

## REVIEW

# In memory of Patrick Manson, founding father of tropical medicine and the discovery of vector-borne infections

Kelvin KW To and Kwok-Yung Yuen

Patrick Manson, a clinician-scientist serving in China (1866–1889), discovered that many tropical infectious diseases require a vector peculiar to warm climate for person to person transmission. He demonstrated the nocturnal periodicity of microfilariae in the blood of patients with elephantiasis. These microfilariae undergo metamorphosis when ingested by the mosquito acting as the vector for the completion of their life cycle. Furthermore, he demonstrated the linkage between the lung fluke and endemic haemoptysis by finding operculated eggs in patients' sputa. He predicted that the miracidium from hatched eggs uses crustaceans, such as fresh-water snails found at tropical conditions, as the intermediate hosts in the life cycle of many trematodes. His vector hypothesis leads to vector control which is now the cornerstone for the World Health Organization's programme for the elimination/control of lymphatic filariasis, dracunculiasis and malaria. Before leaving China, he established the Alice Memorial Hospital, the Hong Kong College of Medicine for Chinese (the forerunner of the University of Hong Kong), and the Hong Kong Medical Society for medical service and education. He also accepted the Hong Kong Dairy Farm for supplying hygienic milk affordable by pregnant women, children and patients.

*Emerging Microbes and Infections* (2012) 1, e31; doi:10.1038/emi.2012.32; published online 24 October 2012

**Keywords:** Patrick Manson; tropical disease; vector

## INTRODUCTION

Manson started as a clinician whose initial involvement in the Far East partly resulted from the colonialistic needs of the British Empire in Asia; however, his work proved to be more than advancing the understanding of exotic diseases by Europeans. His research finding is life-saving. His clinical service changed the perception of the Chinese people to Western medicine. He laid the foundations for medical education in Hong Kong for the centuries to come. We trace the footsteps of Manson who ventured into the tropics, also known as white men's grave in those days, and how he became the indisputable founder of modern tropical medicine.

## AN ORDINARY CHILDHOOD OF AN EXTRAORDINARY CLINICIAN-SCIENTIST

Patrick Manson was born in 1844 at Oldmeldrum, a small market town near Aberdeen, Scotland. His mother, Elizabeth Livingstone, was a distant relative of the great explorer and Christian missionary of Africa, Mr David Livingstone. Manson, as he used to mock himself as 'Scandinavian pirate' owing to his Norwegian descent, was described as a dull but curious child. Among his Presbyterian Christian family, he was noticed to have a good memory for being able to memorize the church sermons at the age of 5 years. As he grew up, he was noted for his interest in carpentry, mechanics, cricket and hunting with shotguns. A minor incident foretelling his career was his shooting and dissection of a lean and ferocious

cat which yielded a tapeworm inside. However, his initial enthusiasm for mechanics led to his apprenticeship as an ironsmith at the age of 15 years. His will power was obviously much stronger than his physique; he soon developed a spinal curvature and right arm paresis after working for the same hours as other adult ironsmiths. Being medically certified as invalid, he had to give up engineering which turned out to be a blessing in disguise when he switched to biological science. His personal experience of illness and disability might have contributed to his decision to go into medicine, a caring profession.

## EARLY COMPLETION OF MEDICAL DEGREE

In 1860, Manson started studying medicine at the University of Aberdeen for 4 years. As he finished his medical curriculum at the age of 20 years which was too young for graduation, he had to spend another year in reading and visiting hospitals, schools and museums before he formally graduated in 1865. He then worked for 7 months as an assistant medical officer at a lunatic asylum in Durham during which time he performed 17 postmortem dissections on patients with psychiatric illnesses for his Doctor of Medicine thesis. He reasoned in his thesis that the severity of the brain pathology in these patients correlates with the diameter of their aneurismal internal carotid artery, which is similar to the situation of a cirrhotic liver and the dilated portal vein due to portal hypertension.<sup>1</sup>

## FROM AN INEXPERIENCED MEDICAL GRADUATE TO A MEDICAL OFFICER WORKING ALONE IN TAKAO OF FORMOSA (NOWADAYS TAIWAN)

In 1866, Manson was inspired by his elder brother who worked in Shanghai to take up a medical officer post in the Customs Service of Formosa. He sailed for 3 months from London across the Cape of Good Hope, Madagascar, and finally arrived at Takao (present day Kaohsiung) of Formosa. His official daily duty was to inspect the ships calling at the port, treat their crew and keep the meteorological record. He also attended to Chinese patients in a local missionary hospital where he was exposed to a wide variety of illnesses from elephantiasis to leprosy for his postgraduate training without any supervision. His only research tool was a combination of clinical skill, hand lens and good record keeping. He took pride in fishing out leeches from the nose of patients painlessly by soaking and relaxing the leeches with hypertonic saline. He successfully treated European patients who developed tropical liver after too much meat and wine (probably fatty liver) with a prescription of heavy exercise and dietary discretion. However, he was quite disappointed by the death of a young Chinese patient presenting with heart failure who died the next day following his treatment. The patient was not improving after weeks of treatment by a traditional Chinese doctor. Later he realized that this and many similar patients were suffering from beriberi as a result of vitamin B1 deficiency only after many years.<sup>2</sup> While he became more and more confident with his successes, he also became humbler and wiser with each of his failures.

