The British Army's contribution to tropical medicine

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ABSTRACT

Infectious disease has burdened European armies since the Crusades. Beginning in the 18th century, therefore, the British Army has instituted novel methods for the diagnosis, prevention and treatment of tropical diseases. Many of the diseases that are humanity's biggest killers were characterised by medical officers and the acceptance of germ theory heralded a golden era of discovery and development. Luminaries of tropical medicine including Bruce, Wright, Leishman and Ross firmly established the British Army's expertise in this area. These innovations led to the prevention of many deaths of both military personnel and civilians. British Army doctors were instrumental in establishing many of the teaching facilities that we now consider to be global leaders in tropical medicine. The impact of the Army in this field has certainly been significant in the past and its contribution continues to this day.

KEYWORDS: Tropical medicine, British Army, history, Fleming, Army Medical Services

Introduction

Tropical medicine is the study of diseases that are most prevalent in the tropics and subtropics.[1] British armies have grappled with these diseases since the Crusades, and even more so during the time of empire.[2] Within living memory, infection was the greatest threat to even the most powerful of military forces. In his account of the Burma Campaign, *Defeat into Victory*, Field Marshall William Slim said, 'In 1943 for every man evacuated with wounds we had 120 sick…A simple calculation showed that in a matter of months, at this rate my army would have melted away.' The importance of tackling the threat of disease has driven the British Army (which includes the Indian Medical Service, a former colonial entity) to make some of the most important advances in the sphere of tropical medicine. This contribution has been colossal and the authors hope that this short paper will merely stimulate further reading.

Pre-microscopy era

John Pringle, dubbed the father of modern military medicine (despite holding no official rank until he was appointed physician-general to the forces), was the British Army's first major contributor to tropical medicine.[3] He lived in the 18th century when many more soldiers died from infections than were killed in battle. Pringle observed the poor living conditions of the army and documented the resultant disease, particularly dysentery (then known as bloody flux). Sanitation was non-existent and soldiers defecated outside their own tents. Pringle linked hygiene and dysentery, thereby contradicting the accepted 'four humours' theory of the day. He ordered that latrines were dug and bedding changed regularly.

The 19th century was a time of colonial expansion and as a consequence the prevalence of tropical disease among Europeans was rife. During the Napoleonic Wars, only some 13% of the 240,000 deaths were trauma related.[4] A notorious example was the Walcheren Campaign of 1809 in the Netherlands which involved 40,000 British troops. This area was particularly known for undifferentiated febrile illness and had been previously described by John Pringle.[5] Of the 8,000 soldiers who were infected, over 4,000 perished and just 100 of these were battle casualties. This led Sir James McGrigor to professionalise the Army Medical Department and he became its first director general. In addition to introducing the stethoscope, field hospitals and an ambulance corps, he greatly improved hygiene standards.[6]

During the Crimean War, many previous lessons were forgotten and military hospitals again became reservoirs for infection, with 77% of deaths (16,323) resulting from exposure to disease-causing agents. This presented an opportunity for nurses caring for the military troops to instil new infection-control methods such as those described by Florence Nightingale and Mary Seacole.[7]

This led to an era during which the description of disease and primitive techniques for disease treatment prevailed. For example, in 1860, Surgeon Major Henry Vandyke Carter was the first to describe isolation techniques for leprosy that were used well into the 20th century.[8] Carter was more famous, however, for the illustrations he produced for the *Gray's Anatomy* textbook. He was also the first to confirm the presence of tuberculosis and malaria on the Indian Subcontinent.[9] Brucellosis was first described by Surgeon General Jeffery Allen Marston (then an assistant surgeon) in 1861 after surviving his own infection with this disease.[10] Charles Murchison was a physician who studied typhoid in London after returning from military service with the Bengal Army. Appointed lecturer at St Thomas's Hospital in 1873, Murchison traced a typhoid epidemic to a polluted water supply. He famously intervened by removing the handle to the pump in the infected area and was thanked by the residents of West London.

