

OUTWITTING THE MOSQUITO

W. H. HATTIE

“**M**OSQUITO Manson”, which might seem to be a peculiarly ridiculous pseudonym, was the title bestowed upon Patrick Manson by admiring friends at a time when they were still a bit doubtful about his pet enthusiasm. Later on, when there was no doubt, England’s King dubbed him Sir Patrick, and other honours were showered upon him in recognition of work which had increased the significance of the earlier and more distinctive title. More than fifty years ago, while in Amoy, Manson proved that mosquitoes were instrumental in the spread of filariasis from man to man, and thus not only solved one of the most puzzling of medical problems, but furnished a key to the solution of several others. From that time he pursued mosquitoes with quite as much zeal as mosquitoes pursue men. While some of his friends wagged their heads dubiously, others took inspiration from him, and joined whole-heartedly in the pursuit. Manson was convinced that filariasis was not the only disease disseminated through the agency of the mosquito, and his conviction soon came to be shared by others. His early work and that of his immediate disciples eventually brought a host of scientists into the investigation of mosquitoes. Resulting discoveries made the elimination of malaria and yellow fever feasible, made trade with the tropics reasonably safe for ship’s crews, made successful colonization of tropical and subtropical countries possible, and permitted the construction of the Panama Canal without the fearful wastage of human life which characterized the venture of de Lesseps.

Manson was not the first to hold the mosquito suspect in relation to the spread of disease. A reference in the Sanskrit *Susrata* suggests a belief in the culpability of that pesky insect in malaria. This takes us back probably at least a thousand years. And what would appear to be a conjuration against mosquitoes is to be seen on a votive object found at Susa, which suggests suspicion of its malefic disposition even in the pre-Christian era. Few of the earlier writers expressed anything more than suspicion, but well-reasoned arguments in favour of the mosquito theory were advanced in 1881 by Carlos Finlay, a physician of Havana, who lived to see others produce experimental proof of the accuracy of many of his deductions. By common consent, however, the credit for the first conclusive demonstration of the

mosquito's guilt, and for giving the initial impetus to the vast amount of productive study of mosquitoes which has been carried on of late years, goes to the modest Scotsman, the "Father of Tropical Medicine." Of his followers, some have achieved more than he, most have followed the pursuit to far distant lands, many have experienced highly thrilling adventures, not a few have given their lives that humanity might be benefited. And this despite George Meredith's dictum that no stretch of cunning can outwit the mosquito.

When Manson, at the age of 22, went to Formosa, and shortly thereafter to Amoy to take charge of a hospital, he became interested in many diseases which were quite new to him. Among these was elephantiasis, a very common malady of the East, characterized by great swelling of the legs and other parts of the body, with resulting deformity and disability. A few years later his interest in this condition was intensified when he read that Lewis had discovered the embryos of filaria in the blood of persons suffering from it. He quickly confirmed the justice of Lewis's claim, and, by a combination of good fortune, intuition and deduction, made the discovery that the filaria embryos are present in the blood at the surface of the body only at night. The story is worth retelling. Two native assistants, in whom Manson had equal confidence, were detailed to examine the blood of patients. One consistently found the embryos in a much larger proportion of cases than the other. Manson sought and found the explanation of this discrepancy. The assistant who found the embryos most frequently did most of his work at night; the other, by day. Further investigation proved that embryos were found, during the day, only in blood taken from deeper parts, although at night they appeared in the blood near the surface. This was a puzzling phenomenon, and its explanation might help in proving whether or no the filaria had anything to do with causing the disease. And if it caused the disease, how did it get from person to person? Manson could not find that it escaped from the patient's body by any secretion or excretion. There must be some means of transmission. After rejecting a number of other possibilities, he directed his attention to blood-sucking organisms. The leech, the flea and the bed bug were found innocent, but there was a strong evidence against the mosquito. One of his chair boys, known to be infected, was bribed to allow mosquitoes to bite him. These mosquitoes were carefully dissected, and live filaria embryos were found in their bodies. The investigation was now well under way.

The rest of the story is long, involving the dissection of many thousands of mosquitoes, the demonstration of the migration of the little worm from part to part of the mosquito's anatomy, its development from stage to stage until it is capable of making its way from the skin to the lymphatic system of man, and then its faculty of taking its place in the mosquito's proboscis so that—when the mosquito bites man—it may gain admission to its new host. In such way did Manson forge the chain of evidence which led to the conviction of the mosquito as the disseminator of filariasis, and incidentally showed why the embryonic filaria appears in the surface blood only at night. For that is the time the mosquito bites, and consequently the time when it is worth the while of the filaria that needs a change of host to be where the mosquito can render the required assistance.

