Malaria is one of the most ancient diseases of man, but it has been just over a hundred years since the causes first became apparent and even more recently that we have begun to systematically attack it and its insect propagators. Active prevention campaigns would not be possible if not for the work of Ronald Ross in the late nineteenth century. His time in India under the tutorage of Patrick Manson, ‘The Father of Tropical Medicine’, was not without its difficulties; and it took him two long years to identify the life cycle of the malaria parasite. Ross had to overcome physical, medical and psychological factors in order to make his discovery, but was regularly supported by Manson, whose four year correspondence documented one of the most legendary collaborations in the history of medicine. Following the discovery, attention was then turned to prevention strategies, which formed the basis for the current campaigns for malaria eradication by the World Health Organisation (WHO).

Keywords: malaria, Tropical Medicine, life-cycle, parasite, malaria eradication

Introduction

Malaria is one of the oldest diseases known to mankind and has had a profound influence on the social, economic, military and health aspects of our history.

The combined work of several eminent figures during Edwardian times, notably Charles Laveran, Ronald Ross and Patrick Manson, resulted in the discovery of the life cycle; and provided a turning point on malaria’s grasp on humanity. This work earned Ross the Nobel Prize for medicine in 1902 and would later provide the means for methods of control and ultimately, eradication of the disease. In the last hundred years, the discovery of insect transmission of communicable disease rates among the most important in terms of its effect on disease control, and hence as a tool in preventive medicine (1).

The following essay aims to address an overview of the history of malaria with particular emphasis on the Ross and Manson allegiance. It also explores the main struggles encountered by Ronald Ross during his research, and his eventual ground-breaking discovery.

The History of Malaria

The history of malaria was, for many centuries, concerned with an understanding of the circumstances under which it flourished, together with some preventive action, and a concurrent clinical understanding of the pattern of fever and associated splenomegaly that dates back to ancient times (2). One of the oldest references to the disease is an ancient script noting symptoms of malaria to the Babylonian god of destruction and pestilence. The ancient Greek, Hippocrates, the ‘Father of Medicine’ accurately described the various manifestations of the disease.
Furthermore, malaria was credited with the decline of ancient civilizations, such as those of Greece and Rome, and several influential figures throughout history; including Alexander the Great and Genghis Khan, are believed to have fatally succumbed to malaria.

Despite its persistent and widespread occurrence, it was not until the late nineteenth century that French scientist Charles L.A. Laveran isolated the parasite and demonstrated that malaria was caused by a protozoan parasite. Scientific discoveries are seldom made in isolation, and continuing research by Sir Ronald Ross and Sir Patrick Manson, furthered the understanding of the malaria parasite. Even so, malaria was remarkable for concealing some of its parasitological secrets, so that the entire life cycle took a complete century to unravel.

**Charles L.A. Laveran**

Charles L.A. Laveran (1845-1922), a French military surgeon from Paris, was the first to visualise the intra-erythrocytic parasite in peripheral blood films taken from a patient with malaria, whilst working in a military hospital in Constantine, Algeria in 1880. He found pigmented bodies of the malaria parasite, and wrote, ‘I had suspected for a long time the parasitic nature of these bodies when, on 8 November 1880, I noticed with joy, motile filaments of an animated nature at the periphery’. In short, Laveran had observed the exflagellation of the parasite, the process that would later prove the key to unravelling the puzzle of malaria. He concluded that malaria was caused by a protozoan that he named *Haemamoeba malariae*. It appeared in different forms in humans, particularly in liver and brain capillaries. He also proposed that the malaria parasite must be found outside of the human body—a vector hypothesis. This constituted a breakthrough in understanding of the disease. However, the realization that it must be transmitted through a mosquito came much more slowly and laboriously.

**Patrick Manson and Ronald Ross, ‘The Malaria Story’**

Patrick Manson was born on 3 October 1844 in Aberdeen. He entered the University of Aberdeen in 1860 to study medicine, graduating in 1865. Following graduation, he commenced work at a psychiatric institute in Durham. However, he longed to travel and practice medicine, and in June 1866 obtained the post of Medical Officer for Formosa (Taiwan), which started a lifelong connection with the tropics and tropical diseases. After five years he was transferred to Amoy (China) where he worked mainly in local missionary hospitals. He was the first to note filarial worms in the lymphatic vessels and microfilariae in the blood of infected people with elephantiasis, and discovered that they could be picked up by blood-sucking mosquitoes and transmitted to others. In Amoy, he gained considerable knowledge of tropical diseases and his research here would ultimately provide the grounds for solving the malaria problem.

