

Nobel Prize in Medicines 1951



Max Theiler

The Nobel Prize in Physiology or Medicine 1951 was awarded to Max Theiler "for his discoveries concerning yellow fever and how to combat it"

Yellow fever is one of many diseases spread by insects which have been and to some extent still are a scourge in certain tropical and subtropical countries. We do not know when yellow fever first made its appearance. The first epidemic that can definitely be identified as yellow fever occurred in Mexico in 1648, where it is believed to have been imported from West Africa on ships which brought negro slaves to America. If this is correct, this was a more dangerous a «ghost going West» than the one we remember from that title in the movies, and it is only to be compared with another one that probably went East at about the same time, syphilis.

In the 17th, 18th and 19th centuries the disease was especially rampant along the shores of the Caribbean, whence it spread intermittently along the sea lanes of the Atlantic and eventually reached large areas of continental South America and Africa.

The history of yellow fever abounds in dramatic events and it has played a certain politico-economic role. An example is the fate of Haiti. The aborigines of this West Indian

island were soon reduced in number through harsh treatment by the whites, who then imported negro slaves. The slave population rapidly increased, and one day they rebelled and slew their white masters. Napoleon sent 25,000 troops to deal with the negroes, who fled into the jungles followed by the soldiers. After a few weeks 3,000 men returned; the rest had died of yellow fever. Even to this day Haiti's population is 90 per cent negro. Another instance is the failure of the Frenchman de Lesseps to build a canal across the Isthmus of Panama because his workmen died of yellow fever and malaria.

The exact nature of yellow fever and its mode of transmission were long obscure. As early as the 18th century the abundance of mosquitoes in places where the disease occurred had been observed, and in 1881 Dr. Carlos Finlay, a Cuban physician in Havana, had written a treatise in which he asserted that the disease was transmitted by mosquitoes, but his assertion drew little attention. When, in 1898, the Spanish-American War broke out, yellow fever caused considerable difficulties for the American army in Cuba. Because of this the American authorities in 1900 appointed a Yellow Fever Commission with Walter Reed, an army surgeon, as its head. The commission could find no bacteria that caused the disease, but instead they found that it was transmitted to persons bitten by mosquitoes which had previously sucked the blood of patients suffering from yellow fever. This particular mosquito was found to be of the species *Aedes aegypti*, which lives in and near human habitations and multiplies in the stagnant water of pools and containers. This discovery made it possible to combat the disease by exterminating the mosquitoes and by isolating the patients in surroundings where there were no mosquitoes. Extraordinary results were quickly obtained by these simple methods. One of these was the extermination of yellow fever in the Panama Canal Zone, a necessity for the construction of the Canal.

The Reed commission, however, made still another discovery - that the infectious agent in yellow fever belongs to a group which we nowadays call virus, and which differs from bacteria in many respects. Shortly before this time, it had been established that a virus causes foot-and-mouth disease, but this was the first time anyone had found that this

newly discovered type of contagion could cause disease in man. We now know that viruses cause many of our most dangerous diseases.

It was thought at first that the Reed commission had practically solved the entire yellow fever problem, but it gradually became apparent that this was far from true. As early as 1911, a group of South American physicians proved that one can be infected by yellow fever not only in the vicinity of human dwellings, but also when working in virgin jungles. Some years later the suspicion arose that this form of disease, which later became known as «jungle fever», exists among wild monkeys and may be transmitted from these animals to man. However, it was a long time before conclusive evidence could be presented showing that this was the case. It has cost much labour to reach this knowledge, most of which has been carried out under the direction of the International Health Division of the Rockefeller Foundation. The dangerous nature of yellow fever is well illustrated by the fact that no fewer than six members of the medical staff of the Health Division have given their lives in the course of these investigations. An important step toward solving the riddle of jungle fever was taken in 1927 when research workers succeeded in transmitting the disease to monkeys experimentally. Here was proof that the theory was not unreasonable and that a means had been found by which its accuracy could be confirmed by further experiments. Monkeys, however, are not only expensive but also difficult to handle; it was therefore welcome news when Dr. Max Theiler in 1930 discovered that yellow fever can be transmitted to white mice, which are easy to handle and are available by the thousand at small cost. In the following year Dr. Theiler demonstrated that mice inoculated with serum from humans or monkeys who had had yellow fever are protected against infection by the contagious substance of the disease. By this discovery a test had been found whereby it was possible to map the occurrence of yellow fever in both monkeys and human beings and which has been invaluable in revealing the epidemiology of jungle fever and the link between that disease and classical yellow fever. We now know that yellow fever is a very common disease among the monkeys of the South American and African forests and that it may spread to humans through the agency of several species of mosquitoes. Where there is

a sufficiently large number of non-immune persons in the presence of *Aedes aegypti*, one individual infected in this way may be the cause of an epidemic of the classical yellow fever. Because monkeys and these species of mosquitoes most often dwell in the tops of jungle trees and cannot be exterminated, jungle fever remains a constant menace, a fact which was well supported by observation, especially in South America. Fortunately Dr. Theiler's discovery implied more than this. He demonstrated that the infectious agent, if transmitted from one mouse to another, becomes so weakened that monkeys can be inoculated without risk, and that this makes them immune to the disease. The next step was to try inoculation on human beings; this was done in 1932 by the Rockefeller group and by Sellards and Laigret in France - in both cases with success. However, the use of the mouse vaccine was thought to involve certain risks. This led Dr. Theiler and his collaborators, Lloyd, Smith, and Ricci, to try to produce a vaccine less potentially dangerous. After much hard work they achieved their purpose by means of a special technique. This variant of the virus, which is quite harmless to man, was called 17D. Inoculation with 17D must, however, be made by injecting the vaccine subcutaneously, whereas the mouse virus can be introduced through a scratch on the skin in the same manner as in vaccination against smallpox. For this reason the mouse virus is more suitable for mass treatment; the French have used this technique in their African colonies, where 20 million out of a total population of 30 million have thus been inoculated. L'Organisation Mondiale de la Santé, which has prepared regulations for the compulsory inoculation of passengers travelling on airlines through countries where yellow fever exists, approves both vaccines.

The significance of Max Theiler's discovery must be considered to be very great from the practical point of view, as effective protection against yellow fever is one condition for the development of the tropical regions - an important problem in an overpopulated world. Dr. Theiler's discovery does not imply anything fundamentally new, for the idea of inoculation against a disease by the use of a variant of the etiologic agent which, though harmless, produces immunity, is more than 150 years old. Jenner used a natural virus variant, cowpox virus, against smallpox, and Pasteur produced a similar

variant of the rabies virus by repeated passage through animals. So far there have been only a few successful attempts to master a disease by such measures, but Dr. Theiler's discovery gives new hope that in this manner we shall succeed in mastering other virus diseases, many of which have a devastating, effect and against which we are still entirely powerless. Max Theiler, therefore, has rendered mankind such a service as Nobel made a condition for the awarding of this prize.

Dr. Theiler. For a period of almost forty years the International Health Division of the Rockefeller Foundation has carried on very comprehensive and fruitful work in combating yellow fever and extending our knowledge of it. Among the many who have made their contributions, you take an especially prominent place, because you have made their contributions profitable and because you have opened the way to greater understanding of the epidemiology of the disease and to an effective prophylaxis against it. The Caroline Institute esteems your research work so highly, not the least for its practical value, that it has found it proper to award this year's Nobel Prize in Physiology or Medicine to you.

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