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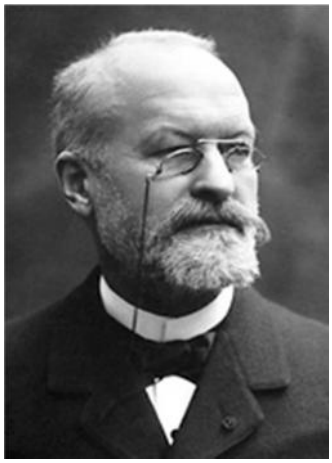
Nobel Prize in Medicine 1907



Charles Louis Alphonse Laveran

The Nobel Prize in Physiology or Medicine 1907 was awarded to Alphonse Laveran *"in recognition of his work on the role played by protozoa in causing diseases"*.

RESEARCH INFORMATION:

The Staff of Professors at the Caroline Institute have this year awarded the Nobel Prize for Medicine to Dr. Charles Louis Alphonse Laveran, for his work on the importance of the protozoa as pathogens.

The Staff has thus chosen to single him out not only as the founder of medical protozoology, a branch of medicine that has reached a striking level of development in recent years; but also as the man responsible for experiments and discoveries - followed up until recently - which ensure his continued pre-eminence in this field.

To appreciate properly the importance of Laveran's investigations into the protozoan causes of disease, one must remember the state of this branch of science at the time of Laveran's earliest work, i.e. about 1880. The body of knowledge relating to the causes of infectious diseases was making rapid progress at that time in the field of bacteriology. Pasteur's «Theory of Germs» had provided the key to the riddle of fermentation processes, and its relevance to infectious diseases had been grasped. So

several pathogenic bacteria had been discovered by 1880: those of anthrax and relapsing fever; other germs, such as those causing tuberculosis, glanders, pneumonia, typhoid fever, diphtheria, tetanus, Asiatic cholera, traumatic fevers, etc. were discovered one after another during the years 1880-90. All these germs were found to belong to the last category of the plant kingdom, the bacteria.

As a result, it was natural to look for the cause of marsh fevers, like malaria, among micro-organisms of that sort. Indeed, several distinguished bacteriologists believed themselves to be on the trail of such a microbe. We recall the so-called malaria bacillus of Klebs and Tommasi-Crudeli, found in the ooze of the Pontine Marshes.

When Laveran, in 1879, began his research at the military hospital of Bône in Algeria, he only set himself the task of explaining the role of the particles of black pigment found in the blood of people suffering from malaria. After 1850, when these particles, called melanins, were discovered, methods had been discussed of determining whether they were only to be found in patients suffering from malaria, or were present in other diseases as well. Laveran first set about solving this problem, which was particularly important to the diagnosis of malaria. During his investigations, Laveran not only found the particles he had been looking for: he also found some entirely unknown bodies with certain characteristics which led him to suppose that parasites were involved. His initial investigations were carried out on fresh blood without using chemical reactions or any staining process. He was none the less successful, using this primitive method of examination, in distinguishing and describing most of the more important forms adopted by these new bodies, which varied so much in their appearance. In 1882, he moved the scene of his investigations for a while to the dangerous marshy regions of Italy. There he again found the same bodies in the blood of people suffering from marsh fever, and his hope of having found the malarial parasite became a certainty. Laveran published his first great work on these parasites, *Traité des fièvres palustres*, in 1884. In this, he draws on 480 examined cases of malaria.

This work is the foundation on which subsequent investigations of marsh fever are based. Laveran showed that the parasites, during their development in the red blood

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corpuscles, destroy them; and the red pigment in the corpuscles is changed into the melanin particles mentioned above. He described all the main forms of this polymorphic parasite, even those which have subsequently been found to be different developmental phases of the parasite. Continuing his work, Laveran concerned himself in the first place with the important problem of the existence of these parasites outside the patient's body. To this end he examined the water, soil, and air of the marshlands, hoping to find the parasite. His perseverance was unrewarded. We should not, however, fail to recognize the merit of this work, despite its negative outcome, since it has fundamentally aided subsequent research. As far as Laveran was concerned, these apparently fruitless investigations led him to the conclusions which he expresses in the book of 1884, and has also maintained on a number of occasions, such as the Congress of Hygiene at Budapest (1894): that the marsh-fever parasite must undergo one phase of its development in mosquitoes, and be inoculated into humans by their bites. Laveran based his conclusion not only on the negative experiments already mentioned, but also on an analogy with the mode of transmission of the Filaria worm, which, according to Manson, is mosquito-borne. When Laveran was recalled from Algeria to Paris, and so forced to interrupt his work on malaria, he had already clearly formulated the problems that had first to be solved in this field.