The malaria parasite identified by Laveran was much more difficult than filariae to trace within the human body. Furthermore, very little was known about biting insects, except that they were numerous in those warm countries where malaria was endemic. Manson had discovered the filariae of sufferers from elephantiasis were ingested by mosquitoes. In view of this, he had cause to suspect that the mosquito was a vector for malaria. It became clear to Manson that the exflagellation described by Laveran could not take place within the bloodstream, but only when the parasite was outside of the human body, and exposed to moisture and a lower temperature, such as within the stomach of some insects.

Manson left China and moved to London where he began practice at Queen Anne Street, and in 1892, was appointed physician to the Seamen’s Hospital Society and put in charge of the ward at the Albert Dock Hospital. Whilst in London, Manson formulated his famous mosquito malaria hypothesis, ‘On the Nature and Significance of the Crescentic and Flagellated Bodies in Malarial Blood’ which was published in the *British Medical Journal* on 9 December 1894. In this he stated that mosquitoes supported an essential phase of parasitic development during which exflagellation took place within the stomach of the mosquito whereby the free flagellum was able to pierce the stomach wall and then somehow develop into a larval malaria parasite. In short, the parasite acquired infectivity towards
humans and without this stage, could not pass from person to person (12). Manson did not speculate on the method by which the larval parasite left the mosquito and entered the next host. It was at this time, Ronald Ross appeared on the scene, and it was Manson’s mosquito malaria hypothesis that would inspire Ross into a frenzy of research and direct him in discovering the life cycle of the malaria parasite.

Ronald Ross was born on 13 May 1857 in India. At eight, he was sent to England for his education, during which time he developed an interest in poetry, literature and the arts. At seventeen, he declared his ambition to become a writer. However, his father had decided he should study medicine and ultimately join the Indian Medical Service (IMS). Thus, in 1875 he reluctantly started at St. Bartholomew’s Hospital in London. He completed medical school and took a job as a ship surgeon on a transatlantic steamship. In 1881, Ross finally fulfilled his father’s wish by entering the IMS, holding temporary appointments in Madras, Burma, and the Andaman Islands.

Western medicine for centuries had espoused the notion that miasma or, the stench of decaying matter, caused epidemics. The name malaria literally means ‘bad air’ in Italian. Outbreaks of malaria within the densely populated cities of Europe were attributed to the miasma from open sewers, dumps, graveyards and open waste disposal. However flawed, the miasmic theory of disease had a positive influence. It compelled public health authorities to eliminate squalor and make water potable.

Having spent a great deal of his life in India, Ross noted that the incidence of malaria was higher in areas of mosquito infestation. Despite early doubts about the parasites’ existence, Ross had a vague notion that there might be some connection between the miasmic theory, malaria and mosquitoes. He became very interested in Laveran’s discovery of the protozoan and took up independent study of malaria in 1892.

During his early years of research, Ross attempted to trace the development of the Plasmodium in the mosquito. He concentrated his efforts on the avian malaria parasite (protoosoma). During this period, he effectively discredited the miasmic theory of ingested foul water transmission, following numerous failed attempts to infect human ‘volunteers’ with water contaminated with malarial mosquitoes and larvae.

It was not until he was on a period of leave in England in April 1894, that he met Patrick Manson in London (13). This was undoubtedly the turning point in Ross’s career.

Manson was, at this time, the established leader of the growing body of British physicians concerned with tropical disease (14). He demonstrated to Ross that Laveran’s parasitic bodies could be clearly identified in a stained specimen of malarial blood (Figure 1), when compared to a sample of healthy blood. Manson provided much of the knowledge that Ross desperately sought, and within a few days, he also showed Ross other forms of the parasite in patients at Charing Cross and Seamen’s Hospitals. It was clear that Manson knew the function of the asexual forms of the malarial parasite within the human body, but not the functions of the sexual forms. Manson had already identified mosquitoes as important stages in the life cycle of filariae, and raised with Ross the possibility that mosquitoes might also carry malaria (15).

