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by William Osler.**

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ROYAL COLLEGE OF SURGEONS ENGLAND
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Yellow Fever and Malaria.

**Evidence given before the Royal Commission by
William Osler, M.D., F.R.S., Regius Professor
of Medicine, Oxford.**

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the Appendix to the Fourth Report of the Royal Commission, p. 157.*

(The questions put by the Commissioners are printed in italics.)

I think that the story of yellow fever illustrates, perhaps, more satisfactorily than any other, the remarkable way in which experiments, carefully devised and carried out, may influence not only our knowledge of the etiology of a disease, but may influence extensively the commercial relations of nations, and save not only thousands of lives but millions of pounds annually. Yellow fever has been the great scourge of the regions round the Caribbean Sea, more particularly Mexico, the West Indian Islands, Brazil, and every few years it has spread into the Southern States of America, and occasionally has reached Philadelphia, and even as far north as Boston. In the early part of the last century on several occasions it reached Europe, and there were extensive outbreaks in Spain, costing some thousands of lives. Many attempts had been made to find out the cause of the disease, but all had failed up to the year 1900, when a Commission was sent to Havannah by the United States Government especially to investigate the cause of yellow fever. That Commission, composed of Drs. Watten Read, Carroll, Lazlear, and Agramonte, recognised particularly the relations of the mosquito to the disease, and they went out with the specific object of determining, if possible, to discover the germs of the disease. The experiments which they devised were carried out in a United States Army Camp in Havannah, and they are among the most remarkable that have ever been made. The camp was entirely isolated, so that there could be no possibility of communication with the outside. It was composed of a certain number of immunes, that is to say, persons who were no longer susceptible to yellow fever—

*In consequence of having had it, do you mean?—*In consequence of having had it—and of non-immunes. That is a common division of the population in Brazil and Havannah—namely into immunes and non-immunes. A man is asked whether he is immune or not.

Does one attack confer immunity as a rule?—One attack confers immunity. In this camp a house was constructed with two compartments, divided from each other by a wire mosquito-proof screen. There were two sets of experiments made in connection with this little house. In the first place, into one side of this hut 15 infected mosquitoes were placed. Those were mosquitoes that had bitten a yellow fever patient within the first three days of the illness. Men were selected, partly from the Army and partly from civil life, who had expressed and signed their willingness to submit themselves to experiments. I may state that one or two of the medical men also volunteered. Into the compartment with the 15 mosquitoes a non-immune went in the morning, in the afternoon, and on the following morning, and submitted himself to the bite.

For an hour, or something of that kind?—I do not know how long, but long enough to get a number of bites. Within five days he had the disease. At the same time, in the adjacent compartment, which was simply screened from these mosquitoes by a wire netting, for 21 consecutive nights two non-immunes slept. They did not get the disease.

Were any precautions taken to keep the ordinary mosquitoes from them?—Yes, of course; the compartment was double-doored and very carefully screened so that there was no possibility of that. I may say that experiments of that nature were repeated on several occasions, demonstrating quite conclusively that, so long as these infected mosquitoes were kept from biting, though there was only a screen between them, the individuals did not get yellow fever. Then, experiments were made on a very extensive scale to determine whether the disease was conveyed by means of fomites, that is to say, whether, as was usually supposed, the disease was carried by infected clothing and by the excreta of the patients and by the vomit. For that purpose the clothing and material soiled by the vomit and by the blood, and by the stools of the patients, were placed in one of these rooms, and a group of non-immunes slept in contact with this clothing, in some cases between the actual sheets of the beds in which these patients had died, for 21 consecutive nights. That experiment was repeated with a second set of non-immunes sleeping, as I say, with the bed linen and with the soiled materials of patients who had died of the disease. Not one of them took yellow fever.

