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ADVANCEMENT OF MEDICAL SCIENCE

BY

L. A. STIMSON, M.D.

VICE-PRESIDENT N. Y. ACADEMY OF MEDICINE; PROFESSOR OF SURGERY, UNIVERSITY OF THE CITY OF NEW YORK

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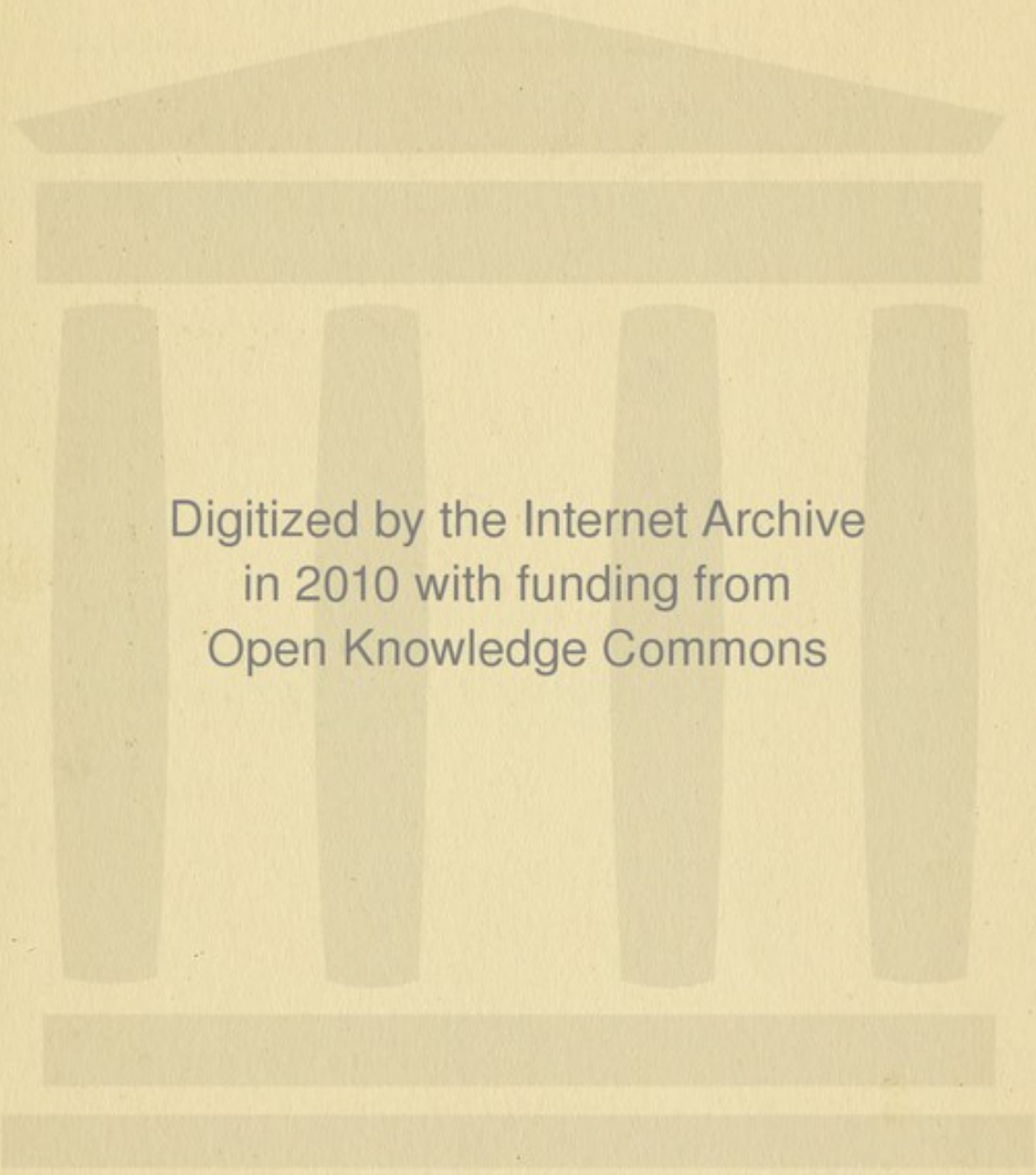

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Mr. President and Fellows of the New York Academy of Medicine:

Among the many wise provisions of those who have brought this Academy to its present standard of intellectual and material prosperity must be counted that which provides for this annual reunion of its members, in order that, laying aside for the moment the special interests that absorb them in the various Sections during the year, they may turn their attention to some matter of general interest and wider import. The same wise foresight throws open the doors to our non-professional friends; and in order that they may be not only welcome, but also interested in our proceedings, it suggests that the topic of the evening and its treatment should be such that the deficiencies of their training and of their opportunities may not wholly deprive them of the possibility of finding pleasure therein.

In casting about for a subject that would meet the requirements of the occasion, that would interest both the professional and the non-professional hearer, and that possessed sufficient intrinsic merit to compensate for defects in its presentation, I was reminded that nothing is more interesting than to review the course of one of the masters of science, to receive his exposition of the principles of his method, to study their illustration in examples drawn from his own experience, to trace the operation of

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[1] Anniversary Discourse before the New York Academy of Medicine, November 17th, 1892. Reprinted from Transactions.

his mind, to learn how even mistakes may be profitable and instructive, and to appreciate at what price notable discoveries and solid progress are made.