Though Manson lived amongst a small community of 16 Europeans, he befriended the local Chinese and learned the local languages including that of the aborigines. At that time, the island was in a state of unrest due to struggles between the Japanese and the Chinese factions for its control. Manson happened to be on good terms with some fine upright native Chinese fellows of similar character and was suspected to buy some ponies for the Chinese forces. In early 1871, he was advised by the British Consul to leave for Amoy (Xiamen).

## THRIVING AND INNOVATIVE CLINICAL SERVICE AT AMOY UNDER IMPROVISED CIRCUMSTANCES

Manson lived in a community of 150 Europeans at Kulangsu at the entrance of the Amoy harbour which was a port serving the much bigger inland trading city of Chang Chow. Besides his official duty as the medical officer of the local Imperial Maritime Customs, he again served the local Chinese patients at the Baptist Missionary Society's Hospital and Dispensary for the Chinese. Though he still received no supervision or mentorship for his daily work, he was joined by his brother David Manson for 2 years and other missionary doctors intermittently.

Amoy was known as just another white man's grave in the tropics which is hot and humid. The streets were narrow, irregular and filthy with excreta and litters. In those days, the only machinery for sanitation at Amoy was the pigs and dogs which ate up the excreta and litters. The inhabitants were in extreme poverty who subsisted on rice and sweet potatoes occasionally flavoured with vegetable pickles and salted fish. The area was highly endemic for malaria, typhoid fever, dengue fever and leprosy. His estimation by survey showed that about 1 in 450 inhabitants were infected by leprosy. In the 1877 cholera outbreak in Amoy, 95% of the population was affected and 2% died. Unfortunately, his younger brother David Manson also died in Amoy in 1878.

Despite the absence of supervision and training for a specialist, he had become a highly competent clinician who was able to make

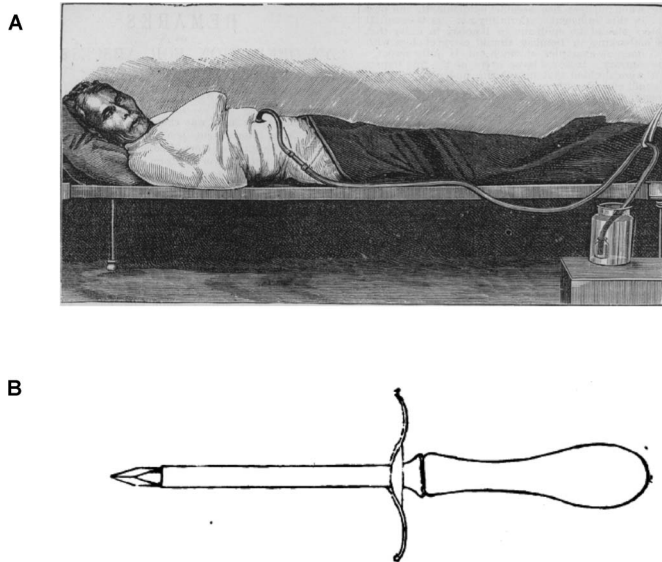
brilliant diagnosis and gave useful treatment under improvised conditions. His competence in anatomy and clinical medicine was exemplified by some quotes in his records. "Given a non-febrile case in which persistent symptoms, no matter how trifling, point to disease in the chest (especially if there is laryngeal irritation), and the cause for which cannot be readily made out, suspect aneurysm of the aortic arch".<sup>3</sup>

He attended to 1980 patients at the Baptist Missionary Hospital in 1871. In 1877, he excised one ton of tissue from patients with elephantiasis, with only 2 deaths out of 61 operations done under chloroform anaesthesia and without support by blood transfusions and antibiotics. Many of these patients could not find a job because of their grotesquely disfigured and enlarged lower limbs and scrotums. They were abandoned by their families because of the financial burden or the superstition about demon possession. In one instance, he encountered a 19-year-old man badly affected by a huge elephantoid tumour who attempted suicide by swallowing arsenic but failed because the excessive dose of poison caused gastric irritation leading to early emesis of the poison. He agreed to be operated by Manson because he did not mind to be killed anyway. This successful operation by Manson earned him reputation and the gradual acceptance of Western medicine by the local Chinese. Besides elephantiasis, he has relieved many patients suffering from the distressing colics due to renal, ureteric and bladder stones by surgical lithotomies. Despite these achievements, he was modest in describing himself as a good carpenter but an indifferent surgeon.

