# SCIENCE

VOL. LVIII DECEMBER 14, 1923 No. 1511

CONTENTS



**SCIENCE: A Weekly Journal devoted to the Advancement of Science, edited by J. McKeen Cattell and published every Friday by**

**THE SCIENCE PRESS**

**Lancaster, Pa. Garrison, N. Y.**

**New York City: Grand Central Terminal.**

**Annual Subscription, $6.00. Single Copies, 15 Cts.**

SCIENCE is the official organ of the American Association for the Advancement of Science. Information regarding membership in the association may be secured from the office of the permanent secretary, in the Smithsonian Institution Building, Washington, D. C.

**Entered as second-class matter July 18, 1923, at the Post Office at Lancaster, Pa., under the Act of March 3, 1879.**

## THE CONTRIBUTIONS OF PASTEUR TO MEDICINE AND HUMANITY[1]

IN his éloge of Littré, Pasteur, speaking of the Greeks, says these words: "Ce sont eux qui nous ont legué un des plus beaux mots de notre langue, le mot enthousiasme—un Dieu intérieur. La grandeur des actions humaines se mesure à l'inspiration qui les a fait naître. Heureux celui qui porte en soi un dieu. . . ."[2]

Enthusiasm—a God within! Happy indeed is he who bears this "God within"! The son of a tanner, a non-commissioned officer of the Armies of Napoleon, Pasteur was born at Dôle in the Franche Compté on 27 December, 1822. His first studies were at the Collège d'Arbois, whither his parents moved while he was yet a baby. In 1839, he entered the Lycée of Besançon, where he received his Baccalaureat ès arts. In 1842, he became Bachelier ès sciences. In the same year he entered the École normale supérieur, fifteenth out of a class of twenty-two. Dissatisfied with this rank he resigned and went to Paris to an institution directed by a compatriot in the impasse des Feuillantines. There he followed courses at the Lycée St. Louis and listened to the lectures of Dumas at the Sorbonne. At the end of the year, he was admitted fourth in rank to the École normale. Not remarkable as a student, he was classed seventh in his examinations for license, and third out of four candidates who were received at the Concours d'agrégation; and when he presented himself for his Doctorat, his two theses received but mediocre appreciation.

But this modest student bore a "God within" which led him on his way. That pathway was singularly straight and direct, for, as has been pointed out by many, the logical sequence throughout all Pasteur's work is striking and remarkable.

Beginning as a chemist he was led fatally into questions of general biology and thence to questions of pathology and therapy, animal and human. To the careless eye the way might seem winding and beset

1 Address delivered at the Sorbonne on May 22, 1923, on the occasion of a meeting organized by the American Committee for the Commemoration of the Pasteur Centenary.

2 "They have given us one of the most beautiful words of our language, the word enthusiasm—a God within. The grandeur of the acts of men is measured by the inspiration from which they spring. Happy is he who bears a God within!"

by digressions, but from the patient labors of his early days to the triumphs of his maturity each observation led so naturally to the other—from his earliest studies in crystallography to his work on rabies—that the story of Pasteur's contributions to humanity and medicine is the story of his scientific life.

### Early Studies in Crystallography

In the course of his studies between 1848 and 1853, while repeating certain measurements of crystals of tartaric and paratartaric acid and their salts which had been made by Provostaye, he observed that the crystals of the tartrates bore hemihedral facets like those of quartz; the crystals were dissymmetrical, the facets occurring only on the right side; solutions rotated polarized light to the right. Crystals of the paratartrates, on the other hand, although chemically identical, bore like facets *symmetrically arranged on both sides; their solutions were optically inactive.* This led Pasteur to fancy that a relation might exist between the asymmetry of the crystals and the optical activity of their solutions—a relation like that between the asymmetrical crystals of quartz and the optical activity of blocks cut from them.

Struck by a statement of Mitscherlich that one of the salts of paratartaric acid gave rise to asymmetrical crystals similar to those of the corresponding tartrates, Pasteur discovered that, in reality, when this salt was crystallized it resolved itself into two groups of dissimilar, asymmetrical crystals of tartaric acid, which were reciprocally symmetrical; that is, each was as the image of the other in a mirror. The one group bore hemihedral facets on the right, the other, which was new to science, on the left. Solutions of the one deviated polarized light to the right, of the other, to the left.

The rotatory power residing in solutions of these crystals, Pasteur ascribed to like dissymmetry in the atomic structure of the molecules.

In this fruitful hypothesis as to molecular structure lay *the germ of the theory of stereo-chemistry.*

More than this, Pasteur observed that in fermentation of solutions of paratartaric acid, associated with the growth of a common mould (*Penicilium glaucum*) the organism, in its development, consumed the dextro-rotatory component of the salt, thus changing an optically inert solution of paratartrates to a laevo-rotatory solution of tartrates.

Considering, in connection with these studies, the optically active character of the principal constituents of living bodies, such as the albumens, the celluloses and the sugars, Pasteur conceived the importance of molecular dissymmetry in the phenomenon of life.

In these initial studies Pasteur one day broke a piece from an octahedral crystal and dropped the injured crystal again into its mother liquid. With the renewed growth of the crystal a special activity was evident at the injured spot; in several hours the crystal had assumed its original form. And Pasteur, whose active mind always cast about for the ultimate significance of his observations and discoveries, called attention to the circumstance that the cicatrization and repair of wounds might well be compared with this physical process.

In 1849 Pasteur was made professor of physics in the University of Strasbourg. There in the same year, he married Marie Laurent, daughter of the rector of the university—a noble woman who throughout his life was his patient and devoted companion and helpmate, his assistant, his adviser, his inspiration.

