The debt Tropical Medicine owes to the Military

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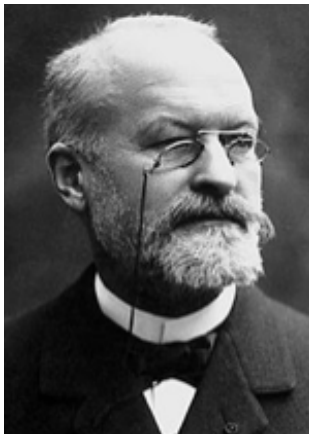
Introduction

Prior to the twentieth century, infectious diseases took a heavy toll of troops and civilians from western countries posted to tropical locations. Indeed, it was generally recognised that in most prolonged campaigns the victorious side was the one experiencing the lesser number of medical casualties. Examples of wastage of soldiers of European nations are numerous.[1,2] Even as late as the mid nineteenth century little had changed, with disastrous medical casualties being experienced in the Crimean and South Africa (Boer) Wars and in 1915 illness accounted for eight times as many casualties as trauma in the concluding months of the Gallipoli campaign.[3]

In the oak-panelled walls of the dining room at the former Royal Army Medical College, Millbank London, there were oil paintings of medical officers who had held appointments at the College. They were majors David Bruce and William Leishman. These doctors together with other military officers from France, the United States, India and later Australia were responsible for many ground–breaking discoveries in Africa, India, Malta, the Caribbean and Australia relating to tropical infectious diseases. Their endeavours stimulated the formation of tropical disease research institutes throughout the world and the recognition of tropical medicine as a distinct medical discipline.

The contribution of six miltary doctors

Charles Alphonse Laveran



Malaria had a profound affect both on colonization and military campaigns and was the subject of intense investigation. Charles Laveran served in Algeria before being appointed to the chair of Military Diseases and Epidemiology at Ecole De Val-de Grace in Paris in 1880. In patients with malaria he noted pigmented spherical bodies that underwent amoeboid movement. These varied in size and some were attached to erythrocytes or occupied most of the cell cytoplasm. Others were free in the plasma, Laveran postulated that the crescent shaped forms in the plasma were fully developed protozoal parasites. He subsequently identified granules in the blood of 148 of 192 patients with malaria and deduced that these bodies were the cause of malaria.[4] This discovery is the first recorded observation that protozoa are the cause of disease.

Until recent times more battle casualties and deaths resulted from infection than from trauma. Even in the concluding months of the Gallipoli campaign, patients with illness outnumbered trauma cases by eight to one. The marked reduction in the prevalence of, and improvement in outcome, of troops with infectious diseases that occurred early in the twentieth century was largely due to the efforts of military doctors. These doctors, often working with poor facilities, were responsible for a remarkable reduction in the impact of a number of serious infectious diseases. Not only did their research findings help improve the health of serving members, but it proved of considerable benefit to permanent residents in tropical and semi-tropical areas.

Ronald Ross

Ronald Ross, the son of a British army officer, studied medicine at St Bartholomew's Hospital, London and joined the Indian Medical Service in1881.Whilst serving with the British Army in India, Ross was encouraged by Patrick Manson to investigate whether mosquitoes might transmit malaria. In 1898 he carried out dissections of anopheles mosquitoes that had fed on patients infected with malaria and on examination of their stomach walls, noted the presence of what he termed 'germinal rods' which he surmised were parasites. Ross found these bodies then passed to the salivary glands where they underwent further

development before being injected into the blood of birds and humans through the wound they made with their proboscis. He postulated that birds and mammals were the reservoirs, and mosquitoes the vector, for transmission of infectious diseases including malaria. Ross confirmed his hypothesis by exposing healthy birds to the bites of infected mosquitoes. Subsequently they too developed malaria, thereby proving his transmission theory.[5] He went on to warn of the risk of exposure to mosquito bites. It remained for Castellani and his Italian colleagues to confirm human transmission of malaria. Ross and Laveran were both awarded Noble Prizes for Medicine for discovering the pathogenesis of malaria..