Manson was also a daring and accurate surgeon who tried to tackle liver abscess which was almost invariably fatal in his era with no organ imaging facilities and antibiotics.<sup>4</sup> His other famous clinical quote was 'Given a febrile case of some standing in which symptoms, no matter how trifling, point to disease in the abdomen, the precise nature of which cannot be diagnosed, suspect abscess of the liver, and carefully and repeatedly examined for it'. He designed the Manson's trocar and cannula for the single-handed blind exploration and treatment of deep seated liver abscess. The trocar and cannula produced at a local iron-smith in Amoy can be fitted to a stylet and perforated drainage tube which could be used for the exploration of hidden liver abscess in the absence of organ imaging and many other surgical conditions (Figure 1). His adventurous, patient, accurate and decisive personality was not just reflected in his clinical practice, but also in his recreation. Manson gained the reputation of being the best snipe-shot in the tiger hunts at Amoy.

## LOCAL CULTURE AND PATIENTS' PSYCHOLOGY, PUBLIC HEALTH PREVENTION AND MEDICAL EDUCATION IN AMOY

Ignorance, superstition, distrust, rumors and jealousy obstructed the spread of Western Medicine in China in those days. There were even rumors that Western doctors dispensed poisons called Shan-si-fan (生死粉, literally, 'the powder of life and death') to Chinese people who then fell ill and could only be cured by Western doctors who had the antidotes. Western doctors were also accused of harvesting the eyes and hearts of Chinese patients for potions, and of drugging and raping Chinese women. Manson soon noticed that traditional Chinese doctors took the history, examined the pulse and tongue of patients, and prescribed in full view in an open street. Taking into account the patients' psychology, he modified his operating theater so that street onlookers and relatives could peep through wide glass windows to watch his operations. The whole process of putting the patient under anaesthesia, painlessness of the surgical procedure, removal of tumours and stones and the recovery from anaesthesia were open to



**Figure 1** Drainage of liver abscess with Manson's trocar and cannula by Patrick Manson (Reproduced from Ref. 4 with permission from BMJ Publishing Group Ltd).

the public. His sharp observation, humanistic concern and adaptive attitude are keys to his success in winning the locals over to western medicine.

Being a seasoned clinician-scientist, Manson fully understood that 'prevention is better than cure'. He popularized smallpox vaccination at Amoy which markedly reduced the incidence and mortality from smallpox. One of his students was appointed as the public vaccinator in Chang Chow. He has trained many native house surgeons and dressers who successfully established their practice elsewhere. Unfortunately, a fervent evangelist at the Baptist Missionary Hospital considered that Manson was overly focused on medical practice and ignored spiritual work. Manson was thus dismissed, but he continued to practice at the Seamen's Hospital which served the European population and seamen.

#### DISCOVERY OF THE LIFE CYCLE OF FILARIAE IN MOSQUITOES

After 9 years of work in China, Manson returned to London in 1875. He was married to Henrietta Isabella Thurnburn. While enjoying the time of being a newlywed, he also acquired the latest techniques in eye surgery. Despite his daring personality and meticulous surgical skills, he was a conscientious surgeon who did not touch the eye till he had acquired such specialist skill in London. While searching for the most updated information on tropical diseases and entomology, he was quite disappointed to find that such information was scarce and poorly organized. However, he bumped onto the work of Timothy Lewis in the British Museum Library on the finding of a microscopic nematode worm, *Filaria sanguinis hominis* (*Filaria nocturna*, *Wuchereria bancrofti*), in the chylous urine and blood of an Indian patient suffering from chyluria.<sup>5</sup> This struck Manson as he had operated on many cases of elephantiasis who also had chyluria. Manson then returned to Amoy with his wife and a compound microscope in 1876.

With his new compound microscope, Manson soon found that sheathed microfilariae were abundant in the blood of patients with elephantiasis (Figure 2). The interesting observation was that such sheathed and vigorously active microfilariae remained unchanged in the blood at body temperature, but then escaped from the sheath at tropical room temperature. He traced the changes of microfilariae in the alimentary tract of female *Culex fatigans* (*Culex quinquefasciatus*)

mosquitoes fed with infected human blood.<sup>6</sup> After dissecting hundreds of such mosquitoes, Manson found that the microfilariae underwent unshedding and metamorphosis from the alimentary tract to the thoracic muscles of mosquitoes. In 1899, Thomas Bancroft demonstrated that these infected mosquitoes can inoculate the parasite back to human by biting.<sup>7</sup> Finally, Manson and others successfully discovered the adult worms of *W. bancrofti* with all stages of microfilariae in their uterus within the lymphatics of patients suffering from elephantiasis. Thus, the complete life cycle of filariasis in humans and mosquitoes was described, which clearly illustrates how human-to-human transmission occurs through the mosquito vector.