What were the numbers of the non-immunes that slept in connection with the fomites?—I think two or three, two soldiers and one surgeon, for 21 consecutive nights; and a second party for the same period. Then these men were subsequently experimented upon by placing them in the section of the house with the infected mosquitoes, and in each instance they took the disease. Altogether 22 soldiers sub-

jected themselves to the experiment and 22 took the disease; fortunately none of those cases proved fatal. One fatal case was a former assistant Dr. Lazlear, who had been for several years in charge of my clinical laboratory. He submitted himself to the bite of an infected mosquito, and three days subsequently developed the disease and died.

*May I ask what interval there was between the exposure to the fomites, and individuals being put into the place with the infected mosquitoes?—*Some days, possibly weeks, intervals; I cannot say exactly.

*What is the incubation period of yellow fever?—*From three to five days. The mosquito to become infective must bite a patient within the first three days of the disease—*Of its having been in contact with the disease, do you mean?—*I mean that the mosquito must bite the yellow fever patient within the first three days of the patient having the disease. The mosquito itself is not infective under a period of 12 days; the mosquito may bite an individual anywhere up to the twelfth day after receiving the infection without being infective; then it remains infective all through the rest of its life.

Of course, the interesting practical point comes out, that this series of experiments has already revolutionised life in those regions. Havannah within the next two years was cleared of yellow fever, the first time in the 300 years of its existence. The French Academy sent a Commission to Brazil to study the disease, and they have reported in harmony with the American Commission—namely, that the disease is transmitted by the mosquito, and by the mosquito alone, and only by a mosquito that had bitten yellow fever patients within the first three days, and that the mosquito did not become infective until after 10 or 12 days subsequently.

*I think in yellow fever the transmission of any organism from the mosquito to man has not yet been followed out?—*No, we do not know the organism; but it must be a protozoon, possibly a spirochæte, which undergoes a slow evolution in the body of the mosquito.

*But nothing has hitherto been discovered comparable with the plasmodium of malaria?—*No, but it is possible that it is a very minute spirochæte, which passes through an ordinary filter.

This is the kind of discovery that will revolutionise conditions of life in the tropics. The discovery of the malarial parasite and the discovery of relations of yellow fever with the mosquito will enable the Panama Canal to be built. Without those two investigations, the probability is that it could not be built. *Or, if built, would cost a tremendous sacrifice of human life?—*It would cost an enormous sacrifice of human life, just as happened with the French. Now there

are 20,000 whites on the Isthmus at work; of course, nearly all of those are non-immune. There has been practically no yellow fever, and what is much more important, because it was not the yellow fever that killed the French to the same extent, there is no malaria.

*In these experiments that you have been detailing to us, animals do not come in; the animal experimented upon was man?—*That is so, only as man is an animal. I am referring to those experiments only as an illustration that it is through the experimental side of medicine, the experimental spirit in medicine, that these great revolutions have been effected, revolutions with which there is nothing else in human endeavour to compare from the standpoint of humanity. There is not anything else in the whole development of the British nation that is going to have so much importance as the discovery of the mode of transmission of malaria. It is going to make the tropics habitable. And all this has come about through the experimental method and the experimental spirit. Without these such investigations could not have been made, and these perfectly phenomenal results could not have been achieved. It was the same spirit that gave us anæsthesia, and the same spirit that has given us antiseptic surgery, and the same spirit which has given us preventive medicine—three things which stand out in the record of human achievement, with which nothing else may be compared—I mean from the standpoint of every-day, common humanity.

*Then your contention would be that this experimental investigation into the interaction between the mosquito and man producing yellow fever would never have been thought of, if it had not been for previous experiments on animals?—*Never. The men who made these investigations spent their lives in laboratories, and their whole work has been based on experimentation on animals. They could not otherwise, of course, have ventured to devise a series of experiments of this sort.

*Could you experiment with yellow fever on animals?—*Yes, recently Wolferston Thomas, from the Liverpool School, working in Demerara, I think, has shown that it is capable of transmission to one of the higher anthropoid apes.

*Do the natives take yellow fever?—*Yes, everywhere; but they often have it in such a mild form, and have it as children. *Still, even in that mild form, the mosquito would transmit it?—*Yes.

