BRITISH MEDICAL JOURNAL

LONDON SATURDAY APRIL 19 1947

LOUIS PASTEUR*

BY

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I feel that it is a very great honour to have been asked to deliver this lecture on Pasteur, but I accepted the invitation with great trepidation, for I felt that I should be unable to do justice to so memorable a subject. We are grateful to M. Leveille for coming to London and setting up this Pasteur exhibition. I saw it in Paris and was struck then with its comprehensiveness and arrangement. But M. Leveille knows that the genius of Louis Pasteur is revered in Britain as it is in France.

Louis Pasteur was just a citizen of France—not an ordinary citizen, as it turned out; and there was nothing in his origin to indicate that when he died—and 50 years after his death—he would be a national hero. His great grandfather, grandfather, and his father were tanners. Perhaps had circumstances been different one of these ancestors might have become famous, but son followed father in an essential occupation. Pasteur's father, who on the battlefield had been decorated with the Legion of Honour, appreciated the advantages of education, and Louis, instead of becoming a tanner, was admitted to the Ecole Normale in Paris, where he seized with avidity the chances of learning, particularly chemistry and physics, under the distinguished teachers of that institution. He obtained his degree, but even then there was no real indication of his coming fame.

Louis Pasteur in his youth and throughout his life believed in hard work. He lived for his work and put his whole heart and soul into it. His was not a 40-hour week. He worked so constantly in his laboratory that it was inevitable that he became a beautiful technician, and throughout his life he had no use for sloppily performed or ill-conceived experiments. His first momentous discovery was the dissymmetry of crystals. Like many others, he had been puzzled by the difference between tartaric and racemic (or paratartaric) acids. These two chemicals appeared to be identical in every way except that, whereas racemic acid solutions had no influence on polarized light, tartaric solutions rotated this to the right. When Pasteur examined the crystals of a salt of racemic acid with the microscope he noticed that the crystals were not quite identical and could be divided into two groups. In one of these groups a particular facet was on the right side while the other group had the same facet on the left. They were in fact mirror images of each other and might thus be compared with a pair of gloves. Pasteur had vision, and with extraordinary care and perseverance he separated his right- and left-handed crystals into distinct groups. Then he made solutions of these and tested them by the polariscope. The solution of the right-handed crystals deviated the polarized light to the right, the left-handed crystals to the left, and when the solutions were mixed in equal proportions there was no deviation—it was back at the indifferent racemic acid.

A New Science

Pasteur had solved a mystery that had puzzled older and more famous chemists. Little wonder is it that he was excited and rushed out and kissed an attendant whom he met outside the laboratory door. You can imagine the feelings of young Louis Pasteur when later he visited the great Biot to demonstrate his discovery. Biot, like a careful scientist, took no risks. Pasteur was given tartaric acid and the chemicals necessary for its crystallization. He made the solutions, which Biot kept in a cupboard till the crystals had formed. Pasteur separated his right- and left-handed crystals and Biot tested them in the polariscope. It was as Pasteur had said, and we can honour Biot for his immediate remark. "My dear boy, I have so loved science all my life that this makes my heart beat." From that day Biot was Louis Pasteur's friend and helper.

But he was not to stay in Paris uninterrupted. He was sent to Dijon and later to Strasbourg as a teacher. In Strasbourg, possibly the most important thing he did was to marry Mademoiselle Laurent, the daughter of his chief. She proved a mainstay throughout his life, and well deserved the tribute of one of Pasteur's disciples: "She was not only an incomparable companion for her husband but also his best collaborator." He pursued his studies in crystallography and he pursued racemic acid. No one knew how to make it. He heard of people in Leipzig and Vienna who were supposed to be able to do so, and off he dashed. But in the end he had to make it himself, and this gained for him the ribbon of the Legion of Honour and a prize of 1,500 francs from the Pharmaceutical Society of Paris.