This landmark discovery of the role of mosquitoes as an intermediate host in the life cycle and transmission of vector-borne pathogens came only with meticulous and painstaking research. He built a small mosquito house covered with fine mosquito-proof gauze. He put microfilariae-infected patients including his gardener, to sleep inside this mosquito house. A light was placed inside this house and the door was opened for 30 min at night. Next morning, mosquitoes with their abdomens engorged with infected human blood were found on the gauze. They were stupefied by tobacco smoke and transferred to labelled glass vials. Then they were dissected and examined under the microscope.<sup>5</sup>

Of the 190 Chinese people that Manson examined, 15 who had microfilariae in their blood samples had some sign of elephantiasis or some indication of ill-health as shown by recurrent fever and oedema. After examining 670 persons, he found that 1 in every 10.8 patients in Amoy was infected and the incidence of infection increased from 1 in 17.5 during youth to 1 in 3 for the elderly. Manson was such an astute clinician-scientist who also discovered the nocturnal periodicity of microfilariaemia. By counting the number of microfilariae in the blood of infected patients, he found that their number peaked at around midnight which coincides with the human sleeping time and the mosquito biting activity.

His eye-opening research findings were published in the Customs Gazette and later the *Journal of Linnean Society of London, Zoology* in 1878.<sup>6</sup> While his paper was read out in the society's meeting, one critic remarked that 'what they had heard represented either the work of a genius or more likely the emanations of a drunken Scots doctor in far-off China, where everyone was aware, they drank far too much whisky'.



**Figure 2** Microfilaria of *Wuchereria bancrofti* with sheath in the peripheral blood of human (Giemsa stain; original magnification,  $\times 200$ ).

With time, his experiments were reproduced and his mosquito hypothesis was widely accepted.

### MANSON AND ROSS IN THE DISCOVERY OF MALARIA TRANSMISSION BY MOSQUITOES

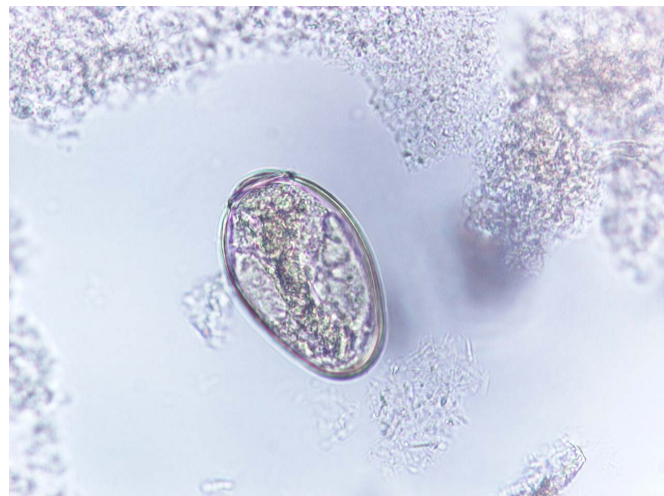
Manson had noticed the exflagellation of the blood malarial parasitic agent (later known to be male gametocyte) for a long time (Figure 3). He communicated this finding to Ronald Ross and encouraged him to take up this important piece of research in India.<sup>8</sup> During the period of mentorship by Manson, Ronald Ross had written 110 letters to Manson. Manson replied with 85 letters on knowledge gaps, experimental methodology, scientific analysis, support and encouragement. After Ross's completion in painting the life cycle of malaria in mosquitoes in 1898, he wrote to Manson, 'What a beautiful discovery this is. I venture to praise it because it belongs to you, not to me'. However, in the years after Ross got the Nobel Prize, he turned against and discredited Manson. When Manson was enquired on this issue, his comment was 'What I have done I have done, I have nothing to add or retract'.

### FROM PATIENTS TO DISCOVERIES: THE LIFE CYCLES OF LUNG FLUKE AND OTHER PARASITES

In 1880, an Amoy official consulted Manson for a facial eruption and a harsh and loud cough. He coughed out blood-stained sputum which missed the spittoon and fell onto Manson's office carpet. Manson picked up the sputum and found large operculated eggs under his microscope (Figure 4). When these were put in water jars, they hatched into ciliated creatures after 2 weeks at tropical room temperature.<sup>9</sup> Manson later found that this fluke *Paragonimus westermanii* (*Distoma ringeri*) in the postmortem examination of a patient suffering from endemic haemoptysis with large operculated eggs in the sputum. He proposed that this lung fluke should have an intermediate host in fresh water crustaceans such as snails for the completion of its life cycle. His hypothesis was finally proven in 1916 by Nakagawa.<sup>10</sup> His fresh water snail theory was later applied successfully to schistosomiasis. Manson has made many important contributions to tropical diseases including the discovery of *Filaria demarquaii* (*Mansonella ozzardi*), *Filaria diurna* (*Loa loa*), *Filaria perstans* (*Mansonella perstans*), the tapeworm *Bothriocephalus mansoni* (*Spirometra [Diphyllobothrium] mansonoides*), *Schistosoma mansoni*, and the



**Figure 3** Exflagellated gametocyte of *Plasmodium vivax* in human blood (Giemsa stain; original magnification,  $\times 1000$ ).



