discovery of the toxic principle from filtered cultures of the bacillus of chicken cholera, which organism he also unearthed, and he thus laid the foundation for our knowledge of toxines. He was an indefatigable worker. He found the cause of boils, the staphylococcus, and finding it in a case of osteomyelitis he pronounced this a "boil of the bone," "a heresy to thus confound internal and external pathology."

The picture of Pasteur in the Academy of Medicine supporting his view of the question of puerperal infection is delightful. "One day, in a discussion on puerperal fever, at the Academy of Medicine, one of the most renowned of his colleagues made an eloquent dissertation on the causes of epidemics in the maternity hospitals. Pasteur, from his place in the audience, interrupted him: "The cause of the epidemic is nothing of the kind! It is the doctor and his staff who carry the microbe from a sick woman to a healthy woman!" And when the orator replied that he was convinced that no one would ever find this microbe, Pasteur darted to the blackboard and drew the organism with its chaplets, saying, "There! There is its picture!"

Thus we have a wonderful example of this clear thinking, unconquerable worker piling up discovery after discovery, each one enough for one ordinary man's fame, and doing it all with a modesty that does the heart good.

---

**United States Steel Company Orders Setting-up Exercises for Office Employees**—Recently the United States Steel Company issued an order that all officers and employees in the general offices shall take setting-up exercises on the company's time in the rooms in which they work for ten minutes in the morning and ten minutes in the afternoon of each day. During the period of these exercises all business of the corporation is suspended, including even telephone messages. This is an important and initiative movement going in the right direction. Corporations and business houses with considerable office force would add to the efficiency of their employees and increase the volume of work by imitating the practice of the United States Steel Company.

---

Science is the topography of ignorance. From a few elevated points we triangulate vast spaces, inclosing infinite unknown details. We cast the lead, and draw up a little sand from abysses we may never reach with our dredges.

The best part of our knowledge is that which teaches us where knowledge leaves off and ignorance begins. Nothing more clearly separates a vulgar from a superior mind, than the confusion in the first between the little that it truly knows, on the one hand, and what it half knows and what it thinks it knows on the other.—Holmes' Medical Essays.

---

A medical school is not a scientific school, except just so far as medicine itself is a science. On the natural history side, medicine is a science; on the curative side, chiefly an art. This is implied in Hufeland's aphorism: "The physician must generalize the disease and individualize the patient."—Holmes' Medical Essays.

# LOUIS PASTEUR—HIS CONTRIBUTION TO ANTHRAX, VACCINATION AND THE EVOLUTION OF A PRINCIPLE OF ACTIVE IMMUNIZATION.

By J. G. FITZGERALD, M. D.
(From the Department of Hygiene and Preventive Medicine and the Connaught Antitoxin Laboratories, University of Toronto)

In no other of the many fundamental contributions which Pasteur made to scientific knowledge has his extraordinary clarity of vision been more manifest than in his work on anthrax.

At the time (1877) when he began his investigations, first, in relation to the nature of the causative agent of the disease and later with respect to the question of protection against anthrax the actual knowledge of causation of communicable and epidemic diseases in general was in utter confusion.

Because of the great economic losses occasioned through the death of sheep and cattle from anthrax, several scientific workers before Pasteur, had interested themselves in the problem of its etiology. None of them, however, had satisfactorily resolved the question. In 1838 Delafond of the Alfort Veterinary College had observed and demonstrated in the blood of anthrax animals "little rods" to which he attached no importance, regarding them merely as a curiosity. Twelve years later in 1850 Davaine and Rayer again saw anthrax bacilli in the blood of animals that had died of the disease, without, however, appreciating their significance.

In the meantime, Pasteur published his paper dealing with the micro-organisms which are responsible for butyric acid fermentation. This paper greatly impressed Davaine and a number of years later in 1863 a physician, in whose neighborhood a number of sheep had died of anthrax, sent a sample of blood from these animals to Davaine, who found in it tiny bodies which he called "bacteridia." These he believed to be the cause of anthrax. This view he made public.

Immediately attempts were made to repeat his work because, of course, if true, it was of fundamental importance, since at this time, 1863, no so-called communicable disease had conclusively been shown to be due to a living micro-organism. At the important school of Val de Grace, Jaillard and Leplat were unable to corroborate Davaine's findings. Davaine himself repeated the work of these other investigators and concluded that the inoculum they had employed had not been obtained from a definite case of anthrax. Jaillard and Leplat at once obtained blood from an authenticated case of the disease and while rabbits died when inoculated with this material, their blood in turn did not show the presence of the little rods or "bacteridia."

About this time, 1876, Robert Koch began his studies of anthrax and introduced the first solid culture medium for the purposes of his investigation. He observed the vegetable and spore forms of the anthrax bacilli and carefully investigated the pathogenicity of anthrax cultures for mice, guinea-pigs and rabbits. These bacilli now were definitely designated B. anthracis, and their etiological relationship to anthrax seemed to have been finally settled.

