced any idea without giving information enabling any one to control it; but instead of losing himself in useless details and explaining clumsily the arrangement of apparatus which everybody could easily imagine, he confined himself to stating exactly the necessary and sufficient conditions. The laboratory of the rue d'Ulm was not large enough to receive numerous investigators, there was just enough room for Pasteur and his assistants.[5] Moreover, Pasteur worked easily only in silence and retirement; near him he admitted only his collaborators; the presence of a stranger to his occupations sufficed to disturb his work. One day when we went to see Wurtz at l'École de médecine, we found the great chemist in the midst of his students, in his laboratory full of activity, buzzing like a beehive.

"How can you work," said Pasteur, "in the midst of such a disturbance?"

"That only stirs up my ideas," replied Wurtz.

"That would drive all mine away," replied Pasteur.

Pasteur was constantly imagining new experiments; he noted his projects upon sheets of a little notebook or upon morsels of cardboard which he carefully preserved. His left hand remaining useless after the paralytic attack of 1868, he confided the execution of experiments to his assistants; an irreproachable experimenter himself, he showed himself very exacting toward others. For him, there was no impossible experiment: when we observed that that which he demanded of us presented very especial difficulties he said, "That is your affair; do it in any way that seems best to you, provided it is well done." And he satisfied himself always that it was well done; he separated out the good from the bad with admirable sagacity.

[5] In the laboratory reserved for *l'agrégé préparateur*, several persons have been admitted to work, notably M. Denys Cochin. Later, when the annex in the Rue Vauquelin was fitted up, Pasteur hastened to receive there Dr. Straus and then Dr. Grancher.

A communication of Pasteur to the Academy of Sciences or to the Academy of Medicine was an event; because he published nothing that was not finished. Each one of his notes takes up only some pages of the *Comptes rendus,* but it contains the substance of hundreds of experiments. Consequently we can read them and reread them, and always find there something of use; often a simple phrase indicates a new pathway, and several of those which are thus noted have not yet been traversed. All Pasteur is in his writings; his imagination reveals itself therein by the profundity and the audacity of the generalizations, by the rigor of his spirit, by the justice of his views, by the soundness of his conclusions and his enthusiasm by the emotion of his language.

Before writing, Pasteur read and reread the experimental notebooks, then he dictated to one of us or more often to Madame Pasteur. He kept the manuscript sometimes during weeks, retouching it without ceasing; when he was satisfied, he read it to us and discussed with us its phraseology; often he received our comments with impatience; but he always took them into account if they were just. Madame Pasteur recopied it in her fair handwriting, so easy to read; Pasteur would never have sent to the publisher a manuscript full of erasures; if he modified some passage he glued over these lines gummed paper, cut to the proper dimensions, and wrote it anew. During all this work of editing, the question under treatment developed singularly, and we, the collaborators of the master, who knew at what point the experiments had abandoned him, were astonished to see it grow and be transformed in the final note.

The ideas of Pasteur were too new not to be opposed; besides, Pasteur did not fear strife; his discussions at the Academy of Sciences have remained celebrated; those which he maintained at the Academy of Medicine were more passionate still. Many physicians, in fact, and not the least conspicuous ones, saw at first with stupefaction and then with indignation this chemist overthrow with so much assurance medical doctrines. To study diseases in a laboratory with chemical apparatus was for them a medical con-

tradiction. On his part, Pasteur, persuaded that he brought the truth, would have believed it a bad action if he had not maintained his point with all his force. Hence those contests with which the heroic ages of bacteriology have resounded; every discovery of Pasteur has been imposed with blows; when he despaired of convincing his colleagues, he addressed himself over their heads to the public of young physicians who followed the lectures.

Under these contradictions he lost his serenity, and as he was sure of the propositions he advanced, he proposed willingly the nomination of academic commissions before whom he would bring his adversaries as before a tribunal.

So much courage and stubbornness rallied partisans to his doctrine, but there remained irreductible opponents who came back without ceasing to the charge. There is nothing astonishing in the fact that Pasteur and they could not understand each other. They were imbued with that medical spirit made up at the same time of skepticism and of respect for traditions. He had the faith of a novice and the assurance which the experimental method gives. He was indignant that any one could remain hesitant in the face of a demonstrative experiment.

He left these seances stirred to the depths; MM. Vallery-Radot, Chamberland and I often awaited him at the exit: "Have you heard?" he would say to us: "To the experiments they have replied with talk!" We returned on foot to the rue d'Ulm and his irritation gradually subsided; immediately he spoke of making still more experiments to throw additional light, for the contradictions excited him to make new researches. These tumultuous seances at the Academy of Medicine were therefore useful, since they were like a stimulant to the activity of Pasteur.

The passion of Pasteur for science carried him away sometimes in outbursts very amusingly naïve. For him, a man who made a bad experiment or a false reasoning was capable of anything. One day when he read to us in the laboratory a work which appeared to him to be particularly bad, he was exasperated and cried out: "A man who can write such stuff I would not be surprised if he should beat his wife," as if to beat his wife were the height of scientific irregularity!

The great force of Pasteur is that he could, without being weary, hold his thought concentrated upon the same object. He followed his idea without allowing himself to be distracted and he brought everything to it; thus from a conversation with persons even the most unfamiliar with science he knew how to draw something useful for his researches. Of him also one can say that he has made

his discoveries by continually reflecting on them. His stubborn thought attached itself to difficulties and ended by solving them as the intense flame of the blowpipe constantly directed upon a refractory body ends by melting it.

In those moments of great preoccupation, Pasteur remained silent, even in the midst of his own family. Nothing could efface the obstinate wrinkles of his countenance until the solution was found. Then his face became luminous, and this concentrated man allowed his joy to overflow, explaining what he had discovered and what he hoped from it. All those close to Pasteur and associated with his scientific life felt the rebound of his preoccupations and participated in the satisfactions of the savant.

One can not understand the career of Pasteur if he does not know of his family and especially of Madame Pasteur. From the first days of their common life Madame Pasteur understood what sort of a man she had married; she strove to remove difficulties from his life, taking upon herself the cares of the household in order that he might keep all the liberty of his spirit for his researches. Madame Pasteur has loved her husband to the point of understanding his work. In the evening she wrote under his dictation and brought out explanations, for she was really interested in the hemihedral facets and in the attenuated viruses. And then she had clearly perceived that ideas become clearer when they are explained and that nothing leads more certainly to the conception of new experiments than the description of those which have been made. Madame Pasteur was not only an incomparable companion for Pasteur—she was his best collaborator.

The work of Pasteur is admirable. It shows his genius, but one must have lived intimately with the master to know of the goodness of his heart.