**Figure 4** Operculated egg of *Paragonimus westermanii* from a sputum sample (wet mount; magnification,  $\times 400$ ).

dermatophytic fungus *Trichophyton concentricum* which causes tinea imbricata.<sup>11–13</sup> The identification of these organisms as human pathogens has provided the basis for the current management and prevention of these infections.

### CONTRIBUTIONS TO MEDICAL SERVICE AND EDUCATION IN HONG KONG

After 5 years in Takao and 11 years in Amoy, Manson decided to move to Hong Kong. He set up a very successful private medical practice which attracted many Europeans and rich Chinese patients. Besides operating at the Civil Hospital for Europeans, he and Sir Ho Kai founded the Alice Memorial Hospital with the support from the London Missionary Society. This hospital served Chinese patients and was also the teaching hospital for the Hong Kong College of Medicine for Chinese which is the forerunner of the University of Hong Kong (HKU). He was the founding dean who gave his inaugural speech on 1 October 1887 at the City Hall, during which Manson emphasized the role of the college in medical education to fight ignorance, superstition and outdated traditions of the feudal Ching Dynasty, the popularization of Western medical practice to ease suffering and its future contributions of research to advance scientific truth for the Chinese and the world. This college will reinvigorate the 0.3 billion of industrious thrifty, persevering and clever Chinese people who invented printing, gunpowder and smallpox inoculation. He also highlighted the importance of a correct attitude in the process of education on science and medicine, that 'high personal character, a reputation for wisdom, humility, honesty and kindness will often do more to recommend our wares (scientific & medical knowledge) than any quality in the wares themselves'.<sup>3</sup> The first batch of Chinese medical graduates from this college included the father of the new China, Dr Yat-Sen Sun. It is interesting to note that the Alice Memorial Hospital served as the meeting place for Dr Sun and his revolutionary comrades. In the spring of 1923, Dr Sun made a visit to the HKU at the invitation of the Students' Union, and delivered his historic speech at the now Loke Yew Hall to more than 400 guests. Dr Sun began his speech by saying that, 'I feel as though I have returned home, because Hong Kong and the HKU are my intellectual birthplace'.

Besides founding the first Western hospital and the first medical school for Hong Kong, Manson also founded the Hong Kong Medical Society in 1886 which later had its regular meetings conducted in Alice

Memorial Hospital. In Manson's presidential address to the Society, he indicated the lack of education and research on tropical medicine which rendered doctors unable to differentiate malaria from typhoid fever. Due to such gaps in training, there was often wastage of quinine for non-malarial fever. His philosophy towards the judicious use of antimicrobials is even more important in the present era of rising antimicrobial resistance. Though newly recognized clinical entities such as tropical (fatty) liver could be easily be treated by heavy exercise and dietary (food and alcoholic beverages) discretion, there was no portal of sharing on such important knowledge between doctors till the founding of this medical society.

Despite his heavy engagement in medical education, he did not withdraw from his medical practice. Soon after the inauguration of the Hong Kong College of Medicine for Chinese, he was summoned by Mr Hung-Chang Li, the prime minister of the Ching Dynasty of China who was suspected to have a tongue cancer, to Tientsin in November 1887. Manson was prostrated by a prolonged bout of gout and had to be carried on board by others. Manson found that Mr Li had a sublingual abscess which was incised and drained. Mr Li was deeply impressed by the knowledge and skill of Manson. Later, Mr Li became the patron of the Hong Kong College of Medicine for Chinese from 1889 till his death in 1901. The college was subsequently incorporated into the HKU which was established in 1911.

### INFECTIOUS DISEASE RESEARCH BLOSSOMING AT THE HKU

With the firm foundation laid down by Manson, the following decades saw a slow but sustained development of research in infectious diseases at the HKU. In 1920, HKU established the chair of pathology for Dr Chung-Yik Wang who published extensively on infectious diseases including tuberculosis and syphilis.<sup>14,15</sup> The first post-second world war chair Professor in pathology (1948) was Dr Pao-Chang Hou who described the relationship between primary cholangiocarcinoma of the liver and *Clonorchis sinensis* infection.<sup>16</sup> In the inaugural speech of the chair Professor of pathology in 1968, Dr James Gibson emphasized that the fatality of infectious disease is higher than the fatalities due to injuries in wars. He proposed the establishment of the Department of Microbiology which is dedicated to the teaching and research of microbiology. In 1976, Dr Chi-To Huang became the founding chair of microbiology who firstly discovered that *Pseudomonas pseudomallei* (now renamed *Burkholderia pseudomallei*) was the cause of a major outbreak amongst the dolphins of Ocean Park in Hong Kong.<sup>17</sup>