In another pretty piece of work which he did later he used a common blue mould, a penicillium. When this was grown on racemic acid it assimilated the right-handed portion leaving only left-handed tartaric acid. A remarkable example of the extraordinary power of selection of a living organism. People may say and did say: "What is the use of all this? Why such a fuss about a little dissymmetry of crystals?" You can answer like Franklin: "What is the use of a newborn child?" Pasteur's first scientific baby, born of tartaric acid, inspired later workers so that a complete new science of stereo-chemistry has arisen explaining structure and enabling synthesis of many organic compounds. In London this work did not pass

* A lecture delivered at the Science Museum on April 10 to inaugurate the Pasteur Exhibition, temporarily transferred to London from the Palais de la Découverte in Paris.

without notice, for it earned for him the Rumford Medal of the Royal Society—and that at 34 years of age.

In 1854 Fate ordained that Pasteur should be sent as Dean of the Faculty of Science to Lille. One of the industries of Lille was the production of alcohol by fermentation of beetroot. In those days the prevalent theory of fermentation was that of Liebig—that it was a purely chemical process in which yeast played no active part. Latour and Schwann had produced good evidence that yeast was a living organism, but Liebig and his supporters would not have it that a living yeast took any part in the fermentation process.

The father of one of Pasteur's students was worried by the irregularities of his fermentations and asked Pasteur to help him. This was the stimulus that set him off on his study of fermentations, which occupied him for many years and led him on to his later work on animal infections. He set to work with his microscope and found that in the unhealthy lactic fermentations the globules were elongated and quite unlike the rounded globules of yeast found in the healthy alcoholic fermentations. Some of the products of these fermentations were optically active. His previous work had convinced him that this optical activity was a property possessed by substances synthesized by living things, in contradistinction to substances synthesized chemically in the laboratory. He was therefore predisposed to consider these ferments as living organisms. In the fermentation of impure substances like grape juice and beer wort there were many complicating factors, so he prepared a culture fluid containing only a watery solution of sugar, mineral phosphate, and an ammonium salt. No organic nitrogenous matter was present. In this simple medium a minute implantation of yeast promptly fermented the sugar, thus confounding the upholders of the purely chemical theory of fermentation, who had maintained that without organic nitrogenous material such fermentation was impossible. Perhaps more important for us in this was the fact that Pasteur initiated the method of working with a simple culture medium in which the chemical changes could be more readily observed. This was an enormous advance and is the method still used by the bacteriological chemists. Thus even in his early work on lactic fermentation he was laying the foundations of bacterial culture.

It is quite impossible to go into details of this work here. It received much criticism, but Pasteur was a fighter as well as a wonderful experimenter and he was able to confound his critics. He had got to the stage when he wrote:

> "I can bear witness to the existence of a large number of distinct yeasts setting up chemical transformations in accordance with their nature and constitution; but most frequently the nourishment suited to one allows others to develop. Hence arise most complicated phenomena, liable to constant variations. If one does succeed in separating one of these ferments and making it grow by itself, it produces the corresponding chemical change with remarkable precision and simplicity."

That is as true to-day as when he wrote it.

Having got so far with these fermentations, and having shown that they were due to living organisms, the next question was, Where did these ferments come from? Did they arise spontaneously or did they come from outside? The question of spontaneous generation had been discussed for centuries. Many and curious were the prescriptions for producing animals. Virgil's method for producing bees was:

> "Kill an ox two years of age, whose young horns are just beginning to curl on his brow, place him in a narrow enclosure strewn with leaves of thyme and rosemary freshly gathered, and soon from his fermenting humours there rises a swarm which fills the air like rain from summer clouds."

Van Helmont had a recipe for producing rats:

> "Cork up a pot containing corn with a dirty shirt; after about 21 days a ferment coming from the dirty shirt combines with the effluvium from the wheat, the grains of which are turned into rats, not minute and puny, but vigorous and full of activity."

This sounds almost as learned as some of the explanations of things which we hear to-day and possibly is as truthful.

In the 18th century Spallanzani had produced experimental evidence that spontaneous generation did not exist, but people were not convinced, and the controversy went on. In 1859 the academy offered a prize for "an endeavour by means of careful experiments to throw new light on the question of spontaneous generation." Pasteur's studies on fermentation fitted him for this new investigation. His seniors, Biot and Dumas, tried to dissuade him, but he went on.