The story of the life of such an one should be of interest to all, and if it dealt with the broader problems of our own science the requirements of this occasion would be fully met by it.

Furthermore, there is in the review of the progress of any science or of the development of any great idea or broad principle something far more worthy of respect and attention than the simple personal element or the momentary interest of the recital. In the world of ideas the novelty of to-day becomes the commonplace of to-morrow. The ideas which came like revelations or inspirations to our fathers are fed to us in our school books, and appear to us to have existed, like the alphabet or the solar system, from the beginning of the world. As we read the history of a past removed from us, perhaps, by but a few generations, we are amazed that men's actions should have been determined by such faulty notions of political, economical, or religious principles, and that they could have been so blind to what is now so clear. And when we read books that within a few years have revolutionized thought, that have been received and acclaimed almost as if they had been divinely inspired, we ask ourselves in vain in what the novelty and the originality could have consisted, so commonplace, so trite even, have those novel and original ideas become. It therefore becomes a pious duty to those who have so raised the general level of our knowledge or of our principles, that while we enjoy the fruits of their labors we should still be mindful of their part in it and should bear their names in constant and grateful remembrance.

The science of medicine is so closely interwoven with other sciences, so many of its most important advances have been made by the aid of those whose names are not upon its roll of members, that we shall never be at a loss to find a worthy and appropriate subject for our study,

our honor, and our gratitude; and there is a peculiar propriety in the public and professional recognition of our obligations to those who are not strictly of us. I offer no excuse, therefore, for asking your attention this evening to a brief review of the life and accomplishments of a man who is by profession a chemist and whose only medical title is that of honorary membership in an academy of medicine. And yet, although so widely removed from us by training and occupation, it has fallen to his lot, in a larger measure, perhaps, than to that of any other man, to open important pathways of research in medicine and to establish a doctrine of causation of disease upon which a mighty and efficient structure of prevention and cure has already been erected. Upon principles discovered and established by him rests the modern treatment of surgical wounds, with the saving already effected of hundreds of thousands of lives, and to him a few years ago (1876) Prof. Tyndall wrote in these words: "For the first time in the history of science we have the right to cherish the sure and certain hope that, in respect to epidemic diseases, medicine will soon be delivered from empiricism and placed on a really scientific basis. When that great day shall come, humanity, in my opinion, will recognize that it is to you that the greatest part of its gratitude is due." And at the meeting, last summer, of the British Medical Association, the author of the address on bacteriology expressed the gratitude of the world to him as the one whose genius had raised that branch of study to the rank of a science. Let us, then, add to-night our tribute of homage and gratitude to

LOUIS PASTEUR.

Born in December, 1822, in a village near the central eastern frontier of France, of humble parents who labored and sacrificed to advance his education as though they foresaw his future, we find him at the age of eighteen already a tutor in the college of Besançon, which had just given him his baccalaureate degree, with a reputation es-

tablished for exceptional ability and industry, and with a maturity of character far beyond his years. His position was a modest one: it lodged and fed him and gave him five dollars a month; but it also gave him an opportunity to continue his studies, and it placed his foot upon the first round of that wonderful ladder of educational and scientific organization which offers to every young lad in France who chooses to attempt to climb it a sure and certain promise of rewards and honors, in accordance with the measure of his ability and industry.

Three years later he won a place in the Ecole Normale at Paris, where almost all his work has since been done, and of which he has become the supreme glory. In this great school, where the students are invited rather to independent investigation than to attendance upon methodical instruction, Pasteur found both stimulus and opportunity for the gratification of his passion for chemistry; and it is interesting and suggestive to see the lad employing in his self-instruction those methods of close observation, rigid self-criticism, and control experimentation which have been the foundation of his later successes, and displaying the same skill and beauty of manipulation, the same strength and clearness of thought, the same absolute honesty, and the same breadth of view. A single incident may be quoted in illustration, and also because it was the first step in his long line of research and discovery, each subsequent one of which was the natural, logical successor of those which had preceded.

Molecular physics and chemistry, and the structure and polarity of crystals, were at that time receiving much attention, and it was held by some of Pasteur's teachers that in the arrangement of molecules was to be found the explanation of all chemical and allied phenomena. Into the study of this subject Pasteur had entered with his usual ardor, when a note was sent to the Académie des Sciences by the mineralogist Mitscherlich which threatened to destroy the theory. Mitscherlich pointed out that, although the double tartrate and paratartrate of

soda and ammonia were identical in chemical composition, specific weight, crystalline form, and double refraction, yet, while the tartrate in solution deviated the beam of polarized light, a solution of the paratartrate did not affect it. Apparently the admitted identity in the number, arrangement, and distances of the atoms in the two substances did not make them identical in all respects.

The crystals of the two acids and of their compounds had already been studied and described in great detail. Pasteur set himself to repeat the investigation, and he discovered, what had been overlooked by all others, that the crystals of tartaric acid, and those of its compounds, were asymmetrical in this sense, that if one was split in two the two halves, while identical in form, were not superposable; they were, so to speak, right- and left-handed respectively; each was identical with the mirror image of the other, as a right hand is identical with the reflection of a left hand in a mirror. A solution of these asymmetrical tartaric crystals deviated the beam of polarized light to the right. We may, for convenience, call them right-handed crystals. The crystals of paratartaric acid he found to be symmetrical, and, as has been already said, they were without action upon polarized light. But on examining the crystals of the salt formed by combining this acid with soda and ammonia, he found, to his great surprise and delight, that they were asymmetrical, and asymmetrical in two forms; there were both right- and left-handed crystals; and a solution of one kind deviated light to the right, and a solution of the other deviated it to the left; when they were mingled the effect of one neutralized the effect of the other. And thus the objection raised in the famous note of Mitscherlich was answered.