Just at this time, 1877, Paul Bert, a very distinguished French scientist, reported that he had been able to destroy anthrax bacilli contained in a drop of blood by exposing them to compressed oxygen; to inject the material remaining after such exposure to oxygen into suitable animals and produce the disease in them without, however, any anthrax bacilli being found in their blood. He concluded, then, that "bacteridia are neither the cause nor necessary effect of splenic fever (anthrax) which must be due to a virus." Confusion once more reigned in regard to the whole matter.

Pasteur undertook to investigate the question. He took a small amount of blood from an animal that had died of anthrax, and with all aseptic precautions planted it in a sterile flask containing a slightly alkaline, sterile culture medium—he used urine for the purpose. In this medium he grew cultures of the anthrax bacilli. He noted the characteristic tangled filamentous skeins of bacilli in the medium. He subcultured his growths by carrying over from flasks in which the bacilli were growing a few drops to other flasks of sterile culture medium, thus seeding it and giving rise to new generations of these micro-organisms.

A drop of culture material from flasks so inoculated, injected into susceptible animals, produced in them the disease anthrax. He thus conclusively established the etiological relationship of B. anthracis to the disease anthrax. He showed furthermore that there were two distinct forms, the vegetative and spore, which anthrax bacilli might assume.

Pasteur, with a number of other investigators, in 1877 constituted a commission to examine into the discordant results of Jaillard and Leplat and Paul Bert. To summarize briefly, they learned that these other workers had been dealing with mixed cultures of B. anthracis and a septic vibrio. The former an aerobe, the latter an anaerobe. Pure cultures of both were obtained by Pasteur and under appropriate conditions, each was grown in artificial media. The septic vibrio was shown to be highly pathogenic for rabbits and this fact explained Jaillard and Leplat's results.

The true explanation of Paul Bert's findings was next given by Pasteur when he was able to demonstrate that compressed oxygen destroyed the vegetative forms but not anthrax spores. Bert had destroyed the vegetative forms. The spores resisted and were capable of transmitting infection. Paul Bert himself to the Societe de Biologie in 1877 announced his mistake and accepted Pasteur's interpretation of the experimental results he had obtained. Many doubts remained in the minds of certain skeptical observers of that time, but today it is realized that this work was of the most fundamental importance and blazed the trail for much of the splendid progress in bacteriology of the next 25 years.

Three years later, in 1880, were begun a series of experiments which were as profoundly to influence the future of specific prevention of disease as did the monumental work of Edward Jenner, carried on nearly one hundred years before. By chance, (and here it is well to recall Pasteur's immortal words "by chance you will say; chance only favors the mind that is prepared") or as his son-in-law, Vallery-Radot, has expressed it: "A chance such as happens to those who have the genius of observation." In examining some old cultures of the micro-organisms of chicken cholera it was learned that these cultures which had been put away and not replanted for several weeks had lost nearly all the virulence or pathogenicity possessed by young, vigorously growing cultures, replanted daily. Hens injected with small amounts of the old cultures of chicken cholera developed some of the symptoms of the disease, but soon recovered. On recovery, if subsequently inoculated with young virulent cultures of chicken cholera germs, these hens remained refractory or immune and developed no symptoms of the disease.

Pasteur at once appreciated the fact that an underlying fundamental principle of active immunization had been demonstrated in his work on chicken cholera. He learned by experiment, that the micro-organisms of this disease could be reduced to any desired degree of virulence by prolonged growth and exposure to an abundant supply of oxygen. He produced in this manner two bacterial vaccines, one of stronger, the other of weaker virulence and by inoculating normal hens with a dose of each vaccine they were rendered immune to spontaneous or artificial infection with living highly virulent microbes of chicken cholera.

While it is true, and Pasteur was the first to proclaim it, that the principle of attenuation of virulence underlying vaccination aganist smallpox, as demonstrated by Jenner, served to guide him in this work, the fact remains that this was the first instance in which a pathogenic microbe was isolated in pure culture, studied and employed as a bacterial vaccine after appropriate attenuation of virulence had been achieved. Furthermore, important facts relating to methods of attenuation were also gleaned during the progress of the work.

During the next year, 1881, in association with Chamberland and Roux, Pasteur applied himself to the problem of vaccination against anthrax. This was a much more difficult task, however, because of the greater virulence of anthrax bacilli. Toussaint, a distinguished French veterinarian, had just published a communication in which he claimed he had succeeded in vaccinating sheep against anthrax. He had taken blood from sheep suffering from the disease just before or immediately after death, heated it to 55 degrees C. for 10 minutes and inoculated normal sheep with this heated blood.