We have not time to go into the multitude of experiments which Pasteur made on this subject or into his controversies with Pouchet or Bastian, but one simple experiment might be mentioned. The neck of a flask half filled with a fermentable fluid was drawn out in a swan's neck form. The fluid was boiled to sterilize it, and then the flask was allowed to stand at a temperature suitable for fermentation. No fermentation occurred, although it promptly appeared in a similar flask in which the neck had not been drawn out. The dust dropping from the air settled on the bend of the drawn-out flask and never reached the fluid, but if the flask was tilted so that some of the fluid reached this dusty bend and was then allowed to run back fermentation promptly started. This made him state: "The dust suspended in the air is the only origin and the first and essential condition of life in infusions." It was at this time also that he said: "It is very desirable to carry these researches sufficiently far to prepare the way for a serious inquiry into the origin of disease." That showed the trend of Pasteur's thoughts about the germ theory of disease.

The First Pasteurization

Pasteur's home was in Arbois—a wine-growing country. He was naturally interested in the production of good wines, and I can assure you from personal experience that Arbois produces good wine, for it was in November last on the occasion of the 50th anniversary of his death that we visited Arbois and indeed Pasteur's own vineyard there. The wine producers were in trouble. Many of the wines rapidly became unpalatable, sour, and ropy. Pasteur investigated this in much the same way as he had other fermentations. He examined with the microscope the bodies found in healthy wine fermentations: these were yeasts. In the spoilt wine he found other minute bodies, and he showed that it was by the fermentations set up by these that the wine acquired a nasty taste. Much more important from a practical point of view was his finding that these secondary fermentations could be prevented by slight heating of the wine. This did not interfere with its flavour but completely stopped the spoilage. This began the process which we know as pasteurization, to the great benefit of the wine industry of France. Pasteur explained also the essentials of the process of making vinegar. Whether made in the French way in casks or in the German way by slowly trickling wine over beechwood shavings it was the same—a minute organism, the *Mycoderma aceti*, provided the ferment, but it required plenty of air for its action. So the vinegar industry also benefited.

Pasteur's work now took a new turn when his friend and supporter, the famous chemist Dumas, who came from the silk country, implored him to go there and investigate a disease which was destroying the silkworms and ruining the country. Pasteur pointed out that he knew nothing of silkworms or their diseases, but Dumas had the greatest faith in the genius of his younger colleague and managed to persuade him. I have not time to go into details of Pasteur's work on silkworms—how he collected information about their life history, how he examined them, healthy and diseased, under the microscope, how for a long time he was confused by the presence of two distinct diseases, or how he finally showed that it was possible to obtain and perpetuate healthy broods by selection of healthy stock and by cleanliness. In spite of the fact that in the middle of this work he was stricken with a form of paralysis from which he never recovered he was able in the space of five years to convince the silk growers that his methods were sound, and the silk industry of Europe was restored to prosperity.

After the Franco-Prussian war in 1871 Pasteur went on a holiday to his friend Duclaux at Clermont Ferrand: there was a large brewery near by. Pasteur, as always, was interested in the fermentations. Like the making of wine and vinegar, beer-making had been largely rule of thumb with little knowledge of what was happening, and the brewers found that often the beer would not keep. It got sour or even putrefied. Pasteur with his indispensable microscope examined deposits from good beer and bad beer and noted the differences. Then he wanted to extend his observations to the larger English breweries, and in the same year he came to London and paid his historic visit to Whitbread's. In Vallery Radot's life of Pasteur it tells how he was well and courteously received, but instead of just seeing round the brewery he wished to see some of the barm of the beer. After examining it with the microscope he suggested that it was not too good. This made them sit up and take notice, for they already knew all was not well. Then he examined other batches, and could say from his simple microscopical examinations whether they were good, bad, or indifferent. He made such an impression that when he returned a week after Whitbread's had purchased a microscope and were beginning to control their fermentations. This microscope is becoming well known from the advertisement at present in the London tube stations, and is actually in this Pasteur exhibition in the Science Museum. This immediate acceptance of new ideas and controls was certainly to the credit of Whitbread's.

Just as with wine, Pasteur found that the souring of beer was due to a secondary fermentation with contaminating microbes. The pure brewers' yeast produced the essential fermentation which made good beer, but if the vessels were contaminated with the souring microbes these grew out later and spoilt the beer. Again, just as with wine, Pasteur found that heating the beer for a short time to 55° to 60° killed these contaminations. This was the origin of pasteurized beer.