Pursuing the investigation, he found a new form of tartaric acid, one whose crystals were left-handed, and which deviated light to the left. He made known his discovery to the Académie des Sciences, and it was referred at once for report to the veteran Biot, the discoverer of the polarization of chemical substances. He summoned Pas-

teur to his laboratory, supplied him with the acids and bases, and told him to prepare the crystals. When this had been done he bade him separate the alleged right-handed from the left-handed, and then, pointing to each little pile in turn, he said: "Do you declare that these will deviate the light to the right, and these to the left?" On receiving an affirmative answer he at once prepared a solution of each and applied the test, and as the predicted result appeared the illustrious old man caught the youth in his arms, saying: "My dear young friend, I have so loved Science all my life that this makes my heart throb."

We can perhaps gain some conception of the sharpness of the scrutiny that enabled Pasteur to recognize these differences from a remark made to him by Mitscherlich. "I studied," said the latter, "those two salts, in their minutest details, with so much care and assiduity that if you discovered anything that I had failed to find, it could only have been by the guidance of a preconceived idea."

The path thus opened was followed by Pasteur with results that were most suggestive of unsuspected underlying principles. He found molecular asymmetry to be the characteristic, the stamp, of life; the invariable, though sometimes hidden, feature of all substances that have the most influence in the manifestations of vegetable and animal life; it is the line of demarkation between living and dead chemistry.

One of the observations made at this time led to the next and most important step in his career. He caused a solution of the paratartrate of ammonia to ferment, and he noticed that, as the process advanced, the solution, which at first was without action upon polarized light, gradually deviated the plane to the left. Of the two forms of the acid—the right and left—of which the salt was composed, only the former was broken up in the process; the latter—the left—remained unchanged, and constituted, therefore, the bulk of the solution.

The explanation was to be sought in the nature of the

process of fermentation. He had proved molecular asymmetry to be peculiar to life, to living chemistry; he found it present and active in fermentation; he sought the life from which it came, and he made the great discovery of the agency of living ferments. At one stroke he swept away all the old theories, including that of Berzelius—the "theory of contact"—and that still older one to which Liebig had given his name and support, and which was held almost universally at the time—that which invoked an atomic movement communicated to the fermentable solution by dead and decomposing albuminoid matter. And in the place of these explanations which did not explain, these theories each of which was limited to some restricted group of fermentations, these solutions which depended upon unproved and unprovable assumptions and each of which raised a new problem to be solved, he gave us a simple theory which rested at every point upon demonstrated facts, and which not only was applicable to all recognized fermentations, but also vastly enlarged the boundaries of that class, bringing within it other processes whose kinship had not been appreciated, and adding a multitude of others whose existence even had not been suspected—the theory, namely, that the process is one that is correlative with life, not, as formerly supposed, with death, and that all these varied manifestations have a common cause, the active growth and multiplication of minute organisms.

The origin of these minute organized ferments was so entirely unknown, their appearance in the fermenting liquids was so mysterious, that Pasteur felt it to be necessary to investigate the theory of spontaneous generation, which was invoked by so many to account for their appearance. He was strongly dissuaded from the undertaking by his best and closest scientific friends, on the ground that the problem was practically insoluble; but he persisted. Never had he worked with more thoroughness, greater watchfulness, keener intelligence, and sharper insight than in the remarkable experiments

which completely overthrew the theory and laid bare the errors and defects in the experiments of those who maintained it. The story, which is far too long to be told here, is one of the most interesting and instructive in the history of scientific research; it has been told and retold many times, and by no one more clearly and attractively than by Prof. Tyndall, who has himself done so much to extend and illustrate it.

Returning from this scientific excursion to continue his work on fermentation, Pasteur took what may be called his first step in the investigation of disease, although the disease was merely one of certain vegetable products, not of man or even of beast. He studied what was called the disease of wines—that sudden change which occurs sometimes after the wine has been kept for years, and which, within a few weeks, wholly destroys its value. It is sufficient here to say that he found the change to be a fermentation, with living, organized ferments, and that he devised efficient preventive measures which are now in general use, the savings effected by which are already estimated by millions.

In like manner, a few years later, he relieved the manufacture of vinegar and that of beer from empiricism and faulty methods, and gave them the security of a scientific basis; and at the end of that work he uttered, with the caution so characteristic of all his statements made before the complete demonstration, this suggestive sentence: "The etiology of contagious diseases is perhaps on the eve of receiving an unexpected light."