In the nineteenth century the suggestion that disease could be controlled by suppressing mosquitoes would provoke ridicule. There had been a number of competing theories about the cause of malaria for centuries. The miasmic theory dominated European thinking since Hippocrates’ Treatise on Air’ from the first century to the late nineteenth century. Notably, the germ theory and specifically, the research on microbial disease of Louis Pasteur and Robert Koch, posed the first significant challenge to the miasma theory. In further development of the germ theory, two scientists, Edwin Klebs and Corrado Tommasei-Crudeli claimed they had isolated a bacterium – Bacillus Malariae – which caused malaria when injected into rabbits. However, following unsuccessful attempts to reproduce their results, the idea was gradually discarded. More bizarre theories proposed about the cause of malaria included sudden storms, changes in the stellar constellations, seasonal rains and mushroom spores.
Sir Patrick Manson and Sir Ronald Ross’ Struggle for the Malaria Breakthrough

Figure 1: A; a blood slide showing a malaria crescent, prepared by Manson in 1894. B; blood slide showing exflagellation again prepared by Manson in 1894 (16).

On returning to Secunderabad, India in April 1895, Ross rejoined his regiment and began his quest to prove that mosquitoes were connected with the transmission of malaria. In Ross’s words this was “the great malaria problem, to study Plasmodium, not in man, but in the mosquito, which had not as yet been attempted” (18). During his research, he regularly corresponded with Manson back in London, with his findings.

Ross had launched himself into a search for mosquitoes and attempted to breed them so that he might feed them on malaria patients. He encountered many minor obstacles along the way which caused considerable frustration including mosquitoes not breeding, dying during development, not feeding on patients, patient’s parasitaemias (parasite load) being too low due to quinine treatment, and patients refusing to be bled (19). Ross remained determined and Manson continued to offer support by letter, advising him to “follow the flagella” (microgametes) (20).

Although his studies on malaria were interrupted, he managed to get mosquitoes to feed on malarial patients and even successfully dissect them, looking for evidence of the parasite within their stomach cavities. In diagnosing the parasite microscopically, Ross relied heavily on a chart that Manson had produced, derived from the work of Laveran (Figure 2).

Figure 2: Drawings by Laveran. Malaria parasites (Haemamoeba malariae) observed and drawn by Laveran. These drawings were later adapted by Patrick Manson and a copy given to Ross to aid in his diagnosis once back in India (21).
Towards the end of May 1896, Ross speculated on the life cycle of the malaria parasite and wrote to Manson saying, “the belief is growing on me that the disease is communicated by the bite of the mosquito...she always injects a small quantity of fluid with her bite – what if the parasites get into the system in this manner?” (22). Although unaware at the time, Ross had made an important discovery. But as he was using *Culex* mosquitoes, his experiments amounted to nothing (23). Manson, believing the disease to be transmitted by water contaminated by parasites from the mosquitoes which rested on it, thought this was unlikely. However, he urged Ross to find other species of mosquito which may be carriers. Ross decided to investigate mosquitoes caught in highly malarious areas in the hope of identifying the causative species.

Whilst attempting to find other species in the malaria-endemic Sigur Ghat, Ross himself contracted malaria, despite having slept under a mosquito net and behind closed windows. Being prone to regular bouts of depression, Ross lost interest in resuming his research and reverted to the art from which he drew the greatest comfort, his poetry. His poem reflects his depressive and sickened state;

What ails the solitude?
Is this the Judgment Day?
The sky is red as blood;
The very rocks decay
And crack and crumble, and
There is a flame of wind
Wherewith the burning sand
Is ever mass'd and thin'd
The world is white with heat;
The world is rent and riven;
The world and heavens meet;
The lost stars cry in heav'n (24)

A cutting from the *British Medical Journal* in 1897 contains an article entitled ‘The Risks of Study of Malaria’, referring to Ross’s attack of malaria (25). Following his recovery, he was brought five mosquitoes of a type he did not recognise. At this point it occurred to him that he may have been using the wrong type of mosquito on which to base his research.