Pasteur, Chamberland and Roux soon learned through experimentation that anthrax bacilli, while they might sometimes be inhibited in their growth by heating to 55° C., were not necessarily killed. Toussaint then employed carbolic acid for the purpose of attenuating the virulence of his cultures. This procedure also proved to be very uncertain. After a long series of experiments in which chief reliance was placed on physical methods, for the attenuation of virulence and inhibition of growth and spore formation (this latter was really the crux of the difficulty) it was ascertained that the growth of anthrax bacilli in a neutral broth medium was inhibited at 45° C. It was also learned that they can be readily cultivated at 42° or 43° C., but at these temperatures spores do not develop. This latter discovery paved the way for the development of a sound method of anthrax vaccination which obviated the necessity of resorting to the procedure of Toussaint, which had proved to be uncertain and dangerous.

Pasteur's method consisted in growing anthrax bacilli in neutral chicken broth at 42° C. for twelve and twenty-four days, respectively, during which time a marked reduction in virulence of the microbes occurs. After twelve days' growth under the above conditions the culture was no longer able to kill rabbits, but was fatal for guinea pigs or mice. After 24 days' growth it is no longer virulent for guinea pigs, but still was able to kill mice. The more fully attenuated cultures constituted the "premier vaccin." Cattle or sheep, when being immunized, were first given a dose of the weaker culture and ten or twelve days later a dose of the stronger one.

On May 5, 1881, at the farm of Pouilly le Fort, near the little town of Melun, was begun the practical test of Pasteur's anthrax vaccine, which has become famous in the annals of scientific medicine. Fifty sheep and ten cows were used for the experiment, twenty-five of the sheep and six cows were vaccinated and twenty-five sheep and four cows were not. The first injections of vaccine were given May 5, the second on May 17. On May 31 a third and final injection was also given. On the same day all the animals were injected with a quantity of living, virulent culture of anthrax bacilli. By June 5 all the unvaccinated sheep were dead and only one of the vaccinated; this one had aborted and died of hemorrhage. All the others remained perfectly well. The six vaccinated cows were quite normal and the four unvaccinated presented enormous oedemata.

Pasteur's triumph was complete and he was acclaimed by the whole of France. The government recognized his great service to science and to agriculture in formally awarding him the Grand Cordon of the Legion d'honneur. In August of the same year he represented the government of the French republic at the International Medical Congress in London. There he received a most remarkable ovation and was the center of interest during the meetings of the congress. The London correspondent of the Paris Journal des Débats wrote to his paper as follows, describing the events: "When M. Pasteur spoke, when his name was mentioned, a thunder of applause arose from all benches from all nations. An indefatigable worker, a sagacious seeker, a precise and brilliant experimentalist, an implacable logician and an enthusiastic apostle, he has produced an invincible effect on every mind."

For the past forty years active immunization on a very large scale against anthrax has been carried on in many parts of the world with much success and with very great economic benefit to the communities concerned.

Since 1881 bacterial vaccines have been developed for the specific prevention of typhoid and paratyphoid fevers, bacillary dysentery, asiatic cholera, bubonic plague, pneumonia, whooping cough and other diseases of microbic origin. Many of these have found a very wide field of usefulness and enormous success has attended the employment of certain of them. The results obtained from the use of typhoid and paratyphoid vaccine among members of the Canadian Expeditionary Force during the Great War, when contrasted with the experience of the South African War of 1899-1901, will serve as an illustration. In South Africa the war last two years and seven months; 548,237 men were engaged. Among these, 59,864 cases of enteric fever occurred. This was an admission ratio of 122.9 per 1000. Among these cases there were 8248 deaths, a ratio of 18.6 per 1000. During the Great War, in a period of four years, 420,000 Canadians were engaged. Among these there were 420 cases of typhoid fever with only 14 deaths. An admission ratio of 1 per 1000 contrasted with 122; and a death ratio of 0.003 per 1000 contrasted with 18.6. Equally satisfactory results obtained in the American Expeditionary Force. In an average strength of 2,121,396 between September 1, 1917, and May 2, 1919, in the A. E. F., there were 213 deaths from typhoid fever. Had the Spanish-American War rate obtained there would have been 68,164 deaths instead of 213. Specific prevention through the use of typhoid vaccine more than any other factor was responsible for this splendid achievement.

These and other like triumphs of specific preventive medicine constitute the mighty oak which has sprung from the tiny acorn sown by Louis Pasteur at Pouilly le Fort in May, 1881.

---

**Health Bills**—The Public Health Service and the National Health Council in their bi-weekly Bulletin of January 20, list the following bills entered in the Nebraska Legislature under the head of "Health Bills":

"1. Medical Practice—H. 17, would permit duly licensed physicians of any school or system of healing, including religion, to treat patients in institutions receiving support from city, county or State."

"2. School Hygiene—H. 39, would amend the law to excuse from physical examination children whose parents object."

---

**Movement in New Jersey to Shorten the Course of Training for Nurses**—A committee of the New Jersey State Medical Society and representatives of nursing organizations of the State, after a number of conferences, have concluded to shorten the period of training for student nurses. They propose to make the shorter period more intensive by eliminating manual labor which may be performed by ward attendants.