The new parasite discovered by Laveran was not a bacterium. Although it was impossible to classify accurately, certain resemblances to other micro-organisms put it in the same group as the protozoa. We know how difficult it is to demonstrate the presence of malarial parasites in blood which has not been treated beforehand with the stains now in general use, but still unknown at the time of Laveran's discoveries, which make these small parasites more readily visible; so one can appreciate at their true value the insight and keen eye of Laveran, who never allowed himself to be misled by the simultaneous successes of bacteriology, or discouraged by the opposition met with from several quarters, notably from workers studying marsh fever.

However, little by little Laveran's theories made headway, and it can be said that the year 1889 marks the date when his discovery finally achieved recognition.

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When Laveran had to leave the marshlands, he saw himself deprived of materials indispensable if he were to continue working on the still unanswered questions, i.e. those dealing with the parasite's developmental cycle, and its existence away from the patient. He then tried to solve them by an indirect approach, by studying animal parasites, especially those of birds: these parasites had only recently been discovered and showed resemblances to the malarial parasites. The numerous observations Laveran made in the course of this research cannot be indicated here: they belong by rights to the specialist sphere of interest. Now, as always happens after a notable discovery, workers multiplied in the new field. Some of the many workers who were able to continue Laveran's work on the spot, in marshy areas, were destined to reach the goal before Laveran by the indirect approach which he had indicated. Thus, in 1897 the American Mac Callum elucidated the sexual reproduction of these parasites; and, in 1898, the impressive work of Ronald Ross, the Nobel Prize winner for 1902, brought the mosquito theory from the realm of hypothesis into that of established fact. One can imagine the interest with which Laveran must have received the preparations sent to him by Ross from India in May 1898, and the joy with which he confirmed that Ross was in fact dealing with malaria parasites in the mosquitoes he was investigating.

Laveran's discoveries concerning malaria had the additional effect of focussing direct and vigorous attention on the hypothesis that other infectious diseases could be brought about similarly by protozoa. In the tropics especially, but in other areas as well, diseases have been recognized for a long time among men and animals, which are similar to malaria in many respects, such as impoverishment of the blood, loss of strength, and associated fever, but which, unlike malaria, are not affected by the classical treatment, quinine, and are clearly shown by the absence of marsh-fever parasites not to belong to the same group as the marsh sicknesses. Since 1890 a whole series of parasites causing these diseases has been described. Once, thanks to Laveran, attention was drawn to the protozoa as agents of disease, discoveries of such protozoa took place in rapid succession. Among

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diseases due to protozoa, the trypanosomiases take precedence. The list of these diseases alone is long, and we will mention only the scourges known as *Nagana*, *Surra*, *Caderas* sickness, and the *Galziekte* of Equatorial Africa, etc. which ravage large parts of Africa, Asia and South America, attacking various members of the Bovidae, horses, camels, donkeys, etc. as well as the big game, antelopes, deer, etc. sometimes wiping out great herds. All these infections are caused by corkscrew-shaped micro-parasites, called trypanosomes, and are transmitted to animals by various types of biting flies. However important these diseases may be to Man from the point of view of commerce and nutrition, yet, among all the trypanosomiases, the endemic disease generally known as «sleeping-sickness» takes precedence from the medical point of view. The sleeping-sickness trypanosome was discovered in 1901 by Forde in a European ship's captain who had navigated the river Gambia for several years. Forde does not seem to have examined the parasite in detail. Later, the same case was studied by Dutton, and following on his reports on the parasite and the disease, an expedition was sent from Liverpool and London to carry the investigation further. This expedition also solved the first problems relating to the disease. There is certainly much one could say about these diseases; unfortunately we may not dwell on them here. Let us rather take a quick look at the part played by Laveran in the elucidation of these problems.

It can be said, it seems to us, that Laveran took up these problems again at the exact point where circumstances had forced him to interrupt his own research on malaria. He had discovered the parasites for the latter group of diseases, but others, notably Golgi and Ross, followed up the biological investigation of the parasites. As far as the trypanosomiases are concerned, the opposite holds good: the parasites were discovered by other investigators, who were able to study the investigations on the spot in a number of different places, but Laveran, more than anyone else, extended our understanding of the finer points of the morphology, biology, and pathological activity of the parasites. He made this work possible by having many artificially-infected experimental animals brought to his Paris laboratory, as well as larger animals which had contracted the disease naturally. Not

content with this great quantity of material, he extended the scope of his investigations even further by studying the trypanosomes of rats, birds, fishes and reptiles; and these investigations often threw light on the true pathogenic trypanosomes at the same time. The trypanosomes thus studied and described by Laveran number about thirty; he discovered a greater number of new species than any other worker we know of. In addition, he discovered a new genus of trypanosomes, the trypanoplasmias.

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