David Bruce

David Bruce made an enormous contribution to medical science. The son of an engineer, he was born in Melbourne in 1855. He studied medicine at Glasgow University and then joined the British Army and was sent to Malta where he was stationed between 1884 and 1889. At that time there was a high prevalence of Malta fever in the general population and in the British Army garrison of 8,000. One hundred and twenty thousand days were lost annually from the illness it caused. Malta (Undulent) fever is characterised by malaise and a relapsing fever, highest at night and accompanied by severe night sweats. Most patients made a full recovery within two weeks although the symptoms could persist and there were some deaths.

Whilst carrying out autopsies of patients who died of a febrile illness, Bruce consistently found a micrococcus in specimens of the spleen, kidney and liver. He grew the organisms in peptone broth then injected three monkeys with a pure culture of the micrococcus. All monkeys developed a clinical picture similar to that seen in Malta fever in man, and one died. These results were confirmed by further monkey studies.[6] The cause of Malta fever had been identified and the disease was re-named brucellosis in Bruce's honour. Sometime later the same organism was found in goat's milk in Malta and was subsequently shown to be present in half the goat population7. As a result, the use of goat's cheese and milk was abandoned after which the prevalence of Malts fever fell to zero. Bruce's discovery was of great benefit to the residents of Malta. In Africa too, the military demonstrated that they were concerned with the health of their troops.

When stationed in South Africa in 1895 Bruce was asked to investigate nagana, a disease causing heavy stock losses in horses and cattle, so impacting heavily on the livelihood of the indigenous population. He took blood samples from infected cattle and noted the presence of flagellated organisms in their blood. He surmised these were trypanosomes which had first been seen in rats by Dr Lowe, another RAMC medical officer. Bruce then inoculated healthy animals with blood from infected cattle and observed that they succumbed to nagana. Other healthy animals brought into an area with a high prevalence of nagana were later found to acquire a large number of trypanosomes in their blood stream.[8] He identified the cause of nagana as trypanosomes and by showing that nagana was transmitted by the bite of the tse-tse fly, Bruce was able to prove that insects can transmit protozoal diseases.

In 1903 Bruce was sent to Uganda to investigate sleeping sickness, which was the cause of high mortality in both colonial residents and the indigenous population. The disease, prevalent throughout Sub-Saharan Africa north of the Zambesi River, is characterised by intermittent headache, lymphadenopathy and a skin rash. Symptoms may last for two years after which CNS involvement can occur through the parasite, Trypanosoma brucei gambiense, invading the brain and causing a chronic meningo-encephalitis and cerebral oedema. Symptoms of drowsiness and behavioural changes may follow. In East Africa, a more aggressive parasite, T. brucei rhodesiense, frequently caused myocarditis and death. Bruce found that all patients with the symptoms of sleeping sickness had trypanosomes in their blood-stream and that injecting cerebrospinal fluid (CSF) from infected humans into monkeys produced an identical clinical picture to that seen in humans.[9] He concluded that nagana and sleeping sickness were the same disease, which was renamed trypanosomiasis. Bruce's work in identifying the tse-tse fly as the vector for nagana and sleeping sickness led to steps being taken to decrease the tse-tse fly population. This greatly reduced disease prevalence in humans and livestock and resulted in enormous economic benefit to the local farmers.

William Leishmann

William Leishman joined the British army on graduating in medicine from Edinburgh University in 1886 and, after a period in India was posted to the Army Medical School at Netley, England. Here he worked under the professor of pathology, Sir Almroth Wright and made a number of valuable contributions to the science of tropical medicine, possibly the greatest of which relates to the disease which bears his name.