It was in 1873 that Pasteur entered new fields by being elected (by one vote only) to the Academy of Medicine. Little did the academicians know when they admitted this chemist of 53 years of age that in another ten years he would have revolutionized many of their ideas.

In his studies on fermentation he had always in his mind that many human ailments were due to microscopic living objects (the word microbe was only introduced a few years later), and human infection had been forcibly brought home to him by the death of two daughters from typhoid fever. By this time Lister had, as a direct result of Pasteur's publications, introduced antiseptic surgery and was creating a revolution in that art. Other workers were contributing to our knowledge of what we may now call microbes, and the " germ theory " was being promulgated.

Davaigne had demonstrated what he called the bacteridium of anthrax. Koch had grown it outside the body and demonstrated its character and mode of growth. It was only in 1877 that Pasteur, in collaboration with Joubert, commenced his work on anthrax. He cultivated a drop of anthrax blood through many flasks of culture medium so that anything dead in the original blood was diluted to extinction. After nine passages it was calculated that the original drop of blood had been diluted in a volume of fluid equal to the volume of the earth, and Pasteur did not stop at nine passages—he did many times nine. The last of these cultures was just as infective for rabbits and guinea-pigs as was the first one. He could then state positively that the bacteridium was the real infecting agent.

Other diseases were being connected up with definite microbes, and one of these, chicken cholera, had an enormous effect on subsequent developments in medical and veterinary practice. Pasteur isolated a microbe from fowls suffering from this disease, and he and his associates had shown that healthy fowls inoculated with cultures of this microbe contracted the disease and died. But on one occasion old cultures were used for these inoculations instead of fresh ones. The fowls did not die. The microbes in the cultures were alive, but for some reason they did not kill the chickens. They made new cultures and again inoculated the fowls—some of the survivors of the last experiment and some fresh ones; the previous survivors again survived, but the fresh ones got the usual chicken cholera and died.

Attenuation and Immunization

A less observant man might have passed this by, but not Louis Pasteur. He recognized that he had by the injection of the old culture immunized the fowls against the disease. Here was a new method of preventing infection. Cultures had first to be attenuated—that is, altered in some way that they do not kill the animals. Then when injected into the animals they give the animal protection, not death. Then Pasteur applied these methods to anthrax, a disease which was killing thousands of cattle and sheep. He had to find out how to attenuate his cultures so that they would not kill the animals. This he did by growing them at a higher temperature than normal. With vaccines made from microbes grown at these higher temperatures he found he could protect animals. But there was disbelief, as there always is with something startling or unusual. How could a chemist without veterinary or medical qualifications discover these things ? He was challenged to one experiment to prove his statements and he readily accepted.

On a farm, Pouilly le Fort, 25 sheep and 6 cattle were inoculated with Pasteur's vaccine and the same number were left untouched. Two weeks after the second vaccine injection all were injected with a virulent culture that was known to cause the disease. Two days after, on June 2, 1881, there was an enormous concourse of people to see the results—senators, scientists, newspaper men, and others. The result was a phenomenal success: all the uninoculated animals were dead or dying while all those inoculated with Pasteur's vaccine were alive and well. I cannot do better than tell you the result in Pasteur's own words from a letter to his children written on the morning of June 2, 1881, before he left Paris to see it himself. " The telegram tells me that when we arrive at 2 o'clock this afternoon all the non-vaccinated subjects will be dead. 18 were already dead this morning and the others dying. As to the vaccinated ones they are all well." For Pasteur 1881 was a memorable year; so it was for me, for it was then I was born.

Chicken cholera and anthrax have been defeated. Swine erysipelas was successfully tackled, and then the cry in regard to all infections was, "Find the microbe and make a vaccine." And for Pasteur a vaccine was synonymous with an attenuated living culture. At that time rabies or hydrophobia was much more prevalent than it is to-day, and it was a dreaded and fatal disease. It was known that it followed the bite of a rabid dog, but beyond that there was complete ignorance. (We in Britain know little of hydrophobia. The quarantine precautions on dogs wiped it out, and we shall be free so long as there are no foolish persons who from mistaken sentimentality deliberately defeat this quarantine.) Pasteur set to work on rabies. He injected saliva from a child suffering from the disease into rabbits. They died, and some of their blood injected into other rabbits was likewise fatal. In the blood of these rabbits microbes were seen, but Pasteur was not deluded as were some others into the belief that he had discovered the microbe of rabies. He found he could get the same result with saliva of children suffering from other diseases or even with saliva from healthy people. Actually he had discovered the pneumococcus—the microbe usually responsible for pneumonia. The actual microbe of rabies eluded him. He could not see it with his microscope. That is not surprising, for we now know that it belongs to the class of viruses which are so small that the ordinary high-power microscope does not reveal them. But he was not beaten. The nervous system of dogs was obviously affected, so he went to the nervous system for his material. He injected material from the brain of a rabid dog into healthy ones and reproduced the disease after the usual incubation period. Then his assistant Roux injected similar material into the brain of a dog, and it became rabid in only fourteen days. The infective agent was concentrated in the central nervous system.