### Fermentations

Later, in 1854, when professor and dean of the faculty of sciences in Lille, the father of one of his pupils laid before him certain difficulties in the making of alcohol from beets and Pasteur began the study of fermentations. Here from the beginning it was his earlier experiences that guided him on the way.

The growth of yeasts in association with fermentation had been known and discussed from the days of Leeuwenhoeck in 1689, but despite the observations of Schwann and Cagriard-Latour, purely chemical and physical explanations still reigned. Fermentation, according to the prevailing ideas of the day (Liebig), depended on the breaking down of the molecule by decay and disintegration, set in motion by the presence of some dead nitrogenous material. Pasteur's observations had shown him that, excepting in the presence of a living substance, molecular dissymmetry, which renders a body optically active, disappears with the breaking up of the original molecule. On the basis of his experience he was convinced that a dissymmetrical disposition of the elementary atoms of the molecule on which optical activity depended, could be created only through the intervention of some vital process. That vital process was the growth of a yeast.

In the fermentation of potato amyl alcohol is produced which is laevo-rotatory; but the molecular constitution of the amyl alcohol is too far removed from that of the sugar from which it is derived to retain the molecular dissymmetry and the optical activity of the sugar molecule. In the creation of such a substance some vital process must have intervened. The question of lactic acid fermentation was especially intriguing to Pasteur because Liebig had asserted that here no yeast was present. But Pasteur showed clearly that this fermentation was dependent upon a living organism, a bacillus, so small that its presence had escaped the notice of others. The organism was the ferment. At first he called it a yeast, so unimportant to him was its form. As Delezenne has said, "It is not in form, it is above all in functional aptitudes that Pasteur found the proof of the specificity of micro-organisms. For the first time morphology made way for physiology in the definition of species."[3] He showed that the ferment reproduced itself, and at the very beginning he asserted: "The purity of a ferment, its homogeneity, its free development without interference, with the aid of a nutrient medium adapted to its individual character, this is one of the essential conditions for good fermentations." And again: "If, in the saccharine, albuminous, clear solution one sow the yeast of beer rather than that of lactic acid, it is the yeast of beer that will develop and with it alcoholic fermentation, although there be no change in the other conditions of procedure. One must not infer from this that the chemical constitution of the two yeasts will be identical any more than that the chemical constitution of two vegetables is the same because they have lived on the same soil." In other words, he pointed out the specificity of these organisms and their specific physiological action. Finally, in an experiment of great beauty and simplicity he demonstrated the growth of micro-organisms with fermentation in a liquid free from organic nitrogenous matter.

"Alcohol fermentation," said he, "is an act related to life, with the organization of the globules (yeast), not with death or the putrefaction of these globules."

In connection with these studies he pointed out that, "Each cell of yeast has properties of species and of race which it shares with the neighboring cells, and, moreover, special characteristics of its own which it may transmit to its progeny." Thus he called attention to variations of species, and in the end gave to the manufacturers of beer the precious principle of the selection of yeasts.

In 1859 he was nominated administrator of the École normale and assistant director of scientific studies.

The development of a method designed to secure pure cultures from fluid media, the use of culture media of known composition, and the careful chemical study of products of decomposition all belong to this early period of Pasteur's life and were achievements of the deepest significance. . . .[4]

### BUTYRIC ACID FERMENTATION—ANAEROBES

Upon these studies followed naturally the demonstration of the dependence of butyric acid fermentation on an organism which could develop only in the absence of free oxygen—the discovery of anaërobes. He showed how, in a fluid medium, the action of anaërobes follows that of the aërobes which use up the oxygen and by the film which they form on the surface of the liquids prevent its further entrance, thus preparing the way for the anaerobes in the depths.

### SPONTANEOUS GENERATION

Then, naturally (1860–1876), came the famous studies on spontaneous generation undertaken against the advice of his doubting masters, Biot and Dumas. On the basis of careful and well-conceived experiments he demonstrated the universal presence of bacteria in air, water, dust; he showed the variations in different regions of the bacterial content of the air; he demonstrated the permanent sterility of media protected from contamination, and he insisted on the inevitable derivation of every living organism from one of its kind. "No," he said, "there is no circumstance known to-day which justifies us in affirming that microscopic organisms have come into the world without germs, without parents like themselves. Those who make this assertion have been the playthings of illusions or ill-made experiments invalidated by errors which they have not been able to appreciate or to avoid." In the course of these experiments he demonstrated the necessity of reliable methods of sterilization for instruments or culture media, of exposure for half an hour to moist heat at 120° or to dry air at 180°. And behold! our modern procedures of sterilization and the basis of antiseptic surgery.

### STUDIES ON VINEGAR

Then came the studies on vinegar, undertaken in an attempt to relieve the embarrassment of an important national industry, and the demonstration that the formation of vinegar was a process of oxidation and dependent upon the development of micro-organism, *Mycoderma aceti*, which forms a pellicle on the surface of the liquid and serves as a conveyor of oxygen from the air without to the alcohol within, from which it gains its sustenance. He resolved simply and practically all the important questions at issue in connection with the protection of the manufacturers of vinegar. In the course of his studies he showed that in the absence of alcohol, its diet of choice, *Mycoderma*, might go farther and attack and disintegrate the acetic acid, the product of its own creation. This not only explained certain annoying phenomena associated with vinegar production, but was the first demonstration of the ability of a living organism to destroy the product of its own development.

It is most interesting to note, by the way, that in

[3] 100th Anniversary of the Birth of Pasteur, Bulletin de l'Academie de médicine, 3, series, tome LXXXVIII.