Surgeon General William Campbell McLean was appointed professor at the Army Medical School in 1860. He taught for 26 years, lecturing on his experiences of tropical medicine in order

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to ensure that the Army learned from past lessons.[11] The Royal Victoria Hospital at Netley was subsequently opened in 1863, establishing a home for military teaching and research in the field of tropical diseases. This critically changed things for years to come as military medical officers now had a centre of excellence where they could learn and expand their knowledge. Surgeon Major H Veale published a report from Netley in 1879, differentiating brucellosis fever from fevers caused by malaria and relapsing fever. He reported that brucellosis did not respond to quinine like malaria and had no spirilla in the blood, thus excluding relapsing fever.[12]

In 1879, there were multiple competing aetiological theories of disease, particularly for cholera. Among these were the 'miasma' that Pringle felt contributed to disease and the 'contagion' theory, which hypothesised that a person could carry a particle and it could enter the body leading to disease. Surgeon Majors David Douglas Cunningham and Timothy Richard Lewis were the first Anglo-Indian scientists trained in fungal microscopy and culture. They believed the cause of cholera to be a fungus-like organism that distributed spores into the air. Ultimately, Cunningham's research was disproven by Robert Koch's discovery of the cholera bacillus. Nevertheless, Cunningham had added much to the aetiology of the disease in India and subsequently used Koch's germ theory to account for the characteristics of cholera.[13]

Golden era of tropical medicine

The germ theory suggested by Louis Pasteur and Robert Koch in the 1880s was quickly accepted and the identification of many bacteria followed rapidly.[14] This was the golden era for tropical medicine. The first discovery of leishmaniasis is believed to have been made by David Douglas Cunningham, who is thought to have seen parasites of the leishmania type in 1885. He did not, however, relate it to the disease.[15] Major (later Lieutenant General) William Boog Leishman was stationed in Dum Dum near Calcutta in 1890, and then returned to Netley in 1899 to take up the assistant professor of pathology post. While examining post-mortem splenic specimens of soldiers who had Dum Dum fever he discovered ovoid bodies.[16] He thought these were degenerated trypanosomes,[16] but Captain Charles Donovan published findings of similar bodies from living and post-mortem splenic samples and disputed this theory.[17] It was Ronald Ross who concluded that the ovoid bodies seen by Leishman and Donovan were a novel protozoan organism and were from cases of kala-azar. He also proposed that the name for the new organism should be *Leishmania donovani*.[18] The vector was only confirmed in 1942 by Colonel Henry Edward Shortt, 16 years after discovering leishmania in the pharynx of phlebotomine sand-flies. Shortt pioneered the use of urea stibamine in the treatment of the disease.

In 1886, Surgeon Colonel (later Major General) David Bruce led the Malta Fever Commission. Shortly afterwards, in 1887, Surgeon Captain Matthew Louis Hughes further characterised this disease.[19] Also in 1887, Bruce identified the causative organism of the disease as the bacterium *Micrococcus melitensis* (later renamed *Brucella melitensis*) when he isolated it from the spleen of a victim.[20] Captain F Smith and Almroth Wright described a serum agglutination test in 1897, which was modified by Wright and Surgeon Major Semple and is the basis for the diagnosis of brucellosis today.[21,22] The Mediterranean Fever Commission reports, published by Major William Heaton Horrocks and Captain James Crawford Kennedy in 1905, showed that one or more goats in every herd contained *Brucella melitensis* in their milk and urine. In addition, they found that 50% of the goats in Malta had a positive serum agglutination test, thereby providing a wonderful example of an excellent epidemiology investigation.[23] There remains some controversy over Bruce's discovery, however, as he failed to credit Kennedy, Horrocks and another investigator Zammit, who actually discovered that goats were the reservoir.[24] Despite this, following his success in Malta, Bruce was asked to lead the Sleeping Sickness Commission to investigate the case of nagana (cattle and horse sickness) in Zululand. In 1895, Bruce subsequently discovered the parasite *Trypanosoma brucei*.[25] However, it wasn't until 1901 that trypanosomes were observed unequivocally in human blood by colonial surgeon Robert Michael Forde. He originally thought that these organisms were worms.[26] Bruce then described the transmission cycle of the parasites in the Tsetse fly while in Uganda in 1903.[26]