*I understand that when the mosquito has once bitten a patient suffering from yellow fever, after the first 10 or 12 days it remains capable of transmitting the disease during its short life?—*Sometimes it is a comparatively long life—many months. *Has that been determined?—*Yes, it will live through many months; it will live through the winter.

*As the fever has disappeared in Havannah, may I ask whether the special stegomyia mosquito has also disappeared?—*No, they have made an active warfare against it, but I think the mosquito itself has not disappeared. *But if the mosquito is capable of transmitting the disease during its existence, after it has bitten a patient suffering from the disease, how can you get rid of the disease, so long as the mosquito lives?—*That is only a matter, I think, of 8 or 9 months. I do not know definitely what the life of a mosquito is. I do not think it is more than over the succeeding winter.

*Is there anything further you wish to add about yellow fever?—*No, I think not. The work in Brazil lately has shown that even in large centres, like Rio, by the mosquito brigades thoroughly carrying out measures such as were introduced in Havannah by Gorgas, the reduction in mortality and in the number of cases has been very striking. *By taking steps to prevent the breeding and multiplication of mosquitoes?—*Yes, and by carefully reporting and carefully isolating the very earliest cases I look forward to the total abolition of yellow fever within five years, and that, from the commercial standpoint alone, will revolutionise the trade of those districts. Every few years that a terrible epidemic arrives and spreads, New Orleans and the Southern States, and the commerce of the whole country, has been paralysed for long periods.

*How do you account for the epidemic's rise and fall, because the mosquitoes were always there, and the yellow fever on which they feed is always there?—*That is the difficult point; it is not easily explained. It depends very much upon how large the immune population is. The greater the proportion of non-immunes, the heavier will the epidemic be, because in a city like Havannah every non-immune within a year of his arrival there took the disease—he could not escape.

*Now that you have discovered that the mosquito is the cause, how do you ensure protection against it?—*By screening the houses properly and scouring out all the pools and protecting the water tanks. *By destroying the habitat of the insect?—*Yes, and particularly in Havannah, by covering up and protecting the water tanks, and by the active energetic fight against the mosquito which has been made so successfully. *Then the object is the extirpation of the mosquito?—*Yes.