Whilst still recuperating, in 1897 he returned to Secunderabad, where unfortunately he contracted cholera. Already weakened, frustrated and depressed, Ross saw little point in continuing. Manson wrote to him with encouragement, imploring him not to give up: “Look on it as a Holy Grail, and yourself Sir Galahad, and never give up the search, for be assured you are on the right track” (26). With a new found determination, Ross contemplated whether he was studying the correct species of mosquito. It was at this point he discovered larvae he had not seen before (27). When the larvae hatched, they developed into brown-winged mosquitoes with spotted wings, unlike any of the thirty-one species he had worked with previously. Ross fed these on a malaria patient called Husein Khan, two of which he dissected immediately and two the following day, observing the exflagellation under microscope. Initially he did not find anything striking on examination. On the 19 August, he dissected another mosquito from a feeding three days prior, and noticed vacuolated cells of about 10µm in diameter in the stomach (28) unlike those of the normal mosquito stomach cells. Ross realised that if these cells were malaria parasites attached to the stomach wall, then they should be growing.

**Mosquito Day, ‘The Beast in the Mosquito’**

On 20 August 1897, Ross had two mosquitoes left. He dissected the first and noted many single large cells, 12µm in diameter within the stomach wall, of a type which he had never seen before (29). In Ross’s memoirs he recorded, “I saw a clear and almost perfectly circular outline before me of about 12 microns in diameter. The outline was much too sharp, the cell too small to be an ordinary stomach-cell of a mosquito. I looked a little further. Here was another and another exactly similar cell” (30). Each cell contained a cluster of black granules found in a crescent form, which Ross hypothesised must be the degraded haemoglobin absorbed by the parasite from the ingested blood. The remaining mosquito he dissected the following day, and found the cells had grown even larger, up to 20µm in diameter. In other words, these cells exhibited one of the evidences of life-growth (31). Ross named this day ‘Mosquito Day’, the day in which his work over the past two years had finally rewarded him with the breakthrough he desperately sought.
Within days, Ross had established the type of mosquito involved, as well as the site of the parasite’s development. The mosquito species *Anopheles* had been identified as the carrier of malaria. With the realisation of his discovery, Ross wrote the following lines in his poem ‘In Exile’ on 21 August 1897:

This day relenting God hath placed within my hand A wondrous thing; and God Be praised. At his command, Seeking His secret deeds With tears and toiling breath, I find thy cunning seeds, O million-murdering Death. I know this little thing A myriad men will save. O Death, where is thy sting? Thy victory, O Grave! (32)

Ross announced his discovery by writing a paper entitled ‘On some peculiar pigmented cells found in two mosquitoes fed on malarial blood’, which he had verified by a colleague, Surgeon-Major John Smyth, before submitting for publication, in the *British Medical Journal* of 18 December 1897 (33).

Ross still wished to continue with his investigations and to understand how the malaria parasite re-entered the human host. Eventually, he concluded that the malaria parasite left the human host by being sucked up through the proboscis during feeding, and injected into the next person via the same route, after an interval of some 10 days (34). During this period, Ross noted that, “within the stomach of the female *Anopheles* mosquito, the parasite reproduced sexually; the flagellum (or sperm), from the male crescent, penetrating and fertilising the female crescent; which then changed shape and bored into the wall of the stomach” (35). Many hundreds of the parasite would be produced, and move from the stomach back to the proboscis, so that it could continue its life cycle within man. At this time, he received orders to proceed to Kherwara in Rajasthan for military duty, an area relatively free of malaria. Ross threatened to resign, but following representations on his behalf by Manson, the Indian Government put him on special duty for a year to investigate malaria and kala azar, a form of leishmaniasis. Ross was forced to continue the later stages of his research experimenting on birds with malaria, and was able to trace the passage of the parasite from the stomach to the salivary gland of the mosquito where it then passed into the skin and blood stream of a healthy bird (36).

In 1898, Ross wrote “These observations prove the mosquito theory of malaria as expounded by Dr Patrick Manson…His brilliant induction so accurately indicated the true line of research that it has been my part merely to follow its direction” (37).

