Medicine in Stamps

Ronald Ross (1857–1932): Discoverer of malaria's life cycle

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When Ronald Ross won the Nobel Prize in 1902, he completed a remarkable turnaround in a career many friends and colleagues assumed would go nowhere. He had no initial interest in medicine, and wished instead to be an artist. Born in 1857 in Almora, India, Ross was 17 when his father, General Sir Campbell Ross, deposited him at St Bartholomew's Medical School in London. He was a poor student and barely passed his qualifying exams, and so he began his career as a Licentiate of the Society of Apothecaries, the easiest medical license obtainable.

FROM POET TO SCIENTIST Ross thought incessantly about dropping medicine for poetry, but his verse, described as "stiff with classical allusion", never gained an audience. He worked as a reluctant clinician in India from 1881 to 1889, serving in the military branch of the Indian Medical Service. The job allowed him the free time he longed for, but offered him little access to leaders in medicine. In 1889, when home in Britain and again contemplating a change to a literary career, he married Rosa Bloxam and returned to school for a Diploma in Public Health. It was a turning point in his life. For the first time, he developed an enthusiasm for medicine and became an ardent contributor to the *Indian Medical Gazette*. In 1894, he met Patrick Manson, the pre-eminent Scottish physician who was to be his tireless mentor and advocate. Manson had carried out important studies on parasites such as trichophyton, filaria, schistosoma and trypanosoma. It was Manson who, using filaria as his model, introduced the concept of arthropods as vectors of disease. And it was Manson who proposed that mosquitoes might play a similar role in malaria.

As late as 1893, Ross remained ignorant of malaria's pathogenesis, subscribing to the view that the disease was caused by intestinal bacteria. This was despite the discovery by Charles Laveran of the *Plasmodium* protozoon on a blood smear more than ten years before. Manson realised that Ross was employing an incorrect technique with his microscope, and in their first meeting, demonstrated the correct preparation of the smear. Confronted with the ringed form of the parasite, Ross underwent rapid conversion to Manson's view.

THE PERSISTENT SCIENTIST Ross's return to India marked the beginning of the most productive period of his career. Following Manson's advice to look at the mosquito as a vector, he began by collecting the insects and allowing them to feed on human "volunteers" infected with malaria. He then dissected the mosquito specimens, imitating Manson's experiments with filaria. Unfortunately, the dissections revealed none of the ringed forms he had hoped to find. In retrospect, Ross failed because the mosquitoes he used were likely *Culex* and *Aedes*, both plentiful in India, but neither capable of transmitting malaria.

But persistence won the day. Undaunted by the initial delays, he pressed on with his experiments. In August of 1897, one of his servants brought him a new type of mosquito. Ross referred to them as "dapple-wings", but in fact, they were *Anopheles*. He allowed the mosquitoes to feed on a malaria patient, and upon subsequent dissection, discovered the parasite in the stomachs of the biting insects. This was an exhilarating breakthrough, and Ross published his findings in a letter to the *British Medical Journal*. He was stalled in further investigation by his inability to locate more anophelines,

and was soon transferred to a semi-desert region of India where malaria cases were infrequent. Expressing his frustration in characteristic verse, he lamented:

God makes us kings
Scornful answer rings
First be my scavenger

At this desperate moment, when Ross's research was on the precipice, his mentor Manson intervened decisively. Pulling strings at the Colonial Office, he had Ross reassigned to Calcutta to pursue his experiments through the final phase. The effort reached its summit in June of 1898. Forced to develop an animal model due to the lack of human volunteers, Ross dissected mosquitoes at sequential points after they had fed on sparrows. By observing the *Plasmodium* parasite at different times in its maturation within the mosquito, he demonstrated the importance of the vector in the normal development of the parasite. His ultimate breakthrough came on July 4 when he discovered sporozoites in the salivary glands of the mosquito. This was final proof that mosquitoes infected through their bite. He informed both Manson and Laveran of his discovery, and at the end of July, Manson presented his results to the British Medical Association in Edinburgh.

ATTEMPTS AT ERADICATION Ross now set as his modest goal the destruction of all *Anopheles* mosquito populations in the tropics. In August 1899, he landed with a small expedition in Freetown, Sierra Leone. Accompanied by an entomologist, the team succeeded in identifying the relevant local species of *Anopheles*, as well as the moderate-sized pools of stale water in which they bred. The overconfident Ross wrote: "*There are only about 100 of these (puddles) altogether, lying mostly in clusters. All could be drained at little cost and most could be swept out with a broom*".

Alas, the vector control effort failed. Ross had underestimated the number and variety of breeding sites; the mosquito was quite adaptive about changing its terrain when confronted by environmental pressure, and pouring oil over stagnant pools was at best a temporary strategy. The colonial government ultimately opted to abandon this effort and instead constructed a segregated suburb in the hills above the city. Ross's first offensive against the mosquito had ended in the retreat of the humans.

Further efforts at eradication proved equally disappointing. A major push by the British in Mian Muir, a barracks town in India plagued by malaria, ended in a spectacular setback. Despite the expenditure by the British Army of vast money and manpower in larva eradication between 1901 and 1909, malaria remained rampant. It was only the larger campaigns launched later in Europe that met with measurable success, although they required the use of pesticides in addition to active treatment of patients and drainage of swamplands.

LEGACY Ross won the Nobel Prize for Medicine/Physiology in 1902, yet the award betrayed the ego that was his chief character flaw. Hearing a suggestion that he should share his award with Manson, Ross responded: "*The work was done by me alone, with Manson's occasional advice, it is true, but not his instructions, as frequently pretended.*" Surely this was overly dismissive given the enormous correspondence between the two, Ross's imitation of Manson's experiments with filaria and Manson's contribution of the mosquito vector theory.

The annual global research budget for malaria now exceeds four hundred million dollars, a sum that is considered by many experts to be too small for the task. Contrast this with the few hundred pounds that Ross budgeted for his eradication programme in Freetown in 1899. The *Plasmodium* parasite has proved remarkably resistant to vaccine development, in part because it deploys sophisticated strategies of immune evasion. It is also increasingly resistant to the drugs commonly used in treatment. Ultimately, the secrets Ross unlocked have led to even more vexing questions about malaria, which Ross the poet called "million-murdering Death."

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