[4] Herter, Johns Hopkins Hosp. Bull., 1903, XIV, 325.

studying enfeebled, "diseased" *mycoderma,* as he called it, he likened the oxidizing activity of the micro-organisms to that of the red corpuscles of the blood whose function it is to carry oxygen to the tissues, and asked himself what might happen in the human body if the diseased red blood corpuscles were inadequate to their task of oxidation.

Fascinating and interesting it is to see how, all along the way, his fertile, active mind sought the parallels between his observations and the diseases and injuries of man.

Certain manufacturers had taken advantage of his previous work and had secured patents for their own interest. To prevent the repetition of such a procedure before announcing a "new industrial procedure for the fabrication of vinegar" he took out a patent himself, and threw it open to the public.

### DISEASES OF WINE

Then he passed to the studies of the diseases of wines (1865) which he found once more to be due to the development of living organisms. It was easy to prevent their development by sterilization, but how could this be done without destroying the wine? In the end he showed how the further development of the bacteria could be inhibited by rapid heating to 55° in closed vessels, at the proper period, and we have the process of *"Pasteurization!"*

### DISEASES OF THE SILKWORM

The silkworm industry, so vital for France, was in sore distress. An epidemic disease increasing in severity was ruining the population of the south, who appealed to the government. Pasteur, a chemist, who knew nothing of the silkworm or its diseases, was requested to undertake the investigations into the nature of the disease and measures for its prevention. For six years, from 1865 to 1871, he gave his whole time to this work.

The silkworms, raised from the egg by exposure to gentle heat at the moment when the first leaves of the mulberry tree are opening, are covered immediately by young leaves upon which they feed. The worms seem to sleep as they clothe themselves with one skin after another from which, in succession, they moult. After the fourth moult, they pass through several days of extreme activity and voracity, following which they climb upon sprigs of heather carefully set out for them and form their cocoons. In the cocoons they remain for fifteen days. After this the moths emerge, sex-union occurs, and six hundred to eight hundred eggs are laid by each worm. If it be decided to use the cocoon for the manufacture of silk they are smothered in a vapor bath six or seven days after the worm has ascended the heather twigs. If, however, it be desired to collect eggs for the next brood, the emergence of the moth is awaited. When a brood appears especially good, through the regular development of its worms and the beauty of the cocoon, it is saved for its eggs.

For twenty years this disease had existed, and despite the importation of eggs from foreign countries, it had become worse and worse; it was known as Pebrine because of little, black, pepper-like spots which developed upon the diseased worms. In the diseased worms and in the eggs there had been found small, round corpuscles (psorosperms) which were regarded as evidence of the disease, and Osimo of Padua had already suggested that eggs should be saved for cultivation only from worms which did not contain corpuscles. But this measure had not been carried out with any regularity, and the true nature of the disease remained unknown.

In two years Pasteur solved the main problem. Although slow at first to recognize the infectious nature of the "corpuscles," he finally demonstrated that they were the infectious agents, that they might be introduced through the gastro-intestinal tract from leaves soiled by diseased worms; that they were hereditarily transmitted through infected eggs. He saw that the secret of protection lay in the microscopical examination of the moths at the time of their emergence from the cocoon, and that where more than 10 per cent. of these moths were "corpuscular," the eggs should not be used. By maintaining the cocoons at a temperature of 25° to 30° R, the emergence of the moths was hastened by five days. Test cocoons were submitted to high temperatures and where the number of diseased moths was too great, the attempt to collect the eggs was abandoned and the entire brood was used for the cocoon.

But this was not the whole story. Although, under these methods, the recovery of the silk industry seemed to be promised, yet there were puzzling circumstances. Sometimes the disease seemed to precede the appearance of the corpuscles; this might indeed occur in experimental infection of the worms. One day, with a despairing gesture, Pasteur announced to his colleagues that they must begin again; there were two diseases!

But in due time he solved the problem of the other disease, a sort of typhoid or cholera of the silkworm, due to organisms widespread in nature. This malady was generally transmitted from worm to worm through the sticky excrement shed by diseased animals upon the leaves upon which they fed. *Flacherie,* as it was called, occurred alongside of *Pebrine* and had thus caused considerable confusion. Flacherie also was an hereditary disease.

With this knowledge the necessary prophylactic measures were soon devised. Pasteur had but to add to his former directions: "One should never use for eggs broods which have shown from the fourth moult to the cocoon, any languishing worms, or which have shown definite evidences of flacherie," and the silkworm industry was saved.

In the course of these studies Pasteur made observations of great interest. He found, for instance, that the period of incubation of the disease varied according to different circumstances; that when the infectious agent was carried from worm to worm through a series, the period of incubation was shortened. Repeated passages of the parasite through successive hosts increased its virulence.

He noted the difference between the period of incubation in worms infected by means of hypodermic injections and those acquiring the disease in the usual manner—*the influence on the period of incubation of the portal of entry:* he recognized that although the infectious agent was widespread, almost always present, the disease did not always arise; some worms seemed to resist infection—in other words, there were *variations in resistance and susceptibility of the host.*

As Duclaux says, he had brought the great questions of contagion and heredity into the field of experiment.

At about this time, the study of a mould, *Mucor-mucedo,* led him to appreciate the *possibility of the anaërobic life of aërobic species and the variations in form of an organism which may accompany the variations of the media in which it lives.*

He then returned to his studies of wine, led by the desire to discover whence came the organisms which caused the alcoholic fermentation of grapes. By simple but ingeniously devised experiments, he showed that these organisms, *Saccharomyces,* were widely distributed and were to be found on the surface of the individual grapes. But they appeared only at a definite time in the development of the grape, at a fixed season of the year. On the other hand, the *mucor* parasites capable also of producing a fermentation were present at all times in the soil.