With the successful control of most tropical diseases in Hong Kong, the direction of infectious disease research has switched to emerging infectious diseases since the 1990s. Among the top three emerging pathogens of global significance, human immunodeficiency virus, influenza A H5N1 virus and severe acute respiratory syndrome coronavirus, the latter two have emerged in Hong Kong in 1997 and 2003, respectively.<sup>18,19</sup> HKU has characterized these two viruses and their associated diseases which directly impacted on patient care and public health policy. The source of this newly emerged severe acute respiratory syndrome coronavirus was successfully traced from human to civets and then the natural reservoir in Chinese horseshoe bats.<sup>20</sup> Similar to the key role of arthropods and animal vectors in the transmission of tropical diseases, wild animals have played a major role in the genesis of emerging infectious diseases. Therefore, HKU has continued to search and has subsequently discovered over 40 novel viruses in animals and human.<sup>20–25</sup> Besides serving the citizens of Hong Kong, the medical school has also tried to improve the medical system and education

in the Mainland through its participation in setting up the HKU-Shenzhen hospital as a teaching hospital in the Guangdong province in 2012.

### IMPROVING THE NUTRITION AND HEALTH OF THE HONG KONG PUBLIC

Life in Hong Kong was very difficult in those days even for the British garrison which was far better provided in terms of nutrition and medicine. The annual death rate in the British garrison varied between 3% and 13.6%, and many deaths were related to infection (Figure 5). Besides advocating sanitation and public health prevention to improve the dire situation, Manson and others established the Dairy Farm at the Pokfulam district in 1886 for providing a hygienic and affordable supply of milk and dairy products for pregnant women, children and patients. The farmers and the first batch of Ayrshire cows were sent from Aberdeenshire of Scotland, and the pasture of guinea-grass grown on the bare hill side of the farm was imported from Queensland. The improvement of nutritional status is vital to our health, including reduced susceptibility to infection.<sup>26,27</sup> A cause-of-death prediction model has named poor nutrition as the underlying cause of most infectious diseases.<sup>28</sup>

### CONTRIBUTIONS TO MEDICAL EDUCATION IN THE UNITED KINGDOM: LONDON'S SCHOOL OF TROPICAL MEDICINE AND HYGIENE

Manson returned to London in 1889 and set up a private medical practice with a laboratory at the top floor in Queen Anne Street. He obtained his membership of Royal College of Physicians by examination in 1889 and became the physician to the Seamen's hospital at Dreadnought for 6 years. He was a strong advocate on the necessity for special education in tropical medicine. In an introductory address delivered at the St George Hospital of London, he said, 'the course of instruction in general medicine usually received in this country is utterly inadequate to qualify for tropical practice. I say so emphatically, basing my assertion on my own experience, my own mistakes, and what I have seen and still daily see of the mistakes of others'.<sup>29</sup> This led to strong repercussions from his colleagues and he had to leave Dreadnought. Though he had to pay the price of honesty and conviction by resignation, he was then given a teaching post for tropical diseases at the Albert Dock Seaman Hospital in 1901. But with time, people were more and more convinced of the necessity of tropical medicine, Manson founded the London School of Tropical Medicine and Hygiene in 1899. At the age of 55 years, Manson had to spend 3 h per round trip and travelled 9 miles to the school two to three times per week for his teaching duties. Similar to most eminent scientists, he was always concerned with how to induce continuous interest in future generations to make keen observations in patients and pursue effective control of infectious diseases.

### RELEVANCE OF MANSON'S DISCOVERIES TO MODERN MEDICINE

The groundwork of Manson has laid a solid foundation for many clinical practices and epidemiological programmes in modern tropical medicine. Global programmes in vector control remain the mainstay in the control and eradication of malaria, filariasis and dracunculiasis;<sup>30–32</sup> 22.8% of emerging infectious diseases since 1940 are vector-borne diseases.<sup>33</sup> Control of arthropod vector-borne diseases includes chemical and biological means, as well as by reducing contact between human and vectors. The best example is the control of mosquitoes, which includes the reduction of the mosquito population by



**Figure 5** A tombstone for British garrisons who died in Hong Kong with fever at the Hong Kong Cemetery of the Happy Valley district.