By this patient, brilliant work, Manson made the year 1879 one of the outstanding years in the annals of Medicine. In the following year came the demonstration by the French scientist Laveran that curious bodies which he and others had previously seen in the blood of malarial patients were living organisms. Long, patient study had again been rewarded by a momentous discovery, but years of work remained before its full meaning was to be realized. By this time the number of those who felt that the mosquito was concerned in the spread of malaria was considerable, but the great majority of scientists remained skeptical. Manson had no doubt, but there was no proof. He stood foremost among those who carried on investigations, and remained steadfast to his faith although several years of diligent research yielded little in support of his theories. Then he returned to England, where he was retained as medical adviser to the Colonial Office. This appointment prevented the continuance of his studies where material was plentiful, but did not lessen his interest. He kept in touch with those in the field, suggesting to them how difficulties might be overcome. Among his co-workers was Ronald (now Sir Ronald) Ross, then attached to the Indian Medical Service, to whom later fell the distinction of proving the correctness of Manson's belief. It is another long story, which cannot be fully detailed here. The *dramatis personae* include many capable scientists, of many nationalities, working in many parts of the world. Just at the end, Manson reappears on the scene to share in the final triumph. Ross, after years of unremitting work, had all but abandoned hope for success, when Manson suggested a study of bird malaria. Sparrows were brought into the experiments, and helped to clear up the difficulties. In 1898 it seemed that the

case was proved. A party sent out by the London School of Tropical Medicine spent several months in a highly malarial district at the worst season, but took no other precaution than restricting themselves from sunset to sunrise in a mosquito-proof shelter, and yet escaped infection. But the studies had been made in malarial districts, and some Thomases doubted whether other possible factors had been quite eliminated. Manson was in England, where there was no malaria. If some infective mosquitoes were sent to him and were made to infect hitherto non-malarial Englishmen, there could be no further doubt. And so, in the last year of the last century, early on a summer morning, two well-known scientists visited a pool in the neighborhood of Rome and captured a number of newly hatched female mosquitoes. Kipling has published abroad that "the female of the species is more deadly than the male," and the male mosquito, in fact, does not transmit malarial infection. After these youthful gnats had been allowed to feed freely on a complacent young Italian who was suffering from malaria, they were sent to Manson. He had two volunteers in readiness, of whom one was his own son, and of whom neither had been out of England. He himself had had malaria in the tropics, and was therefore not a reliable subject for experiment. The Italian-born mosquitoes had no aversion to the blood of Englishmen, and feasted thereon to the full. In due time both volunteers developed malaria, and the last doubt was removed.

Perhaps it should be explained that of the several hundred known kinds of mosquitoes, only about fifty, all belonging to the anopheles group, are capable of transmitting the malarial organism. This was not realized at first, and it can be understood how much time was taken in determining the particular kinds which now engage the attention of malariologists. Ross literally wore out a microscope in his studies. And something should be said of Laveran's organism, commonly called the *plasmodium* or *haemamoeba* of which there are three varieties—each producing malaria of a clinical type different from that caused by the others. The study of the plasmodium also presented many difficulties, and involved full investigation of the several cycles through which it passed in the blood of its victim and in the body of the mosquito. It may be said, in brief, that after it gains access to the blood by the aid of the mosquito's bite, it multiplies rapidly. Myriads of plasmodia enter the red blood cells (which they damage), pass through changes in form, sporulate, and form toxic substances. In time the red cells rupture, and the toxins are set free in the blood stream and produce the malarial paroxysm. When a mosquito

feeds on a malarial patient, some of the organisms pass into its stomach with the blood. In the mosquito, the plasmodium passes through a sexual cycle (in man the cycle is asexual) after which it establishes itself where it is assured a convenient entry through the skin of the next person the mosquito may bite. Part of the life history of the parasite is therefore passed in the human body, and part in the body of the mosquito, and the mosquito is the agent by which it is transferred from man to man.

It would be quite wrong to suppose that all the credit for so remarkable a demonstration belongs to Manson and Ross. They, however, were the acknowledged leaders, and the immensity of Ross's work was recognized by the award of the Nobel prize and Knighthood. It was now possible to devise means of combating one of the most devastating of the white man's foes, with all the implications of reduced mortality, increased efficiency, and the resulting benefit to commerce. Of the measures devised something will be said presently.