And his alert mind, ever seeking analogies between these processes in the vegetable kingdom and human disease, led him to these prophetic reflections:

> May we not, by analogy, be justified in the belief that one day simple and easily applied measures of prevention will arrest these scourges which at one blow desolate and terrify whole populations such as the terrible disease (yellow fever) which has recently invaded Senegal and the Valley of the Mississippi, or that other (bubonic plague), more terrible perhaps, which has raged on the banks of the Volga?

In 1874 there came to Pasteur from Edinburgh a grateful and appreciative letter from Joseph Lister, who called attention to the beneficent results which had followed the application of his principles, scrupulous cleanliness, antisepsis, to the practise of surgery. An era had passed—the old black era of helplessness and uncertainty, of cruel doubt and hope deceived. The hand of the surgeon was freed.

### ANTHRAX

While the old controversies concerning fermentations and spontaneous generation still continued, the victory was already won, and more and more Pasteur's mind turned towards the practical application of his discoveries to diseases of higher animals and man. For this, as Duclaux has so clearly pointed out, he was well prepared. His demonstration of the specificity of micro-organisms, his observations on their life history, and especially of their nutritive demands, his studies concerning the increase and diminution of virulence, of the variation, under different conditions, of the resistance of the host to infection—all these observations and conceptions had taken root in his mind and it is but natural that he should have turned to the study of infectious diseases in the higher animals.

In 1877, he began the study of anthrax—a cruel disease, fatal to sheep and cattle, especially the former. Sometimes nearly half a flock died in one season. There were special regions which seemed fatal, fields or hillsides on which sheep might not feed, over which they might not pass without acquiring the disease. To what was this due? For many years (Delafond, 1838) the existence of little rodlets in the blood of animals dead of anthrax had been known and the question as to the infectious nature of these rodlets had been raised (Davaine, 1850). Pasteur had discovered resistant spores in the bacillus of Flacherie, structures destined to preserve the life of the organism through long periods under adverse conditions. Koch, but a year before, had pointed out like spores in the bacillus of anthrax. More than this, Koch had cultivated the bacilli in the aqueous humor of the eye and in fresh drops of the blood serum of the ox. These cultures he had carried through eight generations, and from them he had transmitted the disease to small animals. But some objectors still raised the question as to whether he might not have carried over some vague virus from one to another of these small cultures.

Pasteur cultivated the bacillus in flasks containing fifty cc of neutral or slightly alkaline urine and succeeded in carrying on these cultures indefinitely from generation to generation. The tenth generation was as capable of transferring the disease as the first. Here one could hardly imagine the transference of a virus other than the bacterium. Fowls were refractory to the disease.

### GAS GANGRENE

During Pacteur's studies concerning the specificity of the bacillus of anthrax, other observers in carrying out inoculations from animals dead with the disease had produced a fatal illness without the presence of the bacteridia. Pasteur discovered in the blood of these animals another organism, a long bacillus, found normally in great numbers in the intestinal tract, which, after death, might enter the blood and develop more rapidly than does the organism of anthrax. When both organisms were introduced at the same time the animal died from septicaemia due to the multiplication of the other bacteridium which he called *Vibrio septique,* before *Bacillus anthracis* had time to grow. The new organism, closely allied to the so-called gas bacillus of Welch, was anaërobic and produced gas in the tissues of the animal infected—the familiar gas gangrene.

In a communication to the Academy of Medicine made on April 30, 1878, Pasteur points out the danger of the entry of such organisms into the tissues, their relation to surgical gangrene, and insists on the importance of antisepsis in surgery. These are his closing words:

> A few weeks ago one of the members of the section on medicine and surgery of the Academy of Sciences, M. M. Sédilot, after having meditated long on that which he had learned in a brilliant career, found a rational explanation in the principles on which rest the so-called germ theory, and that this would give rise to a new surgery, already inaugurated by a celebrated English surgeon, Dr. Lister, who, one of the first, had comprehended its fecundity. Without professional competency, but with the conviction of the qualified experimenter, I shall dare here to repeat the words of our eminent confrère.

These were busy days in which Pasteur's vision, penetrating into many vistas, was constantly making fresh observations and new discoveries.

Fowls he had found resistant to anthrax. But the organism of anthrax is readily killed at high temperatures, and the ordinary temperature of a hen is 43° or 44° C. If the lower third of the body of a fowl be held immersed in water at 25°, the body temperature may be lowered to that of man or those animals susceptible to anthrax. But introduced into a hen with lowered temperature, the bacillus throve and multiplied, and the fowl died.

### Staphylococci and Streptococci

New observations succeeded one another in rapid succession. In 1879, Pasteur discovered in abscesses of the skin little round organisms which grew in clumps like bunches of grapes, whence the name, Staphylococci, and later he found the same organisms in an instance of osteo-myelitis, which, forthwith and quite properly, he called an "abscess of the bone-marrow."

In the *maternité* he found similar round organisms, arranged, however, in chains (Streptococci) in the lochia of women with puerperal fever and in the diseased tissues of those who had died, and he suspected immediately that this organism was the cause of the disease.

At a meeting of the Academy in a discussion on puerperal fever, Pasteur, impatient, interrupted the speaker. "That has nothing to do with the cause of the epidemic; it is the doctor and his personnel who carry the germs from a diseased to a healthy woman." And when the orator replied that he doubted whether such an organism would ever be seen, Pasteur dashed to the blackboard and figuring a chain of streptococci, exclaimed, "There, behold its picture."