environmental modifications, larvicides and adulticides, and the prevention of mosquito–human contact with medicated bed-nets and insect repellants. Alternative biological control strategies under investigation to reduce insecticide resistance and ecological side effects include the use of a bacterial endosymbiont *Wolbachia* to inhibit the replication of the *Plasmodium* in mosquitoes, entomopathogenic fungi and genetically-modified mosquitoes.<sup>34–36</sup> Our understanding of the life cycle of flukes provides the basis for control programmes of schistosomiasis in China, which mainly aims to minimize contacts of snails from excreta of humans or cattle.<sup>37</sup> Though the incidence of paragonimiasis has been reduced substantially with education programmes and mass chemotherapy,<sup>38</sup> it is the control of the vector population and reduction in human–arthropod contacts that are most practicable and sustainable. The importance of vector-borne diseases extends beyond parasites. Mosquitoes transmit many viruses that cause epidemics, such as yellow fever, dengue and chikungunya virus. The problem of vector-borne disease is further aggravated by climate change. The geographical range of arthropod-borne infections has expanded in recent years in both latitude and altitude.<sup>39</sup> For example, chikungunya virus, which was previously limited to tropical countries, has now been found in Italy.<sup>40</sup> Many newly described emerging infections also require a vector, for example the new phleboviruses<sup>41–42</sup> and *Ehrlichia*.<sup>43</sup>

#### A GREAT PERSONAL EXAMPLE OF A CLINICIAN, SCIENTIST AND TEACHER

Manson died in 1922. He was a great physician, surgeon, microbiologist and a discoverer without mentors. His long period of stay in the tropics posed significant risk to his health and safety. He has set the personal example of excellence in clinical service, medical education and microbial research. His scientific contributions on the importance

of vector control to interrupt the life cycle of many tropical disease agents make him well deserved of the title of Father of Tropical Medicine. In the year 2000, the World Health Organization launched a global campaign for eliminating lymphatic filariasis which would not have been possible without the firm foundation laid down by Manson.<sup>31</sup> His contribution to China did not end after leaving China. In 1896, he helped Dr James Cantlie in saving Dr Yat-Sen Sun from the kidnap and imprisonment by secret agents of the Ching Dynasty in London. If not for their effort, Dr Sun might have been executed, and China may not have been liberated from the feudal Ching Dynasty in 1911. In the pursuit of science and medicine, Manson emphasized that most mistakes do not come from not knowing in medicine, but from not looking. It is not the microscope, but the eyes that look through it that counts. Additionally, never refuse to see what you do not want to see, for it is often the finger pointing towards discovery.

#### ACKNOWLEDGMENTS

We are very grateful to Dr Samson S Y Wong (the University of Hong Kong, Hong Kong, China) who proofread this review and supplied three of the figures.

- 1 Jay V. Sir Patrick Manson. Father of tropical medicine. *Arch Pathol Lab Med* 2000; **124**: 1594–1595.
- 2 Arnold D. British India and the “beriberi problem”, 1798–1942. *Med History* 2010; **54**: 295–314.
- 3 Manson-Bahr PH, Alcock A. *The life and work of Sir Patrick Manson*. London: Cassell, 1927.
- 4 Manson P. Remarks on an operation for abscess of the liver. *Br Med J* 1892; **1**: 163–167.
- 5 Lewis T. Filial sanguinis hominis (mature form), found in a blood-clot in naevoid elephantiasis of the scrotum. *Lancet* 1877; **110**: 453–455.