There is not time to go through the hundreds of experiments which Pasteur and his collaborators made, but they found that brain tissue from a rabid dog injected into a rabbit, and then from rabbit to rabbit, became more and more virulent until it reached a certain state when it remained constant. The spinal cords of the rabbits infected with this "fixed virus" were taken out and dried for various times. The longer they were dried the less virulent they became. The dogs were immunized by injection of an emulsion of a piece of the rabid spinal cord which had been dried for 13 days. Next day a piece which had been dried for 11 days was injected, and so on till the dog received the fresh virulent spinal cord. They did not get rabies, and subsequent attempts to give them rabies failed. They were injected with infective material from mad dogs. They were bitten by mad dogs, and they remained well. They had been successfully immunized.

One problem had been solved. Dogs could be immunized against rabies. But what to do? It was an impossible task to immunize the millions of dogs in France. But was it possible to immunize a human being in the same way during the incubation period—that is, between the time he was bitten and the time the symptoms appeared? The incubation period was long—several weeks—so possibly there was time; but the question was not yet solved as to whether the injection of the dried rabbit's spinal cord which did not infect the dog would be equally harmless to man. At last Pasteur's hand was forced. From Alsace came Mme. Meister, bringing her boy Joseph, who had been severely bitten by a mad dog, and imploring Pasteur to save him from the dreaded disease. Pasteur immunized Joseph Meister as he had done his experimental dogs. The injections were harmless, and Joseph Meister did not get rabies. At last it had been shown that it was possible to protect man against infective disease even after the infection had occurred. The immunization of Joseph Meister was not a flash in the pan. It was successfully repeated on many others, and Pasteur's laboratory in Paris became the mecca of people from all over Europe who had been bitten by rabid dogs.

This may be regarded as the culmination of Pasteur's great work. Famous he had been before; but now he was a national hero. Subscriptions were invited for the foundation of an institute in which he could carry on his great work, and they poured in from all over the world. The Pasteur Institute was erected in the Rue Dutot (now renamed the Rue de Docteur Roux after Pasteur's great collaborator). On Nov. 14, 1888, the new institute was opened by President Carnot. A quotation from Pasteur's speech on that occasion summarized his philosophy:

> "To believe that one has made an important scientific discovery; to be in a fever to announce it and to restrain oneself; to force oneself to confute one's own experiment, and only to proclaim a discovery when all contradictory hypotheses have been disproved—yes, this is an arduous task. But when after very many attempts one has at last arrived at certainty, one experiences one of the greatest joys the human mind can feel, and the thought that one will add to one's country's glory makes this joy greater still."

Another quotation from the speech:

> "I would say that two contrary laws seem to be wrestling with each other nowadays: the one a law of blood and death, ever imagining new means of destruction and forcing nations to be constantly ready for the battlefield—the other a law of peace, work, and health, ever evolving new means of delivering man from the scourges which beset him. Which of these two laws will ultimately prevail God alone knows."

How true to-day!

In 1892, on the occasion of his 70th birthday, an enormous crowd gathered in the theatre of the Sorbonne. Our Royal Society was represented by Lord Lister, who said: "Truly there does not exist in the whole world an individual to whom medical science owes more than to you." That was said 53 years ago. It is true to-day except that Pasteur is now with us only in spirit.

In the new institute Pasteur was able to see his assistants and collaborators carry on his great work. His health failed, and on Sept. 28, 1895, he died in peace. His body lies in the Pasteur Institute, the useful monument erected for him in his lifetime: his spirit animates workers in microbiology throughout the world.