Leishmaniasis, which has its reservoir in rodents, dogs and foxes, is caused by a protozoan of the genus Leishmania and transmitted by the sandfly of the genus Phlebotomus in the Old World and Lutzomyia in the New World. Humans are infected when the sand fly injects the promastigote with its bite. There are several forms of leishmaniasis- cutaneous, muco-cutaneous and the more serious, visceral disease. Depending on the subject's cell mediated immunity (CMI) the disease may be arrested or progress to a more severe form. In visceral leishmaniasis, if the CMI response is poor, amastigotes replicate in macrophages throughout the reticulo-endothelial system and may cause enlargement of the spleen and liver, resulting in liver impairment, wasting and susceptibility to bacterial infections. Visceral and cutaneous leishmaniasis are common diseases throughout the tropics and subtropical regions of India, the Americas and the Middle East.

The cause of this group of infections was elucidated by three military doctors. In 1900 Major P Borovsky stationed in Tashkent, Russia, published his findings on Sort sores, painless, erythematous plaques, in the Russian Army Medical Journal.[10] Whilst working at the Royal Army Medical School, London, Leishman noticed similar binucleate bodies in endothelial cells from a section of spleen taken from a soldier with fever contracted whilst serving in Calcutta.[11] He later found these same organisms in infected rats. Major C Donovan, serving in the Indian Medical Service in Madras performed a splenic puncture in a patient with kala-azar and noted similar inclusion bodies.[12] These were later named Leishman-Donovan bodies. Donovan showed the infectivity of peripheral blood by injecting blood from a patient with kala-azar into healthy puppies and later finding parasites in the dog's blood spleen and liver.13 The disease was renamed visceral leishmaniasis. Investigation of the life cycle of the parasite was further advanced by Rogers' discovery of a flagellated stage in the spleen of a patient with kala-azar; however the vector proved elusive until 1942 when Colonel H Shortt serving with the British Army in India, identified it as the phlebotomine sand-fly.[14]

Walter Reed

Alarmed at the prevalence of yellow fever in the Caribbean, Reed, the professor of bacteriology at the Army Medical School in Washington DC, was appointed in 1898 to investigate the premise, proposed by Cuban epidemiologist Carlo Juan Finlay, that the disease was transmitted by insects. Whilst in Havana, Reed noted that only one prisoner in a cell containing eight others contracted yellow fever. Shortly afterward a military physician died of yellow fever after being bitten by a mosquito. Reed surmised that mosquitoes were responsible for the transmission of the disease and infected army volunteers with multiple bites from local mosquitoes. All subsequently developed yellow fever. Working with W Gorgas, another military physician, he disproved that fomites were a source of infection. Gorgas subsequently dramatically reduced the prevalence of yellow fever in Havana by spraying oil on the water to prevent mosquitoes hatching.[15]

Neil Hamilton Fairley

A Melbourne graduate, Fairley made a significant contribution to the science of tropical medicine in both world wars. After the great War he was appointed professor and Director of Special Research at the Hospital for Tropical Diseases in London, but it is in the field of malaria research in World War Two that he is best remembered. Malaria was taking a huge toll of the Allied troops in New Guinea in 1942-1943 and it was the insistence on strict malaria discipline in the field, together with the scientific work at the Land Headquarters Medical Research Unit (LHQMRU) in Cairns Queensland, planned by Fairley, that dramatically reduced its prevalence. In Cairns, army volunteers were infected with strains of malaria prevalent in New Guinea and new chemo-prophylactic drugs were tested for efficacy and side effects. These included the sulpha group, mepacrine (atabrine) and paludrine (proguanil). The unit established an international reputation for the quality of its research which was acclaimed by all the allied forces and its recommendations immediately applied.[16]

Colonel NH Fairley

Tropical medicine was put on a sound scientific footing by military doctors, often working under difficult conditions with minimal scientific equipment. Their findings on the reservoirs, vectors, pathogenicity and treatment of four serious infectious diseases together with the work of many other military medical officers proved a stimulus for the foundation of tropical research institutions. These establishments greatly facilitated the marked reduction in morbidity and mortality due to infectious diseases in the tropics. Valuable research into tropical and other infectious diseases continues with the United States military and the Australian Army Malaria Institute in particular, making valuable advances to tropical disease pathogenesis, diagnosis and management. The military and medical science clearly owe a considerable debt to military physicians.

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