His success in detecting and removing the cause of the deterioration of wine was promptly followed by another equally important economical discovery, one which affects even more forcibly the imagination of the multitude and the emotions and the resources of those who are directly interested. The cultivation of the silkworm is an important industry in France and Italy. In 1853 France produced twenty-six million kilogrammes of cocoons, worth one hundred and thirty million francs. During

the following decade the production was so reduced by a disease of the worms that in 1865 it amounted to only one-sixth of what it had been in 1853—a money loss of more than one hundred million francs annually. The industry was threatened with total destruction. Innumerable researches into the cause of the disease had been made, remedies of the most varied kinds had been tried, and the French Government had even agreed to pay to the inventor of an alleged cure five hundred thousand francs if it should prove efficient. But nothing availed, and each year the crop was smaller. The senate appointed a committee to consider the matter, and that committee at once turned to Pasteur and asked him to investigate the disease. To his objection that he knew nothing about it, that he had never even seen a silkworm, they replied: "So much the better; you will approach the subject without prejudice." The sacrifice that was asked of him was great, for it required the prolonged abandonment of those researches in fermentation which were so plainly leading him to a great future; but he saw his duty and he followed it. He went at once to one of the desolated districts, and was so impressed by the sight of the distress occasioned by the epidemic that he resolved not to return to Paris before he had exhausted every line of investigation. The industry is one that is carried on by a multitude of small proprietors, not by a few large corporations. Every family in the village hatches out as many worms as it can care for, filling every corner in the house with them, from the kitchen to the garret, and they watch them through their four moultings and into their cocoons with the greatest solicitude. Day and night they are afoot, to give them food and protect them against changes in the weather. It is said that during the season the salutation of the villagers when they meet is not "How are you?" but "How are they?" In the close struggle for life in those older communities the gain or the loss of the little revenue from a few silkworms meant

in many a family comparative ease or dangerous want; the general loss of a crop was a public calamity.

Into the details of the investigation we cannot now enter. It was pursued for five years with unflagging devotion and in the face of much criticism and even active hostility. His critics said he was a chemist and should confine himself to his profession. They were surprised at his ignorance, and they showed that his efforts were doomed to certain failure. But these prophecies were not realized, and, on the other hand, his were. A year after the beginning of his work he inspected fourteen parcels of eggs and the moths that had produced them, and gave a written prediction of the health of the worms that would be hatched from them the ensuing year. In twelve out of the fourteen the prediction was exactly fulfilled, and in the remaining two the result was a partial confirmation. He found the cause of the disease to be the infection of the worms by minute corpuscles, and that even an apparently healthy moth might bear the infection within itself, and that, if it were thus infected, the eggs it laid would produce only diseased, useless worms. He showed that safety was to be had only by killing the moths after the eggs had been laid, examining their bodies for the corpuscles, and hatching only those eggs that came from uninfected moths.

At last his success was universally admitted, and to this day, wherever in Europe the silkworm is cultivated, there will be seen, at the proper season, work rooms filled with women and young girls busily engaged with their microscopes in searching for and throwing out the tainted eggs which he taught them to recognize.

Pasteur emerged from this trial again a conqueror, but also, alas! a cripple. In the midst of it, October, 1868, he was stricken with hemiplegia; he slowly regained the use of his limbs, but he bears to this day its traces on his face and in his gait.

Such was his life up to the age of fifty years. It had been one long, unbroken record of successful effort, of

brilliant discoveries in science, of vast additions to the economic resources of the world, and of hearty recognition and appreciation. Had it ended then, he would still have ranked among the notables of science. It appeared, indeed, to be near its end. Crippled in body by paralysis, utterly depressed in mind by the terrible calamities that overwhelmed his country, he no longer had the heart or the strength to work. And yet the future was to show that the past, brilliant as it had been, was only a preparation and training for a still more brilliant series of triumphs in a field of the highest interest, and one, too, from which he would naturally have supposed himself to be wholly excluded, so far as personal effort was concerned, although he had recognized its possible connection with the work he had already done.

There was yet to be accomplished by him an advance in medical science similar to that which had been made by his countrymen three-quarters of a century earlier, an advance of which Virchow has said: "The year 1800 forms a great turning point in medicine. At that time, under the influence of the French Revolution, the great Parisian school was formed; and we must give honor to the genius of our neighbors that they were able at one stroke to discover the principles of an entirely new science. If we now see medicine developing itself in the greater breadth of objective knowledge, we must never forget that the French were the pioneers, as the Germans were in the middle ages."

The same province of France—Franche-Comté, or, to speak more broadly, Burgundy—which had sent Bichat to Paris to begin the work of which Virchow has thus spoken, had now sent Pasteur to give to that work its latest and most striking development. To the objective knowledge of the changes effected by disease was now to be added, by the same method of observation and experiment, a knowledge of the cause of disease, with all the vast possibilities of prevention and cure which flow from such knowledge.

The germ theory of disease is by no means a new one; its origin, indeed, is lost, as Virchow says, in the darkness of the middle ages, and it distinctly appeared, under the name *contagium animatum*, in the sixteenth century. But at the time of which we are now speaking it was still only a theory. Nineteen years ago, in the Anniversary Discourse which the late Prof. Dalton delivered before this Academy, he ventured, as he said, "to cast the professional horoscope for the present and to anticipate, as nearly as may be, what we are to expect from it in the immediate future." He found that "if there be any one direction in which progress is now so marked as to constitute a dominant feature of the present state of medicine, and to embrace a practically new medical idea, I should say it was that of the origin and propagation of disease by independent organic germs. Perhaps it would be wrong to say that this doctrine is even yet distinctly formulated. It is certainly far from being definitely established as a general truth. . . . So far it exists in the form rather of a scientific instinct than of a positive belief, and its gray light hangs about the edge of the medical horizon like the coming dawn of a new period."