Garrison Surgeon Ronald Ross, another father of tropical medicine, proved that malaria was transmitted by mosquitoes[26] while serving as an Indian Medical Service officer stationed in Secunderabad in 1897. This discovery laid the foundations for fighting the disease and he was jointly awarded the 1902 Nobel Prize for medicine. Surgeon Captain (later Brigadier) John Sinton established the Central Malaria Organisation for India and headed the Malaria Survey.[27] He also established that pamaquin reduced the relapse rate of malaria and gave much superior results when combined with quinine. This changed the treatment course of malaria from long periods of quinine alone.[27] In addition, Sinton improved the staining techniques and devised better preparation methods for samples, with the use of thick films producing much more reliable results.[27] He also set up many teaching schools in India, and his paper on *What malaria has cost India* is the basis for its eradication in much of that country. Sinton also founded the Royal Society of Tropical Medicine and Hygiene in 1907. Notability, he is the only person in history to have the postnominals VC and FRS.[28] Major General Gordon Covell took over from Sinton and continued to develop methods of malaria control.[29] Major (later Brigadier) John Boyd also made valuable contributions to the development of malarial medicine, including the staining of malaria blood smears with methyl blue.[30]

Vaccines became a focus of British Army medics who had come to recognise the benefits of disease prevention. This approach led in 1902 to perhaps the greatest victory in typhoid medicine when Almroth Wright, then professor of military pathology at Netley, developed a typhoid inoculation.[31] He later developed the vaccine and convinced the War Office to issue 10 million doses to British troops. It is estimated that Wright saved half a million lives during World War I.[32] During the Boer War, however, the adverse effects of the vaccine meant that 95% of soldiers refused to take it. The official figures show 5,000 cases of typhoid with 1,000 deaths, but Arthur Conan Doyle argues that these figures do not reflect the true level of suffering and it was a major mistake not to make vaccination compulsory.[33]

To this day, our only defence against rabies is a vaccination first developed in India by Major David Semple in 1911. Semple initially cultured rabies in rabbit brains and used the myelin basic protein as a vaccine. He later utilised the phenol or β-propiolactone-inactivated homogenate from infected sheep and goats. This was the most commonly used rabies vaccine in the world until duck embryos and cell culture replaced it.[34]

Whitmore's disease or melioidosis was first identified by Major Alfred Whitmore in 1913. He identified *Burkholderia pseudomallei* as the causative agent, differentiating it from the casual agent

Fig 1. Photograph of Alexander Fleming in military uniform in a field Hospital at Wimereux in 1918. Reproduced with permission from the Alexander Fleming Laboratory Museum (Imperial College Healthcare NHS Trust).

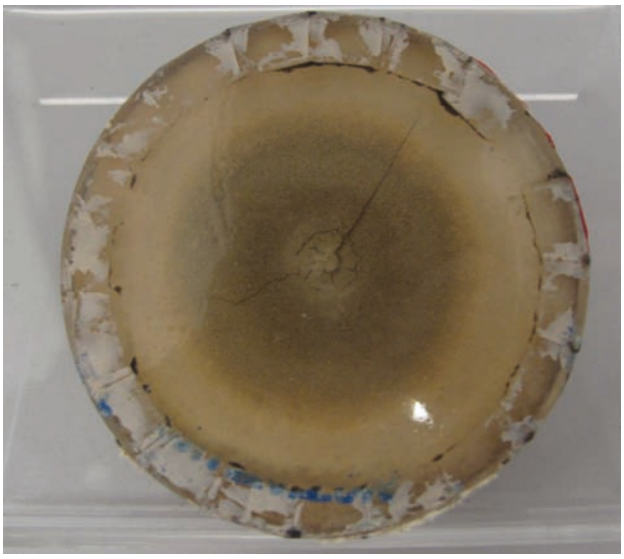

Fig 2. Alexander Fleming's original Petri dish demonstrating no bacterial growth around the *Penicillium* mould. Photograph published with thanks to the Trustees of the Museum of Military Medicine.