In succeeding years Pasteur institutes were opened in many parts of the world to carry out Pasteur's methods, and, quite apart from the immediate benefits which this gave in the preparation of vaccines and the protection of man and animals, they have advanced knowledge in many ways, as can be seen from a study of the exhibits in this beautifully arranged Pasteur exhibition.

The introduction to the catalogue of this exhibition is written by Pasteur's illustrious grandson, Prof. Pasteur Vallery Radot, who is not only a great physician but a great partisan. In this he points out how throughout his scientific life Pasteur was encouraged and assisted by British scientists—Tyndall, Lister, and others. He tells of his emotion at witnessing the embrace of Pasteur and Lister on the occasion of his jubilee with these words: "Was not this gesture a symbol of the bonds uniting our two nations?"

It is good to see the line of the great Pasteur so worthily carried on.

We have surveyed Pasteur's work. Let us see briefly how it has affected us in our lives to-day. People have often speculated on which of Pasteur's many discoveries was the most important. It is very difficult to say. The chemist may say it is his early work on crystals; the pure microbiologist, that it is his refutation of spontaneous generation; the industrialist, that it is his work on fermentation of wine and beer; the agriculturist, that it is his study of silkworm disease or the protection of animals against anthrax and other diseases.

A physician will be doubtful, for almost all of them have assisted him in his work. As a microbiologist and a physician I have the greatest admiration for his last great work on rabies. It was difficult; he had so little to go on; it was so methodically tackled; and it was so successful. His work on fermentations led directly to the cure of diseases of wine and beer. There are teetotallers who may think this is a misfortune, but especially in these disturbed times such beverages seem to provide solace. But his work did more than that. The abnormal fermentations of wine and beer were cured by a process which became known as "pasteurization." We hear of pasteurization now, but it is the pasteurization of milk we hear of. It is by this process of pasteurization that much milk-borne disease is prevented in our large cities; and this we owe to Pasteur's studies on alcoholic liquors.

The Antiseptic System

There was another and even more important direct outcome of Pasteur's fermentation work. Lister, who was then working in Glasgow, read Pasteur's communications, and in them he saw the possibility of keeping germs out of the operation room. In those days nearly all operation wounds were septic and many gangrenous. We have had handed down to us the phrase "laudable pus." Then it was a sign that the patient would probably recover. Now of course pus of any kind, "laudable" or otherwise, is a reflection on the surgeon's methods.

There had been many explanations offered as to the origin of this putrefaction of wounds, but it was Pasteur's work which made Lister see the true light. The infection came from outside, so Lister sterilized as far as he could with carbolic acid and other antiseptics his hands, his instruments, and his dressings. He even used a carbolic spray to sterilize the air. Thus he revolutionized surgery and became one of the greatest figures in British medical science. It was in 1874 that Pasteur received a letter from him saying: "Allow me to take this opportunity of thanking you most heartily for having shown me, by your brilliant investigations, the truth of the germ theory of putrefaction, and for having thus acquainted me with one principle which can lead the antiseptic system to final success." How much life and suffering has been saved by the methods which Lister and his successors initiated as the result of Pasteur's teaching!

In his studies on spontaneous generation and on bacteria he and his colleagues introduced methods which we all use to-day. Notable among these was the introduction of the autoclave for sterilizing material by steam under pressure. This is in constant use to-day in hospitals, in laboratories, and in industry.

Let us now come to the later and most directly medical work—the protection of animals and man against infection. The experiment on anthrax at Pouilly le Fort in 1881 proved without a shadow of doubt that animals could be protected with vaccines. That was settled once and for all, but we still argue about the details of vaccine therapy; and even now there are hundreds of laboratory workers engaged in exploring the uses of various vaccines and the best way of producing them.