In 1806 at the *maternité* one woman in four died of infection; to-day at the Baudeloque (Calmette) the mortality is one in two thousand.

In the words of Descour, "Thanks to Pasteur, maternity hosiptals are no longer ante-chambers of death."

### Chicken Cholera—Vaccination

Next, Pasteur took up the study of a disease of poultry, chicken cholera, a disastrous epidemic malady which played havoc in the poultry yards. A parasite had been discovered by others and suspected of being the cause of the disease. Toussaint had shown that the disease could be transmitted by the blood of the diseased chicken; but he had failed in his efforts to cultivate the germ. He sent Pasteur the head of a cock dead of chicken cholera. Pasteur found the small bacillus which failed to grow in ordinary media but developed rapidly upon that which his insight soon suggested, a broth made of the muscles of the chicken itself. The infectious agent entered by the gastro-intestinal tract, passed out through the excrement and was thus scattered about the poultry yards.

In guinea pigs the organisms of chicken cholera produced only local abscesses, but retained their virulence; and Pasteur pointed out how such infected pigs might, through discharging abscesses, spread the disease—the first example of carriers.

One day, after a vacation, he inoculated some fowls with an old culture which had stood, untouched, for some weeks; the birds were but slightly ill—and recovered. What had happened? He inoculated the same fowls with fresh cultures; they remained unaffected. But fresh fowls, inoculated for the first time with these same cultures, died in the usual manner. The old cultures had lost their strength. *Inoculation with these old, attenuated cultures had conferred immunity!* Pasteur had made his greatest discovery, that of the possibility of preventive vaccination!

It was no mere accident. To his prepared mind the experiment had immediately suggested itself. The analogy with Jenner's vaccination against smallpox was instantly grasped—an analogy in a disease known to be due to a micro-organism! The attenuation of the virulence of the cultures depended on their age. According to the age of the cultures, every degree of attenuation could be obtained. The characteristics of each generation of cultures were hereditary and fixed. Pasteur, as Roux has said, obtained races of virus as gardeners obtained races of flowers.

It was not so much that a method of preventing a disastrous disease of poultry yards had been found; the door had been opened.

Pasteur had meditated and speculated on many possibilities. Among other things he had noted that in certain cases, instead of killing rapidly, chicken cholera passes into a chronic state, the fowls succumbing only after weeks and months of languor. But when the parasite is grown from these birds, its virulence, contrary to what one might expect, is exalted to a maximal degree. And he observed that this interesting example of the combat between host and parasite found an analogy in those instances of rabies with long periods of incubation. Rabies already was in his mind. He was ever reaching for analogies. Among his papers of this period is a project for the study of plague such as that later and so fruitfully carried out by his pupil, Yersin.

### PROPHYLAXIS OF ANTHRAX

At the same time Pasteur was still pondering upon the subject of anthrax. The neighborhood of a pit in which diseased animals were buried was notably dangerous. He had demonstrated living spores on the surface of the earth as long as twelve years after burial of the animals. How could these spores on the surface of the earth stand the dispersing influences of wind and rain? Where did they come from? Could it be that they arose from the depths? If so, how?

One day while walking in such a field freshly harvested, he noticed certain spots which differed from others in colour. These were the areas in which diseased animals had been buried. He examined them closely. The soil was thickly covered with the castings of earth worms; and the truth flashed upon him. It was the earth worm in its silent labor of aëration and drainage of the soil, burrowing to the depths and bringing again to the surface those particles which it deposits in its little spiral castings, it was the earth worm that brought to the surface again the spores of anthrax. He demonstrated spores in worms and in castings—and straightway an important measure of prophylaxis became apparent, namely, that diseased animals, if they could not be disposed of otherwise, should be buried only in dry, barren, sandy soil.

### VACCINATION AGAINST ANTHRAX

The minister of agriculture demanded that Pasteur investigate a method of treatment of anthrax introduced by a veterinarian in the Jura. In the course of this study he was given two cows which had recovered from the disease. They resisted inoculation with virulent cultures. They were immune. Vaccination was possible. But how produce the vaccine? The spore-producing characteristics of the anthrax bacillus rendered this procedure difficult and puzzling. The organism does not grow at temperatures above 44°. Between 42° and 43°, however, the spores are no longer formed. If cultures are kept at this temperature for about a month, the time comes when they cease to grow on transference. With the age of the culture, virulence for sheep, rabbits and guinea pigs diminishes rapidly and progressively until it disappears. The characteristics of the organism at each age are stable, but the virulence may be raised immediately by passing them again through successive living subjects, beginning with the young, which are most susceptible, and passing the organisms through successively older animals. The analogy with the bacillus of chicken cholera was complete. Might not the cause of some spontaneous epidemics be the reëstablishment of virulence in an organism which had reached a degree of attenuation so great as to be almost if not quite innocuous?

It was but a step to vaccination against anthrax with attenuated cultures. And when he was ready, the efficiency of the measure was demonstrated in dramatic fashion. Before a large audience, fifty sheep were inoculated with a highly virulent culture of anthrax. Twenty-five of these sheep had previously been vaccinated with attenuated cultures. The non-vaccinated sheep all died; the vaccinated all recovered. A reliable measure of prophylaxis against anthrax had been established.