Ross had been attracted to the study of malaria as he saw many of the diseases in India as preventable. He believed that, “of all diseases, malaria was in many areas, a scourge far greater than either plague or cholera, and caused more sickness, misery, and death than any others” (38). On demonstrating mosquito transmission of *Plasmodium*, Ross turned from parasitological research to field control and studied methods for controlling malaria and established public health programs for eliminating malaria. He estimated that most malarial fever could be eradicated at almost no cost, except that of a little energy on the part of the local authority, with attention to sanitary matters, (39) drainage of soil, destruction of larvae and by other protective measures (40). In 1899, he released a booklet entitled ‘Residents Malaria Precaution Guide in Epidemic Regions’, outlining such protective measures. The ‘mosquito theory’ was also put into use within a few years, with great success (41). It had taken two long years of strenuous research, but with the satisfaction of what he had achieved in India, Ross resigned in 1899, two years after his discovery.

Back in the UK, it fell upon Manson to explain to the general populace the meaning of Ross’s discovery. He devised a very dramatic and convincing experiment, which would leave no doubt as to the mosquito’s involvement in the transmission of malaria. He let *Anophecline* mosquitoes, which had fed on patients with malaria, feed on two volunteers who had never previously been exposed to the disease (42). One such volunteer was Manson’s son, Dr Thornburn Manson. Following their exposure, they subsequently developed malaria with the parasite present in their blood.
In view of the effort taken to discover the life cycle of the malaria parasite, primarily due to lack of knowledge, Manson addressed an audience at St George’s Hospital in 1897, on ‘The Necessity for Special Education in Tropical Medicine’. The Secretary of State, Joseph Chamberlain, was fully receptive of Manson’s views on the need for specialised training, and in March 1898 he addressed the General Medical Council (GMC). Unfortunately, the GMC was not prepared to see tropical medicine made an obligatory subject of the medical curriculum. Chamberlain however, refused to back down and instead addressed the governors of all British colonies. He pointed out that a school should be established in which, medical officers newly appointed to the Colonial Service should be given appropriate instruction before leaving England; leading medical schools in the UK given teaching in tropical medicine; and medical reports from tropical colonies be designed to increase knowledge of important tropical diseases (43). Subsequently The London School of Tropical Medicine was established. Manson outlined the teaching and research in Tropical Medicine, upon which the present school is still based (44).

In November 1898, Alfred Jones, a wealthy ship-owner announced his intention to contribute £350 per annum for three years to promote the study of tropical diseases in Liverpool and in May 1899, The Liverpool School of Tropical Medicine opened its doors, five months earlier than the London School. That year, Ronald Ross took up the position of lecturer in Tropical Diseases (the Alfred Jones Professor of Tropical Medicine) at the school on Manson’s recommendation.

Four years after his discovery, Ross demonstrated the vast possibilities of the outcome of his research. In Ismailia, he implemented his ‘sanitation drive’ initiative whereby he cleared and levelled streets to eliminate the risk of rain water forming puddles. He then identified all potential breeding grounds around the town and had oil poured over any sites where malaria larvae could breed. The outcome was to free Ismailia of malaria at a time when complete evacuation of the town was imminent. Ross believed the solution to eradication of malaria was to supply natives with kerosene and attack areas heavily infested with mosquitoes. An article entitled ‘Malaria at Ismailia’ in the British Medical Journal outlined his plan (45). In doing this, Ross had shown, by practical application, the immense value of the principles of disease control he had established.

Not only had the scourge itself been banished from areas it used to render uninhabitable, but the proof that the infection is conveyed to man by the bite of a mosquito had led to research along similar lines into the causation of other endemic and epidemic diseases, and promised equally beneficial results in respect to both prevention and cure. Ross believed within a year or two, malaria would be eradicated in all large towns of the tropics. He had visions of Foreign and Colonial and War departments bending their backs to the task, but this was not to be the case (46).