In his enumeration of the facts which seemed to him to justify this anticipation, Dalton laid especial stress upon what he termed Pasteur's brilliant researches in fermentation and spontaneous generation. It must be remembered that these researches had gone far beyond the simple demonstration of the presence and agency of germs. Pasteur had not merely found the germs; he had isolated them, had devised methods to obtain pure cultures, and had studied their natural history in detail. In short, he had laid the foundation of the modern system of bacteriology. The work was already bearing fruit in the field of medicine. The study of the dust of the air and the proof of its agency in exciting putrefaction had led Lister to the antiseptic treatment of wounds, the importance of which was just beginning to win recognition. The interest in the subject was especially quickened in 1872 by

some striking experiments made in Paris which showed that septicæmia could be produced in animals by the injection of infinitesimal quantities of the blood of other animals that had died of the disease, and every laboratory was occupied with the subject. In the address just quoted Prof. Dalton said that between the years 1870 and 1873 more than two hundred papers were published upon septicæmia. Pasteur naturally followed this movement with the keenest interest. More than ten years previously he had foreseen the possibility and had expressed the wish that he might be able to carry his researches sufficiently far to prepare the way for a radical investigation into the origin of disease. But he had no thought of taking a personal part in it, for, although the University of Bonn had conferred upon him the degree of doctor of medicine, and the Paris Academy of Medicine had made him an honorary member, he was, as he said, not a physician. He limited himself to making suggestions to those who sought his counsel. I recall one of them, made at that time, that the dressings to be applied to wounds should be sterilized by heat. It now seems almost too commonplace to deserve mention; it was then an absolute novelty.

After a year or two, however, the interest became too deep or the pressure too great, and he entered the new field. Faithful to his method of experimentation, as contrasted with that of observation, he turned first to certain infectious diseases of animals, for in them observation and inference could be controlled and verified by experiment as it could not be in man.

It had been known since 1850 that the blood of cattle affected with splenic fever, or "charbon," contained vast numbers of a rod-shaped micro-organism to which the name *bacteridium* had been given. The disease had long been prevalent in Europe, and in France alone it annually destroyed horses, cattle, and sheep valued at from fifteen to twenty millions of francs. It is communicable to man, the so-called "malignant pustule" or "anthrax." Davaine

and Rayer had noted in 1850 the presence of the bacilli in the blood, but had drawn no inference from it. Thirteen years later Davaine was reminded of them by reading Pasteur's description of the microbe of butyric fermentation, and suggested, in a communication to the Académie des Sciences, that they were the cause of the disease. The matter had been rather tepidly discussed from time to time for several years, experiments had yielded conflicting results, and the claim of a causal relation between the bacillus and the disease was far from having been established. The question derives a peculiar interest from the fact that in 1876 it became the subject of some of the earliest studies in bacteriology of one whose fame in connection with that branch of science has since become world-wide—Prof. Koch. In the same year Pasteur began his investigation, and in the following year he was able not only to demonstrate the agency of the bacillus in producing the disease, but also to explain the contradictory results obtained by previous experimenters. He showed that the bacillus, to employ his own term, was *aërobic*—it needed free oxygen to live—and that consequently the death of the animal, by cutting off the supply of free oxygen, led to the death of most of the bacilli within it in a few hours. According, therefore, to the length of time that had elapsed between the death of the animal and the taking of its blood for inoculation would the experiment succeed or fail. He showed that the deaths that followed the late inoculations were due to an *anaërobic* microbe—one that did not need free oxygen—and thus was explained the absence of the anthrax bacillus from the bodies of those victims; the deaths were due to septicæmia, not to charbon. The investigation gave to science not only the full story of the bacillus of charbon but also that of a microbe of septicæmia, and the life history of each was traced with a completeness that made it possible to explain all apparent contradictions and obscurities. He made pure cultures, he traced the bacillus through all its stages, recognized those in which it is

vulnerable and those in which it can successfully resist the action of powerful antiseptics, and, in a word, discovered much that has since been again and again rediscovered and is often credited to others. He even followed the bacillus of charbon into the grave of its victim, and thence through the bodies of earthworms back to the surface of the soil, and even upon the blades of grass that grew over it.

Coincidently with the study of charbon he carried on that of chicken cholera, and he allowed himself to step aside for a moment from these two diseases, which can be studied so thoroughly upon animals, to discover the microbe of furuncles, of suppuration, and of osteomyelitis in man. With the latter he did nothing beyond the identification and the cultivation—his methods of further study were unavailable; but the study of charbon and chicken cholera was pursued until he had discovered and established a great principle whose possibilities for good elude even the grasp of the imagination. This great principle is the attenuation of virus, the reduction of the virulence of the microbe to a point at which inoculation with it will not kill, and yet will confer immunity against a subsequent attack. This discovery, the crowning work of his life, was made, like all his others, not by chance, but by prolonged search with this definite object in view. He had long meditated on the immunity against small-pox conferred by vaccination, and on the immunity against recurrence conferred by a number of infectious diseases, and had sought to discover how far the latter was true of the diseases he was studying. The first results were obtained with the microbe of chicken cholera. If this microbe is cultivated in sterilized broth and successive cultures are made at short intervals, the virulence remains unchanged; a drop of the twentieth culture will kill as surely as a drop of the first. But if the interval is lengthened, if the second culture is made after the first has stood for a few weeks or months, its virulence is less; and if this second culture is kept for a similar length of