When Spain surrendered Cuba to our American friends, she provided them with an opportunity to make the most dramatic of all demonstrations of the mosquito's bloodguiltiness. Yellow fever had long been more or less prevalent in Havana, but it practically disappeared soon after the American occupation. This was attributed to the excellent sanitary measures carried through under the direction of the late Dr. William Gorgas. Within a year or two, however, a large immigration from Spain greatly increased the proportion of non-immune persons in the population, and one of the worst epidemics of yellow fever in the history of Cuba quickly developed. Gorgas was, of course, greatly disappointed. He was aware that Finlay had, years before, set forth good arguments in favour of the mosquito theory of transmission, and knew of the work of the Manson and Ross school, but he had felt that good sanitation would be sufficient to eradicate yellow fever. Very good sanitation had failed, so he made it even better, but to no avail. His disappointment was shared by the Washington authorities, who sent a commission to investigate. On the commission were Drs. Walter Reed, James Carroll, Jesse W. Lazear and Aristides Agramonte, whose names should live for evermore. They first put to the test the long cherished ideas that the disease was spread from person to person, and that articles of clothing, etc., which had been soiled by the discharges of patients were capable of transmitting the infection, and were soon convinced that both of these ideas were wrong. So they decided upon investigating the mosquitoes, which were now so much in the public eye. Par-

ticular attention was given to the variety which Finlay had years before declared to be the villain in the plot. In fact, mosquito eggs supplied by Finlay were used for breeding purposes. He had experimented by picking partly-fed *stegomyia* mosquitoes from the skin of yellow fever patients, and immediately transferring them to the skin of healthy volunteers. The volunteers were bitten, but remained healthy, and Finlay therefore failed to prove his contention. Reed and Carroll, knowing of the work on filariasis and malaria, suspected that a period must elapse after the yellow fever germ was taken into the stomach of the mosquito before it developed infective power. They soon proved this to be a fact. Carroll and Lazear now repeated on themselves experiments which had previously given negative results. Carroll permitted himself to be bitten by mosquitoes known to be carrying infective germs. Within a few days he was desperately ill with typical yellow fever. For days his life hung in the balance, but he recovered. Lazear, while working at the bed side of fever patients, saw a mosquito alight on his hand. He allowed the insect to bite him, and awaited results. In five days he became ill, and a few days later he died. The danger of such experimentation was thus made apparent to everyone, but more of it was necessary—and there were plenty of volunteers whose pluck did not save them from death or permanent disablement. A means had been found for curing malaria, but yellow fever still killed the majority of its victims, and obviously the first step towards finding a cure lay in determining its cause. Humanity owes much to those who heroically risked "winged death" in the crucial tests which proved the *stegomyia* (now known as *Aedes aegypti*) to be almost the sole agent concerned in the transmission of yellow fever. In one of these tests a number of volunteers slept in a filthy hut and in the soiled beds in which patients had recently died, but protected themselves against mosquitoes. All escaped infection. Of other volunteers who lived under rigid sanitary conditions, but were unprotected from mosquitoes, nearly all were infected. It was thus shown that danger does not lie in the discharges from fever patients.

The germ of yellow fever has not yet been actually demonstrated. It is not a bacillus, as was at first thought, nor the leptospira described by Noguchi, but is so small that it cannot be seen even under a high powered microscope. Nevertheless it can be used experimentally to produce the disease, and the facts known about it are quite amazing. After the patient has been ill for three days, the germs in his blood lose their infective power, and even if a patient be bitten by a mosquito during the first three

days of illness, the germs which enter the mosquito's stomach are not immediately capable of causing disease. About twelve days must be passed within the body of the mosquito before the germ is able to produce infection. Had Finlay known of these things, he would have had a complete case nearly twenty years before Reed and his associates brought out the truth so dramatically.

Although Gorgas at first scouted the mosquito theory, he cooperated wholeheartedly in the work of Reed's commission, and watched its developments with the keenest interest. It was not long before he realized that he had been wrong, and from that moment devoted himself unremittingly to devising measures for controlling mosquitoes. With but one variety of mosquitoes to manage, and that one singularly domestic in its habits and of limited flying-range, the task was comparatively easy. Perhaps the principal difficulty was to get the cooperation of the citizens, but Gorgas was tactful and soon had the support of nearly everyone. Within a few weeks Havana was again free of yellow fever.