All Pasteur's vaccines were living attenuated cultures, and it was only in the case of rabies that they were used on man. Living vaccines have drawbacks. Although they can be attenuated so that they do not cause disease, this requires care and skill, and, human nature being what it is, sometimes one is a little careless, and instead of the living vaccine protecting it might actually give rise to the infection. As "superior" human beings we might occasionally allow that with cattle, pigs, or sheep, but no one would willingly look with complaisance on the possibility of one's child succumbing to the injection of a protective vaccine. But after Pasteur's time it was found that even if the microbe in a vaccine were killed protection against many diseases could be obtained. The great advocate of immunization with killed cultures was our countryman and my own master, Sir Almroth Wright. At the end of the last century he showed that typhoid fever could be prevented by inoculation with a killed typhoid vaccine. This was a safe procedure. The microbes in the vaccine were dead and could not infect. Now the use of typhoid vaccine is world-wide, and this great scourge of armies in the field has been reduced to comparatively negligible proportions. This is not all due to typhoid vaccine. Hygiene has an important place; but so has the vaccine. In many other bacterial diseases, also, killed bacterial vaccines have been and are being used extensively. The use of these dead vaccines was further extended by Wright to the cure of infections which had already established themselves, and large numbers of these infections have been so treated.

Rabies was in a rather different category. That was a virus disease. Pasteur could not find the microbes, so his vaccine was an emulsion of infected tissue containing a large amount of the virus. This same procedure is used to-day in virus diseases such as dog distemper, yellow fever, and influenza. Instead of the dried rabbit's spinal cord which Pasteur used, the vaccine may be made from a mouse's lung or from material obtained from a chick embryo infected inside the eggshell. Some of these virus vaccines confer a solid immunity, and as we become more and more acquainted with the viruses we shall be able to produce more and more potent vaccines. By means of the electron microscope we can now see the viruses. By various methods we can measure them, and we are gradually learning more and more about them; but the general principle of the virus vaccine to-day is much the same as that of Pasteur's original rabies vaccine.

Antitoxins and Antibiotics

This process of immunization has proceeded beyond vaccines. In Pasteur's lifetime his colleagues, Roux and Yersin, discovered a powerful toxin made by the diphtheria bacillus. Animals immunized with this toxin produced antitoxin, and every child suffering from diphtheria is now treated with this antitoxin. Much more recently it was found that this poisonous toxin could be treated with formalin, when it ceased to be poisonous but still evoked in animals the production of antitoxin. The name of Ramon of the Pasteur Institute is associated with the immunization of children by injection of this anatoxine, as he called it, or toxoid as we call it here. Many people have improved the method; it is harmless; and it certainly gives a good protection against diphtheria. It is a very serious responsibility for a parent at the present day to refuse to have his or her child immunized against this serious infection. The same method is used for protecting against tetanus or lockjaw, and it was Ramon who showed its merits in the immunization of man. In the recent war all our armies were immunized and there was almost no tetanus. Thus another scourge of war was eliminated.

Then there is another method of dealing with bacterial infection in which I am myself particularly interested. I mean penicillin. Penicillin belongs to the class of substances called antibiotics. These are substances produced by living bodies which have the special property of killing or interfering with the growth of micro-organisms. It was Pasteur and his colleague Joubert who in 1877 first described this phenomenon of bacterial antagonism. Pasteur did not pursue this subject; he had other more obviously important matters in hand. If he had gone on with it, who knows but that we might have had penicillin in the last century or perhaps even before I was born.

I have said nothing about the laboratory accommodation which was provided for Pasteur during his life. At the end perhaps it was adequate, but in the earlier years when he made his great studies on fermentation it was lamentable. Nowadays it would be considered disgraceful that any scientist, much less a scientist already famous, should be so badly housed. An American newspaperman described my own laboratory as like the backroom of an old-fashioned drug store, and yet my laboratory is adequate and reasonably modern. What would they have said about Pasteur's attic? It only shows that it is not the grandeur of the laboratory but the grandeur of the man that matters, and that the marble halls so common in certain parts of the world are quite secondary to the brain of the worker.

We have seen something of Pasteur's scientific accomplishments. We have seen something of what they have led to, and something of the debt which the world owes to his genius and perseverance. Not even a partial paralysis could daunt him, and much of his best work was done after that illness. Pasteur was the founder of a science, "microbiology." He was a chemist who gradually became a biologist. His successors were mainly biologists, but in recent years microbiological science is becoming more and more chemical. In the short space of 70 years it is completing a circle from chemistry through biology to chemistry again. But Pasteur was not only a scientist. He was an artist of considerable merit and he was a very human man, adoring his family and his home and his country. His father, his wife, his children, and his grandchildren were very dear to him, and it is a great pity that his grandson, Professor Pasteur Vallery Radot, could not be with us in London to-day.