time, the third, made from it, will be less virulent. Inoculation with the first kills all the fowls that are inoculated; inoculation with the second kills only a part of them; inoculation with the third kills still fewer; and finally a culture is obtained, from inoculation with which all the fowls recover after having been ill for a day or two. These survivors are then able to bear inoculation with the strongest culture: they have acquired immunity. Moreover, the microbes of diminished virulence thus obtained, the "domesticated" microbes, as they have been called, can be indefinitely cultivated and continued; it is not necessary to begin again with those of full virulence and repeat the attenuation. In short, a new disease, or a new form of disease, had been created, one that bore to chicken cholera the same prophylactic relation that cow-pox does to small-pox, and there was no danger that this protective disease would ever disappear and be lost; so long as chicken cholera existed its "vaccine" could be re-created, if necessary, by appropriate cultivation.

Jenner's vaccination against small-pox was the shrewd application of a chance observation of a certain relation between two existing diseases; Pasteur's discovery of the means of attenuating a virus and conferring immunity thereby was effected by long-continued, intelligent experimentation guided by wide observation and profound thought. The former was the brilliant utilization of a fact that had already been observed by others; the latter was the original discovery of a principle. If cow-pox were to die out vaccination would be at an end, but in the attenuation of a virus the disease is made to protect against itself: the bane bears its own antidote.

Pasteur at once sought to extend his study to other microbic diseases that conferred immunity when the attack was survived. He found by experiment that charbon was such an one, but unfortunately the mode of development of its microbe is different from that of the microbe of chicken cholera; the latter multiplies wholly by scission, the former develops partly by "spores" which

withstand exposure to the air and retain virulence notwithstanding prolonged delay in cultivation. He was forced first to find a mode of development in which the spores would not be formed. The personal side of the story of the search has been touchingly told by one of his children. Days and weeks were passed in experimentation. Pasteur became more and more absorbed and preoccupied; he went about with what his daughter called "his expression of impending discovery." To the timid questions of those who were waiting and watching with so keen interest, his only reply was that he could not answer, that he dared not formulate his hopes. At last he returned one day from his laboratory in triumph, and tears of joy rose to his eyes as he told the story of success.

The difficulty had been overcome by cultivating the germs in broth at a temperature of about 108° F.; this gave a steadily diminishing virulence, any grade of which could be subsequently maintained by suitable cultivation, and among these grades were some that were too weak to kill but yet were strong enough to protect.

The announcement of the discovery, on February 28th, 1881, was promptly followed by a challenge to a public test that should prove its truth or expose its falsity. Fifty sheep and ten cows were provided; half of them were inoculated with the attenuated virus, and three weeks later all, the vaccinated and the unvaccinated, received each an injection of full strength. It was done in the presence of a great crowd of farmers, veterinaries, physicians, journalists, and legislators, and two days later they reassembled to see the result. That result was a complete confirmation of the prediction. Of the twenty-five sheep that had not been protected by inoculation, twenty-two were dead and three were dying; the unprotected cows were living, but evidently very ill; all the protected animals, sheep and cows, were in perfect health.

A veterinary surgeon, who had been loud in expression

of his disbelief, was so overwhelmed by the success of the demonstration that he immediately offered himself for inoculation, and was saved from it only by the forcible interference of his family.

A few months later Pasteur sent one of his assistants to Berlin to repeat this demonstration before a committee appointed for the purpose, at his request, by the Minister of Agriculture; the committee, of which Virchow was a member, confirmed his statements at all points.

A third veterinary disease, the measles of swine, was next studied, its microbe discovered and cultivated, its virulence attenuated, and protection obtained.

It will be readily believed that, while he was thus so earnestly and successfully studying diseases of the lower animals, Pasteur was not unmindful of those affecting man. As I have already mentioned, he had isolated and cultivated the microbes of suppuration, of furuncles, and of osteomyelitis, and in addition he had studied those found in the blood of patients affected with typhoid or puerperal fever. In the latter he had recognized several distinct varieties—one of them the micrococcus of suppuration—and in a communication to the Académie des Sciences he had advised the employment of antiseptics in midwifery. He had already made the suggestion at the Maternité, where it was followed by the happiest results. But he felt himself disqualified from pursuing these lines of research by his lack of training in medicine, and by the impossibility of employing in them the instrument which he had learned to handle with such marvellous skill—experimentation. The only diseases of man that he could thoroughly investigate were those that also affected the lower animals. One of these had attracted his attention while he was engaged upon those that have been already mentioned, and when that work was finished he gave himself up wholly to it; and during the last few years it has become the one subject with which his name is chiefly associated in the minds of all save those who are professionally familiar with his other work. There is

much in this fact, too, that is saddening, for in connection with it he has suffered much, like other benefactors of the world, from those who, honestly perhaps, but none the less cruelly, ignorantly, and blindly, have grossly misstated his results and misrepresented both him and his methods.

