Medicine in Stamps

Charles Laveran (1845–1922): Nobel laureate pioneer of malaria

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Malaria is a tropical disease, as ubiquitous as it is deadly. The best estimates put the death rates from nature's top killer at several millions each year, the most vulnerable being young children and pregnant women. For the longest while, the prevailing theory linked the disease to foul air in swamps and marshes – hence the name marsh fever or malaria, which means "bad air" (*mal aria*) in Latin. But we now know that the proximate cause is a lowly one-cell organism, a protozoon, transmitted by biting mosquitoes. It was Sir Ronald Ross who solved the mosquito vector puzzle, but this was made possible through the work of French physician Charles Laveran, who in 1880 correctly identified the *Plasmodium* parasite as the causative agent of malaria.

EARLY YEARS On June 18, 1845, Charles Louis Alphonse Laveran was born to a family with rich military and medical pedigrees. In 1863, he entered the Public Health School at Strasbourg, earning his MD degree four years later. Soon after he graduated, the Franco-Prussian War broke out and young Laveran enlisted in the army, his entry rank being medical assistant-major. He was soon deployed to Metz, an important fortress in France, as an ambulance officer. Metz eventually fell to the Germans, who allowed Laveran to return to Paris where he started work at St. Martin Hospital. In 1874, he became Chair of Military Diseases and Epidemics at École du Val de Grâce – a position previously held by his father.

FROM ALGERIA TO MALARIA Four years later, the military sent Laveran to Algeria, where he made his ground-making observations on malaria, a disease rampant among Algerians. Following his arrival in Bône in 1878, he wrote: "*I had the opportunity of making autopsies on subjects who had died from pernicious attacks, and I was struck with the fact that melanaemia [the presence of black pigment in the blood, causing a brown colouration of certain organs] was a lesion peculiar to and very characteristic of [malaria]*." In his later Nobel lecture, Laveran emphasised that "*Melanaemia is almost always sufficient to show from microscopic examination if death is the result of paludism* [i.e. marsh fever, from the Latin "palus," meaning marsh]."

This first key observation led to additional research in Bône and Constantine, culminating in the eventual discovery of the malarial parasite. Laveran found that the pigmented granules enclosed within hyaline cysts in erythrocytes were in fact amoeba-like microorganisms. On the momentous date of November 6th, 1880, while examining these pigmented bodies, he noticed "*moveable filaments or flagella, whose extremely rapid and varied movements left no doubt as to their nature*." In rapid succession, Laveran spotted the organism in 148 of 192 cases that he examined, including specimens that originated from the marshes of Rome and surrounding areas of Italy. In 1882, he was able to convince Louis Pasteur and Emile Roux, pre-eminent scientists of the time, of the protozoal aetiology of malaria by demonstrating the parasite in a rare case of malignant malaria. In his important publication of 1884, *Traité des fièvres palustres*, Laveran described his experience in a total of 480 cases. His conclusions: the malaria parasite would enter and grow within red blood cells, causing them to swell and liberate spores into the bloodstream, and would go on to invade other red cells. He named the infective organism *Oscilliaria malariae*; the genus was subsequently changed to *Plasmodium*.

OTHER PROTOZOAN DISEASES In 1896, after administrative positions at Lille and Nantes, Laveran left the military to continue his academic pursuits at the Pasteur Institute. Welcomed as belonging to "*independent spirits desiring to undertake disinterested research*," he

pioneered important studies on protozoa such as Sporozoa and trypanosomes. Although the important sleeping-sickness trypanosome was actually identified in 1901 by Forde, it was Laveran who helped to elucidate its life cycle and transmission.

Laveran also studied other pathogenic protozoa of domesticated and wild animals, e.g. deer, horses, camels and donkeys, and showed that in many instances, the disease was transmitted by biting flies. Altogether, he is said to have studied some thirty different varieties of trypanosomes, including pathogens of reptiles, birds, even fishes.

VALIDATION AND RECOGNITION Laveran's findings were at initial odds with the contemporary notion that malaria was caused by a bacterium. In an era of rapid discoveries of bacterial infections such as anthrax, tuberculosis, typhoid and cholera, it was predictable that colleagues would spurn his assertion that there existed an entire new class of pathogens. In time, however, other investigators confirmed his results. The only remaining mystery: how did the malaria parasite gain entrance to the host in the first place? Laveran had himself raised the possibility of a mosquito vector, but it was the later work of Patrick Manson, Giovanni Grassi and Ronald Ross that definitively chracterised the life cycle of the parasite and the role of the *Anopheles* mosquito.

In 1889, Laveran received the valuable Bréant Prize from the French Academy of Sciences. He subsequently became a member of the Academy and eventually the president of the Academy of Medicine. In contrast to recognition by the international scientific community, the military medical service failed to acknowledge his accomplishments. However, vindication came in 1907 when Laveran won the Nobel Prize for Physiology or Medicine "*in recognition of his work regarding the role played by protozoa in causing disease*," thus joining Sir Ronald Ross, who received the Prize five years earlier for his studies on the role of the *Anopheles* mosquito.

Laveran gave half his prize money to the Pasteur Institute to help establish the Laboratory of Tropical Medicine, and devoted the rest of his career to the continued study of malaria and other protozoan diseases. He visited endemic parts of France, and guided educational programmes for disease control. During World War I, as a member of the Commission on Hygiene and Prophylaxis, he directed measures at malaria prevention in areas where French troops were stationed. And in 1908, he founded the Société de Pathologie Exotique, serving as its president for the next twelve years. For his efforts, he was made Commander of the Legion of Honor in 1912, a prestigious service award created by Napoleon Bonaparte himself. Three years later in 1915, on his 70th birthday, he became Honorary Director of the Pasteur Institute.

CURTAIN CALL Not much is known about Laveran's personal life. He married in 1885, soon after returning from Algeria, but did not have any children. He apparently enjoyed art and literature. According to accounts, he was an independent and diligent worker, but somewhat cold and detached. Still, to peers and family, he was described as cheerful.

On May 18, 1922, Charles Laveran, aged 76 years, died in Paris. He lies buried at the famous Cimetière du Montparnasse in Paris, in the company of many of France's elite, like philosopher Jean-Paul Sartre and Statue of Liberty sculptor Frédéric Bartholdi. His legacy is immortalised in his approximately 600 works on human and veterinary parasitology, in particular his landmark insights into the aetiology of "marsh fever."

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