of glanders (*Burkholderia mallei*) by the microscopic and clinical features.[35] Whitmore initially discovered that the disease differed from glanders when he performed a post-mortem on an opium addict with several abscesses. He noticed that there were numerous subcutaneous abscesses and a primary lesion with a cheesy consolidation in the lungs. This was later confirmed by several more post-mortem examinations on further victims of the disease.[35]

Fleming and the post-antibiotic era

Alexander Fleming (Fig 1) made three huge contributions to medicine. The first was made while serving as a captain working with Almroth Wright in the British Army Laboratory in Boulogne-Sur-Mer during World War I. Fleming described an experiment which showed that perioperative antiseptics were increasing mortality in wounded soldiers. In 1916, he and Wright proposed that deep wounds harboured anaerobic pathogens and that antiseptics destroyed the macrophages and neutrophils that contributed to immunity. This reduced competition for the virulent pathogens and caused overwhelming sepsis.[36] He instead suggested debridement and washing the wound out with hypertonic saline, particularly to clean deep wounds as this treatment modulates and increases the white cell response. The bacterial proliferation typically associated with the antiseptics was prevented. Initially, this suggestion was not accepted but soon became standard practice. Second, when testing nasal secretions, Fleming discovered that some mucous samples had properties that inhibited bacterial growth. This was the first documented description of a lysozyme.[37] Lastly, one of the most important discoveries in medical history: in 1928 Fleming returned from holiday to find that a staphylococcus culture had become contaminated with a mould (Fig 2). He noted that the bacterial areas immediately surrounding the fungus had been destroyed and he had in fact discovered penicillin.[38]

In 1931, Captain Sydney Price James hypothesised that sporozites enter the reticulo-endothelial cell of the liver of the infected host in malaria. He suggested that they undergo further development in the liver prior to dispersal in the blood stream accounting for the incubation period.[39] Colonel Henry Edward Shortt built on this work, and in 1947 was able to prove that malaria has an exoerythrocytic stage.[40] He explored the liver of rhesus monkeys that were inoculated with *Plasmodium vivax* and found the elusive exoerythrocytic stage, subsequently confirmed in human volunteers.[41] Two years later, he also found this stage in *Plasmodium falciparum*.[42]

Major Leonard Rogers founded the British Empire Leprosy Relief Association (BELRA) in 1923. This organisation is now known as Lepra and continues to provide support to people with the disease. Rogers inspired others to recognise the early stages of leprosy and investigated the efficacy of chaulmoogra oil for its treatment.[43] It was not until the 1960s that Captain Dennis Ridley, who served during World War II, introduced a new landmark classification of leprosy,[44] which had six stages and became the gold-standard reference system. Ridley was also the pathological expert for studies that led to the development of multidrug chemotherapy for leprosy, which is the current international standard of care.[45]

In more recent times, the British Army has been heavily involved in conflicts in Iraq and Afghanistan. The most significant contributions of Army medics there was the characterisation of 'Helmand Fever', which was found to be sandfly fever, acute Q fever and rickettsial infections (including typhus). Much work has been done to decide the subsequent treatment of these diseases.[46] Operation Gritrock saw the British Army deploy to Sierra Leone in 2014 during the major outbreak of Ebola virus.[47,48] The Army engaged this threat by devising novel education models including an online e-learning package and simulation training.[47,49] Army personnel also created a logistical chain that saw patients enter and leave the facility by designated routes among other innovations.[47] These methods became internationally acclaimed and accepted as standard practice. The region was declared disease-free by 2015. In addition, 45% of cutaneous leishmaniasis occurring in the UK is seen in British military personnel. The British Army retains its currency in treating this disease and maintains of its renowned specialist status.[50]

Conclusions

It could be argued that the British Army Medical Services have contributed more to the advancement of tropical medicine than any other organisation. For over 200 years, the Army has assumed key roles in the discovery, treatment and prevention of major diseases. Perhaps even more importantly, army clinicians have been responsible for the development of education and research facilities worldwide that continue to improve the lot of mankind. ■

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