This disease is hydrophobia. His study of it was seriously hampered at first by the difficulty of obtaining a pure culture of the microbe from the saliva and by the great length of the period of incubation under the then known methods of inoculation. He finally obtained the microbes from the nerve centres of animals dead of the disease, and made his cultures, not in flasks of sterile broth as he had done with the microbes of other diseases, but in the bodies of other living animals. He found that in a rabbit, inoculated from a rabid dog, the period of incubation was fourteen days; successive inoculations from rabbit to rabbit gradually reduced this period to a week, and when some eighty or ninety successive inoculations had been made (covering a period of more than two years) he had obtained a disease of uniform virulence. That is, if a small portion of the spinal cord of a rabbit that had just died of this disease was mixed with a little water and injected into a vein of another animal, the latter would certainly develop and die of the disease. He then sought to attenuate this virus so as to make it protective, and he found that this could be accomplished by drying the spinal cord; that if an animal received successive injections, under the skin, of portions of cords that had been dried in sterilized air for shorter and shorter periods, beginning with fourteen days, it could ultimately receive with impunity an injection of full strength. He found, next, that the protective action of these inoculations was more rapid than the deadly action of the poison introduced by the bite of a rabid dog; that, in other words, an animal that had been recently bitten by a rabid dog could be saved from rabies by these inoculations.

But to extend this protection from animals to man was

a step which he long hesitated to take. It was at last, in a measure, forced upon him. On the morning of July 4th, 1885, a little boy on his way to his school in a village of Alsace was attacked and severely bitten by a rabid dog. A physician cauterized the wounds with carbolic acid and advised the parents to take the child to Paris, where, as he said, was the only man who could do anything for him; he lived in the Rue d'Ulm, and his name was Pasteur. The advice was followed, and on the morning of July 6th the mother and child presented themselves at the laboratory. Pasteur, deeply moved by the distress of the parent and strong in the confidence his experiments had created, asked the advice of two professors in the School of Medicine who were familiar with his investigations. Both approved of the attempt, and the lad received his first injection that same day. On each succeeding day another and more virulent inoculation was made; and as the danger, if danger there was, was thus daily increasing, so increased likewise the anxiety of Pasteur. His days were agitated, his nights sleepless; and even long after the treatment had ended and the child had returned to his home Pasteur wrote to him every week, and then every fortnight, for news of his well-being.

Thus began the application of the remedy to man. The announcement of its success to the Académie des Sciences created a profound sensation; and when a second patient came to Paris for treatment—a brave young shepherd who had been bitten while defending some children from a rabid dog—the public press was filled with accounts of it, and for the time it was the topic of chief interest in the city. This interest promptly brought an important practical result. The number of patients applying for treatment became far too great for the limited accommodations of the École Normale, and a public subscription was opened, under the auspices of the Académie des Sciences, for the erection of a special building for the treatment of the bitten and for bacteriological study of infectious diseases. Subscriptions to this fund poured in

from all quarters; one of the largest gifts came from the Czar, in recognition of the saving of the lives of sixteen Russians who had been bitten by a rabid wolf; another came from the Emperor of Brazil, in recognition of the high scientific value of the work; another from Alsace-Lorraine, from which had come Pasteur's first patient; and a multitude of others from corporations and individuals throughout France. As has been said by a biographer, this time the prophet was not without honor in his own country. Far from it! In May, 1886, a festival was given at the Trocadéro in aid of the Institut Pasteur, at which the greatest celebrities of the literary, musical, and theatrical world of Paris assisted; and when Coquelin recited a poem in honor of the Master, the audience rose and joined in the greatest ovation that had ever been offered to a man of science.

But this subject, interesting as it is, must not now be followed further. The Institut Pasteur was established, and during the years 1886–1891 there were treated within it 11,029 individuals who had been bitten by rabid animals. Of these 98 have died. I quote from a report of the Board of Health of the city of Paris.[1] Comparing this mortality of less than one per cent (0.88 per cent) with the mortality among those not treated, as ascertained by the authorities of the city of Paris for the years 1887 (15.90 per cent) and 1888 (13.33 per cent), or with that given by medical writers (15 per cent), it appears that the work of this charity has already resulted in the saving of about 1,500 men, women, and children from death in one of its most terrible forms. In reply to a question addressed him a few weeks ago, M. Pasteur writes me that during the year 1891 201 persons living in Paris were treated at the Institut, with no deaths, and that during the same period, in the same city, four persons had died of hydrophobia from among the very limited

[1] Rapport sur les cas de rage humaine constatés dans le Département de la Seine de 1880 à 1891. Conseil d'hygiène publique et de salubrité, 1892.

number of those who had been bitten and had not been treated by inoculation. In addition to these 201 Parisians more than 1,300 other patients, coming from greater or less distances, were treated at the Institut Pasteur during the year, and similar institutions have been at work in seventeen other cities.

It would be interesting and profitable to study in detail the means and the methods by which these vast results have been obtained, but time forbids more than a brief reference to them.

Of his method, the experimental method, which he used with such transcendent skill; the method handed down to us by the great experimenters of the past—Galileo, Pascal, Newton—he has given us a description and an appreciation. "Admirable and sovereign method," he calls it, "which is always guided and controlled by observation and experience freed from every metaphysical conclusion; a method so fruitful that great minds, dazzled by its conquests, have believed that it could solve all problems.

"One can do nothing without preconceived ideas, but we must have the wisdom to believe in their deductions only so far as experience confirms them. Preconceived ideas, under the rigid control of experimentation, are the vivifying flame of the sciences of observation; their danger is in fixed ideas. Do you remember Bossuet's fine saying: 'The greatest disordering of the mind is to believe that things are because one wishes them to be'? To enter upon a path, and to stop every moment to make sure you are not going astray—that is the true method."