Manson and Ross and their co-workers had shown that if men would screen themselves from mosquitoes they would escape filariasis and malaria. This was too much to expect of most men, so they directed efforts to discover methods which would not be defeated by man's indifference and carelessness. Breeding and other habits of mosquitoes—and fully fifty varieties had to be considered in the case of malaria—were carefully studied. Mosquitoes follow the common habit of insects in indulging in four stages of existence. Eggs are laid on the surface of water, where, too, the larval and pupal stages of development are passed. From the pupa the mosquito emerges full grown, and at once takes to the air. By drainage and other means of preventing the accumulation of water, breeding places in the near neighborhood of human habitations were eliminated, and where drainage was impracticable a little oil spread over the surface of the water prevented the larvae from breathing and consequently destroyed them. As the range of flight is restricted, such measures proved fairly effective where the expense involved could be met. Most malarial mosquitoes bite only at night; and where people could be persuaded to spend the night in screened houses, an additional factor of safety was provided. But many of those who live in malarial districts are indisposed to exertion, are not indisposed to believe that "whatever is best," and are rather disinclined to cooperate with foreigners. Few of these people, however, are quite indifferent to live stock, and some Machiavellian leaders in this particular mosquito war set up an agitation for a more intensive raising of ducks. As ducks are semi-

aquatic in habit and greatly relish a meal of mosquito larvae, they play a real part in keeping the mosquito population within bounds. The campaign for more and better ducks was reasonably successful, and its advocates were correspondingly gratified. But then there are fishes that have no mean appetite for larvae. Who could object to the stocking of near-by streams and pools with fish? In sequence to this happy thought came a study of the different fishes in respect of their ability to consume larvae, and certain minnows (the top minnow is now considered to be the greediest of all) were found to have an astounding capacity in this particular. The idea of having a few pet minnows in the family water barrel appealed so strongly to the youngsters that parental objection was overcome. So strategy was not neglected. By such varied and sometimes devious ways, much has been done to outwit the mosquito. Were it not for native prejudice, indifference and fatalism, malaria might now be extinct wherever there is the will among the governing classes. Yellow fever is much easier of control, as but a single variety of mosquito is ordinarily involved, and it is peculiarly domestic in its habits. It is doubtless because of the limited range of flight of the *Aedes aegypti* that yellow fever has always been essentially a disease of cities and towns. The limited opportunities for country bred mosquitoes to feast on yellow fever patients proved the salvation of most rural districts.

The outstanding demonstration of the possibilities of control of mosquito-borne infections is associated with the construction of the Panama Canal. DeLesseps's attempt was characterized by frightful mortality amongst his workmen; and before his work had progressed very far, men could be induced to go to the canal zone only by the promise of high wages. The wastage of money of which DeLesseps is accused was occasioned largely by the wastage of human life. When the United States undertook the task, it was with the knowledge that proper sanitation must be considered first.. They had Gorgas, whose work in Cuba has already been referred to, and to him they very wisely assigned the direction of medical activities. Although he had sometimes to contend with a hostile officialdom, he stuck steadfastly to his task. With the advantage of nearly complete control over the Canal Zone, native prejudice interfered little with his plans, and within a short time what had been known as the white man's grave had been converted into a veritable health resort. Had he failed to outwit the mosquito, the death rate would doubtless have been as great as in the time of DeLesseps, and it is questionable if public opinion

would not have resented such sacrifices of life and demanded that the work be abandoned.

Of course Gorgas had other infections to contend with, and his success in reducing the prevalence of pneumonia led to an invitation to advise in the control of that disease in the Rand, where he won fresh laurels. While there he received notification that he had been appointed Surgeon General of the United States army, a position he held with great distinction throughout the war. On his release from this responsibility he immediately turned again to yellow fever, and in 1919 set out for the western coast of Africa, where the disease was prevalent. While in London, *en route*, he became ill and was admitted to the Queen Alexandra Military hospital. There he was the recipient of an honour of unusual interest—he was visited by King George, and invested with the insignia of Knight Commander of the Most Distinguished Order of St. Michael and St. George. Unfortunately he did not live long to enjoy this honour. His death occurred a few weeks later, and a funeral service at St. Paul's, such as is provided for a Major-General, marked once more the esteem in which British people held this very good American citizen.

From even so incomplete an account of what has been accomplished, may it not be concluded that man's cunning may yet stretch sufficiently far to outwit the mosquito altogether?