There have been admirers who claimed for Pasteur more than he had done. That is unnecessary and does not help his memory. He did in his lifetime sufficient to make ten men great. That is enough. It is a pity to gild the lily. He was one of those rare individuals thrown up at intervals throughout the world's history to restore order out of chaos. He was a great Frenchman, but it is not only France which has to thank him. The whole world is deeply in his debt, and we here in London take this opportunity of rendering homage to the memory of our great benefactor, Louis Pasteur.

Negotiations have been completed for close co-operation between the Prince of Wales's General Hospital, London, N., the largest voluntary general hospital in North-East London, with 260 beds, including its convalescent home at Nazeing, Essex, and the Bearsted Memorial Hospital, London, N., which is a voluntary maternity hospital. The first stage of this hospital's new building at Stoke Newington is now rapidly nearing completion and will be opened in July. The new building when completed will have a total of 100 maternity beds and will be the most modern maternity unit in Britain. It is proposed that in addition to general medical and surgical service, already supplied by the Prince of Wales's General Hospital, these two hospitals will eventually provide a complete obstetric and gynaecological service for the district. With this association the following hospitals will now participate in the North London Postgraduate Medical Institute, which provides senior postgraduate teaching under the aegis of the British Postgraduate Medical Federation of the University of London: Prince of Wales's General Hospital; North Middlesex County Hospital; Chase Farm Hospital; North-Eastern Fever Hospital; Bearsted Memorial Hospital.

EFFECTS OF CERTAIN DIETS ON THE LOSS OF NITROGEN IN URINE AFTER EXPERIMENTAL BURNS

BY

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After burns or other injuries the urinary excretion of nitrogen may be definitely increased. Cuthbertson (1930, 1936), Peters and his associates (Leach *et al.*, 1943; Clark *et al.*, 1945), and others have observed that the extent and depth of burning affect the amount and type of nitrogenous material excreted. Investigations by Taylor and his associates (1943), Co Tui *et al.* (1944), and Elman, Charnas, and Davey (1943) have shown that large amounts of protein must be administered after extensive burns if nitrogen equilibrium is to be maintained. Croft and Peters (1945) reported that the increase in nitrogen loss after burning could be reduced substantially by giving methionine, or a protein supplement, to rats maintained on a moderate or low-protein diet. In their studies, rats of either sex, weighing from 100 to 150 g., were placed on a basal diet containing 10% casein and 10% dry yeast until a satisfactory nitrogen balance was obtained. Under ether anaesthesia a standard burn covering approximately one-third of the body surface was produced in water at 73° C., and the effects of various supplements added to the diet were then studied. In control groups of animals an increased nitrogen excretion in the urine occurred. In groups receiving a supplement of 1% methionine or 18% casein little increase was noted, while groups receiving supplements of alanine, cysteine, or an amino-acid mixture including only a little methionine showed no significant difference in nitrogen excretion from the controls. This observation that one amino-acid can replace the extra protein supplement "supports directly the hypothesis that the nitrogen loss is due to the raiding of tissue protein molecules for methionine." The finding that neither alanine (as a source of amino groups) nor cysteine (as a source of sulphur) had the same effect suggested to Croft and Peters that the other well-known function of methionine—that of methylation—was responsible for the effect observed.

Experiments have been performed in this laboratory on rats maintained on both normal and deficient diets. The results confirm only in part, and extend and modify, the conclusions of Croft and Peters. Prof. Peters has kindly examined some of the results of our experiments, and his comments have been most helpful.

Experimental

1. *First Methionine Series.*—Young female rats of a Wistar strain, weighing between 100 and 150 g., were placed on a diet of 15 g. of fox chow a day until a moderately constant urinary output of nitrogen was secured. This usually occurred in from 10 to 14 days. Under ether anaesthesia they were then subjected for a period of 30 seconds to water at 73° C., in a manner similar to that described by Croft and Peters. Most of the animal's back, amounting to about one-third of the surface area of the body, was immersed in heated water. On the day of the burn and daily thereafter a buffered solution of methionine equal to 1% of the diet was injected subcutaneously into six of the nine rats used in the experiment. The animals were weighed daily and urinary nitrogen estimations were made at 48-hour intervals for ten days after the burning.