### SWINE FEVER

In March, 1882, Thuillier, at Pasteur's request, began the study of swine fever, a fatal and widespread disease. The pathogenic organism, a small bacillus, was soon isolated. Pasteur remembered his observations on the organism of rabbit septicæmia which he had found a year or so before in the saliva of a child with rabies. Although harmless for old guinea pigs, this organism was virulent for the young. Passed through a series of young animals, the virulence was so far raised that it became pathogenic for the old as well. But he had made this striking observation: *In the course of its passage through guinea pigs the organism had lost its virulence for rabbits.* In these regions where swine fever prevailed, epidemics were frequent among pigeons and rabbits. The bacillus of swine fever killed pigeons rapidly and by passing the organism through a series of pigeons, its virulence, both for pigeons and for swine, could be raised to a degree considerably above that attained by strains carried alone from hog to hog. The same bacillus killed rabbits, but, although on successive passages through rabbits its virulence was augmented for them, the virulence for swine became progressively diminished, so that in the end an attenuated organism was obtained—capable of transmitting to swine a mild disease only, from which they recovered with an immunity lasting at least a year. A method of vaccination was at hand. Swine fever in its turn was conquered.

## Rabies

That the mystery and the hopelessness of rabies had long been in Pasteur's mind is clear from the occasional references to the disease that appear in his earlier studies.

In 1880 the opportunity came to observe a patient in the wards of Lannelongue. From the sputa, as has been mentioned, he had obtained the bacterium of rabbit septicaemia which later turned out to be the pneumococcus of Fraenkel. All further attempts to cultivate a pathogenic organism failed. By introducing subcutaneously bits of the central nervous system, he had transferred the disease, but the period of incubation was distressingly long and uncertain, amounting sometimes to months.

Finally, by introducing bits of the substance of the medulla of affected animals under the dura mater of the brain, he succeeded in transmitting the disease with certainty, with an average incubation period of about fourteen days.

And then, guided by his experience with other organisms, which he had studied, he succeeded, by repeated passage from rabbit to rabbit, in obtaining a virus of great strength and of an incubation period of a maximum of seven days.

By passage through monkeys the virus could be attenuated to such a degree as to be nearly harmless on subdural introduction into the dog. *These injections conferred immunity.*

He reflected on the long incubation period following the bite and the short period which elapsed between the inoculation and the outbreak of the disease when the strong virus from rabbits was used. Might one not, by subjecting the cords of these rabbits to the action of oxygen in dry air, produce an attenuated virus which would yield a safe vaccine? And with such a vaccine with a short period of incubation, might one not hope, even after the patient was bitten, to produce immunity against the more slowly developing virus introduced by the bite?

Cords of rabbits dead with malignant rabies of an incubation of seven days were subjected to the action of oxygen in jars containing a little caustic potash. Attenuation was readily obtained.[5] By subcutaneous injection daily of bits of these cords of progressively increasing virulence, it was possible to immunize dogs to the most virulent material even if introduced under the membranes of the brain.

At this point in his studies there was brought to his laboratory a little Alsatian boy who, sixty hours before, had been terribly bitten by an obviously mad dog—bitten in such a manner that the development of the disease seemed certain.

Pasteur took counsel with his friends, and acted. He suffered, in silence, cruel anxiety. In nine days the little boy had finished his treatment and had received, finally, injections of the most virulent material, material tested step by step on control animals. The boy was saved. Others followed. The almost universal success of the treatment if begun early, was proven beyond a peradventure.

In 36 years, out of nearly 45,000 patients brought to the laboratory at various periods after the bite, the mortality had been but three per thousand.

The name of the master and the fame of his accomplishments were on the lips of all the world. Honors poured upon him. National subscription built the Institute, that Institute of which he has said: "There is not a stone which is not the material evidence of a generous thought," and there and in all lands thousands of his disciples continue the work that he initiated.

This, in brief, is the story of Pasteur's contributions to medicine.

And the man?

An artistic nature, gifted with powers of design that, early in life, seemed to point to another career.

A sensitive, poetic spirit which betrays itself again and again in the charm of his language. But the emotions of the artist and the poet were controlled by an overpowering love of truth and the censorship, in matters of science, of a Puritan conscience.

He was a noble example of the disinterested student. When asked by the emperor why he sought no material advantage from his discoveries he replied: "In France men of science would consider such an act unworthy."

He was intensely human—human, if one may say so, in his very humanity, for with all his love of pure science, he was forever asking himself how he might use his achievements for the benefit of his country and his fellows; human in his tender-heartedness and gentleness and love for animals; human in his impatience toward opposition, for he was not always patient

[5] In the sense, possibly, only of a diminution in the *number* of organisms.

under criticism, especially if that criticism were born of prejudice or supported by careless or ill-formulated experiments or observation—against such opposition his polemics were sharp; nor in hours of work was he especially tolerant of those futile interruptions which are the despair of the student; human in his devotion to his parents and to his family, and in his profound patriotism.

From the foundation of the institute to the day of his death, in 1895, his quiet life among his friends and his students in the laboratory was a long triumph. As it has been said of Jeanne d'Arc, so was it true of Pasteur—he had become a legend while yet he lived.

Early in his career he had risen again from a physical blow that too often saps the vigour and initiative of the strongest. The "God within" carried him forward and onward over obstacles and through trials that would have baffled another.

Now, he was tired. The loving homage of grateful humanity was almost a burden. But he lived to see the first of the harvest, and he died with the world at his feet.

In the 40 years of his active life Pasteur laid the basis of our knowledge of infections and infectious agents from which such inestimable blessings have flowed; he "revivified the biological sciences" (Herter), but more than this, as Widal has well said, he introduced into medicine accuracy and precision of technique and the habit of experimentation—"the realization of the necessity of precision and the means of satisfying it."

From the seed that he sowed, what a harvest has come forth! Improvements of technique introduced even during his life time have brought increasing certainty and accuracy into our methods. One after another the plagues of humanity are yielding their secrets to inquiring students. The questions of immunity and susceptibility on which he had but begun to ponder have expanded into profound and complicated problems which for their explanations are turning us more and more back to the fundamental chemical and physical principles with which he began.