**Nobel Prize**

Following his twelve years in the IMS, Ross spent most of his time lecturing at the Liverpool School, promoting tropical medicine and organising important medical expeditions to the tropics (47). In 1902, he was awarded the Nobel Prize for Medicine for his work on malaria, by which he had shown how the parasite entered the organism and thereby laid the foundation for successful research on the disease and methods to combat it. As well as Ross, both Manson and Laveran had been nominated for the award. However, although Laveran had discovered the parasite, he had not demonstrated the route of entry into the human host and its further development. Similarly, Manson had only shown that the parasite exists in different developmental stages but had not identified the complete life cycle of malaria. Consequently the Nobel Committee unanimously suggested that the award go to Ross (48). In his acceptance speech, Ross controversially identified Laveran as his primary mentor. For any ambitious scientist, the ideal mentor is one who poses no competitive threat to their own accomplishment. In selecting a respected, foreign scientific forbear, Ross reinforced his claim to originality. He did however acknowledge Manson’s mosquito hypothesis:

“…I will begin with the great name of Laveran, who more than twenty years ago discovered the cause of malaria and created a new branch of science – Laveran, the true man of science who
has honoured me by permitting me to call him my master...And particularly Manson in England, whose profound induction formed the basis of my own humble endeavours, and whom I shall also esteem as one of my masters (49).”

Following this, Ross received a knighthood in 1911, served as a consultant in malaria to the War Office during World War I, and later became director of the Ross Institute and Hospital for Tropical Diseases, founded in his honour.

The Ross/Manson Dispute

Manson had been Ross’s professional voice for three years whilst he was in India, presenting his discoveries to medical colleagues (50) and had helped him find a position at the new Liverpool School of Hygiene and Tropical Medicine on his return. Inevitably, over two decades the creative friendship founded on a teacher-pupil basis gradually cooled, evolving naturally into one of equals.

After taking the post at the school in 1899, dissatisfaction between Ross and Manson grew and relations between the two became increasingly strained until Manson’s death in 1922. To Ross, even with a Nobel Prize, knighthood and membership to the Royal Society, his appointment was at Liverpool and not in London, where Manson was well established. He resented the fact that, unlike Manson’s, his medical practice had not thrived, and that his life as a researcher seemed undervalued and underpaid. Ross also took a disdainful view of teaching, claiming he was naturally an investigator. Those that knew him at this time, described him as frequently hostile and a man “quick to take offence and capable of magnifying a petty affair out of all proportions” (51).

Throughout the remainder of Ross’s life he was constantly bitter about other malariologists not supporting his ideas of malaria control efforts. And he hoped that the difficulties that he had faced would enlighten future generations of scientists (52). By the end of 1927, Ross suffered a stroke leaving him wheelchair bound, and financial worries embittered his few remaining years. Ross died on 16 September 1932. His death was noted throughout the world.

The Struggles of Discovery

Malaria as a disease, was not unveiled by one individual person, but by several people who discovered separate parts of its pathology at different points in time. Laveran had made incisive observations on the parasitic nature of malaria. Manson implicated mosquitoes as vectors for the disease. Nevertheless, it took Ronald Ross to pull together the research into one final concept. This process was filled with struggles related to travel, available knowledge, personality, military commitments, ill health and the ultimate desire for recognition of accomplishment.

In the early years, although familiar with the malarial endemics in his home country, India, Ross knew very little about it. His written requests for Laveran’s journals and research, in order to broaden his knowledge, took a long time to be processed. Moreover, when it eventually arrived, the notes and diagrams were not comprehensive enough to form a basis to commence research. Ross even admitted he had limited medical training, when he wrote that his knowledge of the subject of tropical medicine was “far from complete” (53). Therefore, lack of knowledge and information hindered Ross’s attempt to identify the parasite microscopically and delayed the first stage of his research.