In these impatient times such a method seems all too slow; but see how far and how safely it has taken him. Doubtless his mistakes, his false routes, might be counted by thousands; but he himself detected and corrected them, and no step definitively taken has ever had to be retraced, no statement that he has ever made has proved to be incorrect. His caution in approaching a conclusion is equalled only by his assurance after it has been reached;

each is absolute. His comments upon puerperal fever were made almost with an apology. "I tell you these things," he said, "as they appear to me. But I do not forget that I am ignorant of medical science, and I earnestly ask for your judgment and your criticism." How different his tone when he felt himself master of the subject! "What!" he cried with magnificent scorn one day in the Académie de Médicine—"what! Do you say that I may have worked twenty years on a subject and yet should hold no opinion on it; that the right to verify, to control, to discuss, to interrogate, shall belong only to him who does nothing to throw light upon it, to him who, with his feet on the fender in his library, has only read, with more or less attention, the results of my labor? You say that in the present state of science it is the part of wisdom to hold no opinion [on spontaneous generation]. Well, as for me, I hold one, for I have earned the right to hold it by twenty years of assiduous labor; and it would be well for every impartial mind to share it."

To those who were not aware of the thought and labor upon which it rested, such absolute confidence might seem foolhardy and arrogant; but those who tested it soon learned to respect it, and those who had once met him in debate shrank from again falling into his redoubtable hands. "Come with me," said a man once—"come with me to the Academy and see me strangle Pasteur." "Take care," was the reply—"take care, my friend. Pasteur is a man who makes no mistakes."

Absolutely open and sincere, solicitous only that the truth should be known, he never hesitated to make public his reasons and his processes, to submit them to any open test, and to stand or fall by the result. When the discussion on fermentation was at its height, Pasteur went in person to Munich to show his experiments to Liebig. When spontaneous generation was in question, Pouchet was invited to make experiments in concert with him.

Challenged to a test upon a large scale of his proposed treatment of the silkworm disease, he had himself carried

upon a mattress across France and Italy to Austria, and from an estate which had not previously been able to raise enough silk to pay for the eggs they had to import, he there made in one season a net profit of twenty-six thousand francs.

We have seen his public tests at Paris and Berlin with the attenuated virus of charbon. When Koch at that time said that the theory of attenuation was too good to be true, Pasteur sought him at a scientific meeting at Geneva and publicly challenged him to a discussion. Koch declined, saying he would reply in print. A few months later he published a pamphlet accepting the discovery as one of the highest scientific value.

Few men have had so many scientific controversies, and no one, perhaps, has come out of them so uniformly successful and with his success so uniformly conceded. The latter fact is due in part to the resolution with which Pasteur has held himself and his opponents down to statements capable of proof or disproof. Sooner or later the debate would reach a point at which he could force an issue on some one decisive fact, and then he always demanded the appointment of a committee to determine that fact.

Heated as these discussions often were, ardent as was his support of his own views, and pitiless as was his exposure of error, it is a pleasure to note that on his side the personal element, in the unworthy sense, is always absent. His interest is in the truth, not in himself; and if he is intolerant of frivolous or prejudiced contradiction, if he grows impatient at times over the mental sluggishness of those who can only grope and crawl where he has run, it is only because of his burning zeal for the establishment and the advancement of the truth.

The work that we have thus followed has been done in almost exactly a half-century of life, the period between the ages of twenty and seventy years. And how magnificent it is when it is summed up!

In science he has laid at rest the theory of spontaneous

generation which for centuries had blinded and misled, and in its place he has given us a new world, that of "the infinitely small"; he has made clear the nature of fermentation, and by that explanation he has brought into one group of exquisite simplicity what had previously been a chaotic mass of unrelated processes and changes.

In medicine he has given us the science of Bacteriology; he laid the foundations of antiseptic surgery, by which hundreds of thousands of lives and countless limbs have been saved; he demonstrated the microbic nature of certain diseases, and he gave us the principle of protection by an attenuated virus with its vast possibilities for good, and he has himself applied that principle in one disease to save from a terrible death hundreds of our fellow-creatures.

I hesitate to close such a record with a reference to material gains, and yet, in the words of Prof. Huxley, Pasteur's discoveries would be sufficient in themselves to make good the war indemnity of five thousand million francs paid by France to Germany.

In the address which he made ten years ago on his reception into the French Academy, after an eloquent declaration of his faith in God, his belief in immortality, and his conviction of the reality of those lofty preoccupations which are put aside as non-existent by the positivists, Pasteur said:

"The Greeks understood the mysterious power of these hidden things. They gave us one of the most beautiful words in our language, enthusiasm—ἐν θεός, a god within.

"The grandeur of human actions is measured by the inspiration which gives rise to them. Happy is he who bears within himself a god, an ideal of beauty, and who obeys it—ideal of art, ideal of science, ideal of patriotism, ideal of the virtues of the Gospel. Those are the living springs of great thoughts and great deeds."

Pasteur's whole life has shown that he possesses such an ideal and that it directs every act.

May the happiness that he predicated of such a possession, the happiness that he has so abundantly earned by his devotion to the truth and by the benefits he has conferred, be his reward !

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