The scope of preventive medicine, which, one might almost say, began with Jenner and Pasteur, has widened until problems of public hygiene have become, throughout the world, matters of civic, national, international concern.

And finally, as Calmette has said:

> Dans l'ordre social l'oeuvre de Pasteur n'a pas été moins féconde. En nous faisant connaître la cause des maladies, en nous montrant que ces causes sont justiciables de notre intervention, elle a complètement modifié les anciennes conceptions du devoir social vis-à-vis des malades.
>
> Cet ensemble de notions nouvelles, derivées de l'oeuvre de Pasteur et imposées à nos consciences par les sentiments plus vifs de solidarité que dévelope la civilization, constitue ce que nous appelons l'hygiène sociale. On peut envisager celle-ci comme la base même de la politique, science encore au berceau, quoique née déjà bien des siècles avant Aristote, mais science qui a ou plutôt qui devrait avoir pour essentiel object la conduite des peuples.[6]

Prophetic words! To-day in a world distracted, crippled, poisoned by the venom of war, there has risen one star of real hope—those efforts under the League of Nations, through the activities of the International Red Cross, to extend this work of Social Hygiene in its broadest sense. In this one field all have joined hands. In this one field jealousies, suspicions, selfishness, self-interest, are drowned in a common will to unite in combating the ravages of disease; in making the world a safer, better place to live in, that man may be stronger, wiser, saner; that the future may be spared some of the tragedies that we have known.

How far these beginnings may lead, we know not, for the future is veiled from the eyes of men. But this we know; they can lead only to better days.

The world is one in its will to strive for the continuation of the work of Pasteur.

France gave to the world this man—France, to whom humanity and civilization owe so much of that on which they rest—France, serene, wise, radiant with the beauty that was Greece—France, to whom we of the western world owe our existence as a nation—We salute you in the name of your greatest son! Through him you have laid the foundations of the true science of politics that shall one day bring a fuller measure of peace and happiness to a troubled world!

William Sydney Thayer

## REPLY TO AMERICA

A half century ago on the other side of the Atlantic a nation began to take cognizance of itself, young, confident in its healthy vigour, impatient in its forward march, reaching out eagerly towards the future, knowing no obstacle to its will to attain generous ends.

[6] "From a social standpoint the work of Pasteur has been no less fruitful. In revealing to us the causes of disease, in showing us that these causes may be controlled, it has profoundly modified the old conceptions of the duty of society to the sick.

"This body of new conceptions springing from the work of Pasteur and imposed on our conscience by the more acute sense of solidarity developed by civilization constitutes that which we call social hygiene. This one may regard as the very corner-stone of politics, a science yet in its cradle, although born centuries before Aristotle; a science, however, the essential object of which is, or rather should be, the conduct of peoples."

One of its own poets[1] prophetically said: ". . . ,
Whence to arise inevitable in time, the towering roofs, the lamps,
The solid-planted spires tall shooting to the stars."

And soon Europe felt herself fanned by the breath which from the Pacific to the Atlantic animated the new world. America brought a new youth to the universe.

At the same time there arose on the soil of France a man whose genius was to penetrate to the very foundations of life and to liberate humanity from the bonds which enslaved it to deadly plagues. This man who had made himself—a "self-made man" according to your fine expression—was gifted with most exceptional virtues, without which he could not have built up the gigantic structure of his work which was to be the greatest revolution in the domain of the mind that the world had ever known.

Enthusiasm dominated his character and magnified his life. He had faith in his mission. He went straight to his end towards the great horizons that his genius divined already at the age of 26. His poetic imagination gave wings to his thought, but he knew how to discipline himself, and, by a severe control, to become his own implacable adversary. Tenacious, indefatigable in his pursuit of truth, he knew not discouragement and repeated continually to his disciples: "No effort is lost." Skepticism alone was hateful to him and to his fascinating spirit. His mind full of speculations, the most prodigious that had issued from the human brain had, always practical realizations for its goal, for he was ever obsessed by a sense of duty to render service and considered science as a dispenser of blessings. He was audacious and like all great leaders of men he knew how to play his all at the decisive moment. He was attracted by all that is great and beautiful. His motto was: "Look upwards, peer into the beyond, seek always to raise yourself." He loved his country with a passionate love, and wished that upon her might shine the lustre of his discoveries; but he did not distingiush love of country from love of humanity. His generous soul looked toward the intellectual and moral union of all nations. His pity covered the world, that pity forever active which prompted him to say: "One does not ask of an unfortunate, 'Of what country or of what religion are you?' One says to him: 'You suffer.' That is enough; you are mine, and I will help you.'"

America recognized herself in this son of France. All the virtues that make peoples great, these she found united in him. She took him for model and guide. He became her ideal.

From his laboratory in the École Normale, empty, without endowment, without credit, Pasteur had written: "Concern yourselves, I beg of you, with these sacred dwellings that we designate with the expressive term, *laboratories*. Demand that they be multiplied, that they be adorned; these are the temples of the future; the temples of wealth and happiness. There it is that humanity grows and becomes better. There it learns to read in the atcivities of nature manifestations of progress and universal harmony, while these activities of themselves are too often those of barbarism, fanaticism and destruction."