An additional obstacle to overcome, once his research had commenced with Manson’s aid, was the fact that Ross had to study the disease in the mosquito, not in man. This had seldom been attempted before. Manson’s research and discovery of the filariasis involved experiments conducted on his gardener, Hin Lo who was infected with the filaria. The mosquitoes who fed on Hin Lo’s blood were then dissected, and the abdominal contents microscopically analysed. No great detail was taken of the anatomy or function of the mosquito. Ross had to learn the complete anatomy of the biting insects. In addition, despite the fact that the science of entomology received great impetus in the 19th century, largely as a result of the publication of ‘The Origin of Species’ in 1859 by Charles Darwin, little was known about entomology. The majority of early
entomologists were more concerned with the discovery, identification, habitat and life cycle of insect species, rather than the possibility of disease transmission. Furthermore, there was no reliable literature specifically dedicated to mosquitoes. This lack of additional guidance forced Ross to investigate a previously unexplored area of science, combining entomology with parasitology. The vast number of different species of mosquitoes made this a very demanding task.

Additionally, the geographic distance between Ross and his tutor, Manson, resulted in a long wait for correspondence. Manson was the established leader of tropical medicine and could not leave London, whereas Ross had to remain in the IMS and continue his research.

Like any other researcher, Ross encountered both minor administrative and practical obstacles. Problems such as the mosquitoes not breeding or feeding off infected blood properly, further delayed his work, and added to his frustration.

Moreover, being in the IMS, Ross was forced to conduct his research only in areas where his regiment was posted. Some of his designated posts were in relatively malaria-free areas, leaving him few subjects to study. This understandably slowed his progress to the extent that he threatened to resign from the IMS if he was not allowed to proceed with his research. Ross struggled to be placed in malaria-endemic areas, as the military believed his scientific research to be secondary to his military duties.

Matters were further complicated by Ross contracting both *falciparum* malaria and cholera within the same month. The aftermath of both diseases almost ended his research as he temporarily lost all motivation and saw no purpose in continuing. Nevertheless, with Manson’s continued encouragement, Ross overcame this psychological obstacle, and made ultimately made his final discovery within a relatively short period.

Controversially, Ross’s struggles would continue even after he discovered the malaria lifecycle, received a Nobel Prize and returned to England to focus on prevention of the disease. During his travels abroad, Ross was considered to be Manson’s protégé, whereas on his return to England he expected to receive the same level of respect as his tutor. However, Manson was already well established in the capital and when Ross was placed at the Liverpool School of Tropical Medicine he felt sidelined, despite all his hard work. This resulted in the end of what had been a long and successful allegiance between the two. It is quite likely that, had they closely collaborated in working on malarial prevention, Ross would have seen the result of his research put into action on a more widespread basis. However, Ross’s difficult personality traits prevented this, and can in some ways be considered his greatest struggle of all.

**Conclusions**

Prior to Manson, tropical diseases were assumed to be diseases of warm climates, and not much consideration was attributed to them in the UK (54). Manson argued that tropical medicine was not simply a branch of bacteriology, as was the common view; but an independent branch of medicine. On the strength of his convictions, schools of tropical medicine were established in the UK and several European countries, and journals, societies and international meetings gave separate identity to this discipline (55).

With hindsight, it seems likely that Manson’s 1894 article (56) on the malaria parasite precipitated Ross’ visit to him that year, and acted as a major incentive to his subsequent work in India, resulting in one of the greatest contributions to medical knowledge since the days of Pasteur (57,58). It is certainly clear that Ross was a visionary, years ahead of his time. Not only had he discovered how malaria is conveyed, but he saw his discovery as the starting point that could make malaria control (even eradication), an achievable goal (59,60).

The correspondence between Ross and Manson documented one of the most legendary collaborations in the history of medicine (61). Had the cooperation between them continued, and Ross’s personal difficulties put aside, maybe a preventative measure could have been in place earlier, and further lives saved. Since Ross and Manson enjoyed special stature, one may wonder if their non-collaboration and disagreements after
1900, (62) may have halted the development of British Tropical Medicine. The initiation of malaria prevention programmes was further hindered by two world wars, the loss of the tropical empire and by the shift in biomedical research power to the United States (63).

Unfortunately, Ross was not able to see the full impact of his life’s work and died still holding the conviction that malaria could be eradicated if only governments would commit themselves to expand and implement his discovery. However, once successful, the eradication of malaria will count as one of the greatest triumphs in medicine of all time. That Ross could even foresee this possibility is characteristic of his imagination and creative mind (64). In the years since Ross’s discovery, the situation for those who suffer from malaria has changed significantly, but still not enough.

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