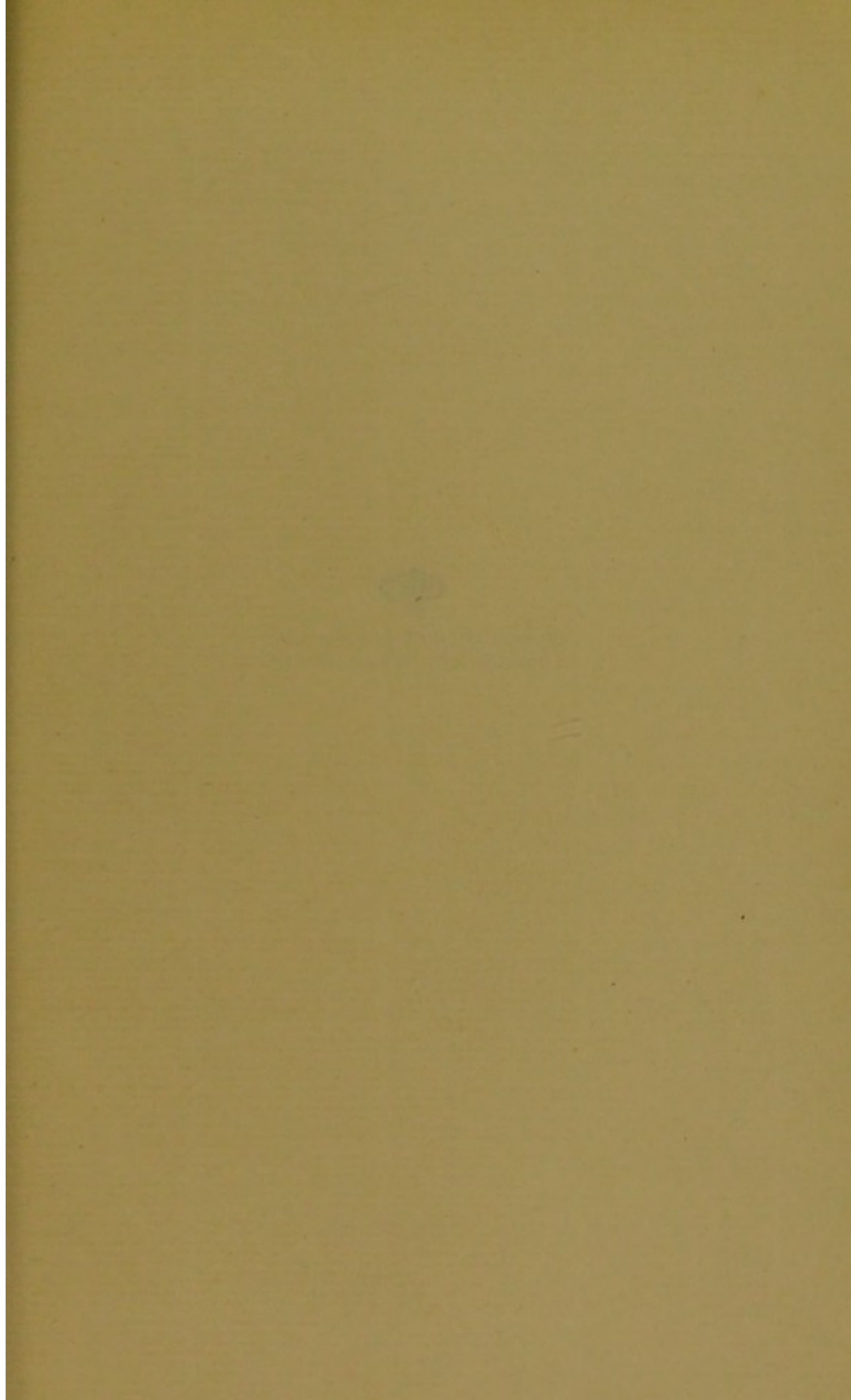
*The mosquito does not fly very far, I suppose?—*Some of them go long distances, particularly when carried by the wind. Then of course, they are carried by ships, and get into the holds, and get from one country to another in this way. *Is it not the case that in the mosquito which is connected with yellow fever the changes from the*

egg to the complete insect occur very rapidly?—Very rapidly. And also that its breeding places specially are not running waters or large pieces of water, but small pools, and even the water left in hollow utensils, which are not thrown away, around private houses?—Yes.

Might I ask has there been at present any distinct diminution in the multiplicity or numbers of mosquitoes?—Yes, in all these regions, particularly where an active crusade has been waged, as in Havannah, in cleaning out these places where they have been breeding. They have become diminished in number?—Yes.

I suppose they never swarm as the midge does in this country?—Oh, yes, they do, and even in the cities, in countless myriads. Is it held to be possible to exterminate them?—Yes, I do not think there is any question about it. It has already been done in many places. Ross worked at that in Ismailia; and even in the West of India under the most unfavourable conditions, the reduction in the numbers of mosquitoes has been very remarkable.

Do you suppose that if it were a fact that disease of a serious nature could be communicated by the midge in England or Scotland, their numbers could be seriously attacked and diminished upon the moors and bogs, and places where they swarm?—In the immediate neighbourhood of houses it could be done. A thing which has been demonstrated, parallel with that, is the reduction in the number of cases of malaria. Take, for instance, a place called Sparrow's Point, in Chesapeake Bay; within the last five or six years, since we have known how malaria was transmitted by the mosquito, the number of cases has been diminished almost to vanishing point there, entirely by clearing up the pools and waging war against the mosquito. There has been a remarkable reduction in the cases of malaria there. The mosquitoes, of course, have been diminished too?—Yes. Are those pools the breeding places?—Yes. This discovery is making Africa, of course, habitable for the white man. Many of the young men who have been out on the recent scientific expeditions have by carefully protecting themselves lived for years there without having an attack of malaria.





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