Then one saw rising on the soil of America, on every side, universities and professional schools such as the Johns Hopkins, great laboratories, those admirable institutions such as the Rockefeller Institution, which are your pride and your glory. The dream of Pasteur became a reality and more. Your laboratories were animated by the intellectual sons of Pasteur, Flexner, Theobald Smith, Noguchi, Carrel, MacCallum, Loeb and so many others. Their discoveries were the offspring of the methods of Pasteur. All Pasteur's discoveries in chemistry, in agriculture, in medicine, in hygiene, America applied them and developed them. Deadly epidemics she knew no more. Her children by thousands were snatched from the clutches of death. She pushed back the limits of human life and diminished suffering. Her unhealthy spots were transformed into prosperous regions. She became the land of promise that we coveted. In a few years she realized an expansion such as one had not seen in the history of mankind. No conception seemed too daring for her. With her realization kept pace with thought. Her most audacious enterprises were so many successes.

Perseverance in effort, tenacity in the pursuit of the end to be attained, certitude that all is possible to him who knows how to will; enthusiasm for all causes that were just and true; love of country combined with love of humanity; all the guiding qualities of Pasteur, your children reached out to grasp them. And before your universities, in your public places, in your laboratories and your hospitals and your colleges, everywhere stands the tutelary effigy of him whom you venerate.

How deep was my emotion, 18 months ago, when I found in your country that cult of Pasteur, a cult springing from comprehension, admiration and love! You who came to fight by the side of that people which gave Pasteur to the world, it was your desire some months ago in Philadelphia, in New York, in Chicago, it was your desire to-day in this ceremony which will remain dear to all Frenchmen, that your hearts should once more thrill in unison with ours, and—one of those touching thoughts which are so characteristic of you—you have sent two of your distinguished pathologists whom we venerate and love, Professor Welch and Professor Thayer, to celebrate our Pasteur, who is yours, too.

In this hymn of gratitude which has been rising

[1] Walt Whitman: "Leaves of Grass."

from all nations for the last six months—that which Pasteur would have appreciated beyond all—it is as a resurgence of hope of humanity for peace and concord among the peoples of the world. And at this moment does it not seem to you, gentlemen, that Pasteur is here among us, as he was thirty years ago on his seventieth anniversary? Do you not hear him say to you as he did then, those words which should become a reality: "You bring me the deepest joy that can come to a man who believes invincibly that science and peace will triumph over ignorance and war, that the peoples of the world will come together, not to destroy but to build, and that the future is to those who have rendered the greatest service to suffering humanity."

PASTEUR VALLÉRY-RADOT

PARIS, FRANCE

## THE AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

### THE CINCINNATI MEETING

PREPARATIONS for the third Cincinnati meeting, which will celebrate the seventy-fifth anniversary of the founding of the association, are in an advanced stage. The meeting is to open on Thursday, December 27, and will close on Wednesday, January 2. The general secretary and the permanent secretary recently visited Cincinnati and conferred with members of the local committee that has charge of preliminary arrangements. The local committee, under the able chairmanship of Professor Louis T. More, has everything well in hand. Especially has Professor Edgar Dow Gilman, secretary of the committee, rendered very efficient and invaluable service to the association and to the thirty societies that are to meet with the association at Cincinnati. Nearly all the meeting rooms have already been assigned, and arrangements have been made for the several general sessions, for the exhibition of apparatus, etc., and for the registration offices.

The preliminary announcement of the approaching meeting, a booklet of eighty-five pages, has just been issued from the permanent secretary's office. Copies have been sent to all members of the association and to others who are members of societies that are to take part—as far as the requisite lists have been furnished by the societies. The booklet contains more information concerning the approaching meeting than has been possible in the case of any similar announcement in past years. Also, it has been possible to publish this announcement earlier than in recent years, because of improving cooperation among the Washington office, the local committee and the section and society secretaries and committees.

The most important message carried by the announcement is perhaps the statement that reduced railway rates are available for those who are to attend, from practically the whole of the United States and Canada. These are to be secured on the certificate plan, as in recent years. A first-class, full-fare, one-way ticket to Cincinnati should be purchased and a *certificate* for the American Association for the Advancement of Science meeting, on *standard certificate form,* should be secured. The certificate is to be left at the validation desk in the registration room, upon arrival; it will be endorsed and validated without further attention from its owner and may be secured at the same desk on a later day. The railway agents at Cincinnati will sell each holder of an endorsed and validated certificate a continuous-passage return ticket for one half of the regular fare, by the same route as that followed in the trip to Cincinnati. Thus the round-trip will cost those who attend the meeting an amount equal to one and one half times the regular one-way fare. This privilege will be available to all who are members or associates of the association in good standing, or who are members of any society or organization meeting with the association at this time, or who are members of any society officially associated or affiliated with the association, or who are delegates from institutions or personal guests of persons entitled to reduced rates. Registration will be necessary in order to secure the reduced railway rates, and all who register will receive the badge for the meeting and a copy of the general program.

Several new features will characterize the seventy-fifth anniversary meeting. There will be a prize of one thousand dollars awarded to some person presenting a notable contribution to the advancement of science, either before the association as such or before one of the societies. It is planned that several supplements to the general program will be issued as the meeting proceeds, thus bringing to publication any program material that may be received too late for inclusion in the regular edition, additions, corrections, etc. An exhibition of scientific apparatus, products and books is being arranged and a good number of exhibits are already entered. It is hoped that the exhibition may be a very important feature of this meeting and that future exhibitions may be of progressively greater importance. Those desiring to enter exhibits should make arrangements with Professor R. E. Oesper, chairman of the sub-committee on exhibition, the University of Cincinnati. Professer Oesper has given much time and attention to preparations for this feature of the meeting. The association's collection of portraits and autograph letters of its past presidents will be exhibited for the first time at Cincinnati.

The opening session will occur on Thursday evening, December 27, under the presidency of Dr. Charles D. Walcott, secretary of the Smithsonian Institution.