- 6 Manson P. On the development of *Filaria sanguis hominis* and on the mosquito considered as a nurse. *J Linn Soc (Zool)* 1878; **14**: 304–311.
- 7 Mackerras IM, Marks EN. The Bancrofts: a century of scientific endeavour. *Proc R Soc Qd* 1973; **84**: 1–34.
- 8 Ross R. *Memoirs, with a full account of the great malaria problem and its solution*. London: London J. Murray, 1923.
- 9 Manson P. Distoma ringeri. *Med Times Gaz* 1881; **2**: 8–9.
- 10 Nakagawa K. Human pulmonary distomiasis caused by paragonimus westermanni. *J Exp Med* 1917; **26**: 297–323.
- 11 Castellani A. Note on the aetiology of some tropical dermatomycoses (*Tinea cruris*, *Tinea flava et nigra*, *Tinea imbricata*). *Proc R Soc Med* 1913; **6**: 31–39.
- 12 Manson P. Report of a case of bilharzia from the West Indies. *Br Med J* 1902; **2**: 1894–1895.
- 13 Haynes DM. Framing tropical disease in London: Patrick Manson, *Filaria perstans*, and the Uganda sleeping sickness epidemic, 1891–1902. *Soc Hist Med* 2000; **13**: 467–493.
- 14 Wang CY. An experimental study of latent tuberculosis. *Lancet* 1916; **188**: 417–419.
- 15 Wang CY. A precipitation test for syphilis. *Lancet* 1922; **199**: 274–276.
- 16 Hou PC. The relationship between primary carcinoma of the liver and infestation with *Clonorchis sinensis*. *J Pathol Bacteriol* 1956; **72**: 239–246.
- 17 Huang CT. What is *Pseudomonas pseudomallei*. *Elixir* 1976; **70**: 70–72.
- 18 Yuen KY, Chan PK, Peiris M *et al*. Clinical features and rapid viral diagnosis of human disease associated with avian influenza A H5N1 virus. *Lancet* 1998; **351**: 467–471.
- 19 Peiris JS, Lai ST, Poon LL *et al*. Coronavirus as a possible cause of severe acute respiratory syndrome. *Lancet* 2003; **361**: 1319–1325.
- 20 Lau SK, Woo PC, Li KS *et al*. Severe acute respiratory syndrome coronavirus-like virus in Chinese horseshoe bats. *Proc Natl Acad Sci USA* 2005; **102**: 14040–14045.
- 21 Lau SK, Woo PC, Yip CC *et al*. Identification of a novel feline picornavirus from the domestic cat. *J Virol* 2012; **86**: 395–405.
- 22 Lau SK, Woo PC, Yip CC *et al*. Isolation and characterization of a novel Betacoronavirus subgroup A coronavirus, rabbit coronavirus HKU14, from domestic rabbits. *J Virol* 2012; **86**: 5481–5496.
- 23 Woo PC, Lau SK, Choi GK *et al*. Natural occurrence and characterization of two internal ribosome entry site elements in a novel virus, canine picodistrovirus, in the picornavirus-like superfamily. *J Virol* 2012; **86**: 2797–2808.
- 24 Woo PC, Lau SK, Choi GK *et al*. Complete genome sequence of a novel picornavirus, canine picornavirus, discovered in dogs. *J Virol* 2012; **86**: 3402–3403.
- 25 Woo PC, Lau SK, Wong BH *et al*. Feline morbillivirus, a previously undescribed paramyxovirus associated with tubulointerstitial nephritis in domestic cats. *Proc Natl Acad Sci USA* 2012; **109**: 5435–5440.
- 26 Katona P, Katona-Apte J. The interaction between nutrition and infection. *Clin Infect Dis* 2008; **46**: 1582–1588.
- 27 Schlaudecker EP, Steinhoff MC, Moore SR. Interactions of diarrhea, pneumonia, and malnutrition in childhood: recent evidence from developing countries. *Curr Opin Infect Dis* 2011; **24**: 496–502.
- 28 Black RE, Morris SS, Bryce J. Where and why are 10 million children dying every year? *Lancet* 2003; **361**: 2226–2234.
- 29 Manson P. The necessity for special education in tropical medicine. *Lancet* 1897; **150**: 842–845.
- 30 World Health Organization. *Dracunculiasis. The global eradication campaign*. Geneva: WHO. Available at <http://www.who.int/dracunculiasis/eradication/en/> (accessed on 16 July 2012).
- 31 World Health Organization. *The Global Programme to Eliminate Lymphatic Filariasis*. Geneva: WHO. Available at [http://www.who.int/lymphatic\\_filariasis/disease/en/](http://www.who.int/lymphatic_filariasis/disease/en/). (Accessed on 16 July 2012).
- 32 World Health Organization. *About WHO Global Malaria Programme*. Available at [http://www.who.int/malaria/about\\_us/en/index.html](http://www.who.int/malaria/about_us/en/index.html) (accessed on 16 July 2012).
- 33 Jones KE, Patel NG, Levy MA *et al*. Global trends in emerging infectious diseases. *Nature* 2008; **451**: 990–993.
- 34 Walker T, Moreira LA. Can Wolbachia be used to control malaria? *Mem Inst Oswaldo Cruz* 2011; **106**: 212–217.
- 35 Alphey L, Beard CB, Billingsley P *et al*. Malaria control with genetically manipulated insect vectors. *Science* 2002; **298**: 119–121.
- 36 Farenhorst M, Mouatcho JC, Kikankie CK *et al*. Fungal infection counters insecticide resistance in African malaria mosquitoes. *Proc Natl Acad Sci USA* 2009; **106**: 17443–17447.
- 37 Wang LD, Chen HG, Guo JG *et al*. A strategy to control transmission of Schistosoma japonicum in China. *N Engl J Med* 2009; **360**: 121–128.
- 38 Blair D, Agatsuma T, Wang W. Paragonimiasis. In: Murrell KD, Fried B (ed.) *World class parasites. Vol 11. Food-borne parasitic zoonoses: fish and plant-borne parasites*. New York: Springer 2007: 117–150.
- 39 McMichael AJ, Woodruff RE, Hales S. Climate change and human health: present and future risks. *Lancet* 2006; **367**: 859–869.
- 40 Burt FJ, Rolph MS, Rulli NE, Mahalingam S, Heise MT. Chikungunya: a re-emerging virus. *Lancet* 2012; **379**: 662–671.
- 41 McMullan LK, Folk SM, Kelly AJ *et al*. A new phlebovirus associated with severe febrile illness in Missouri. *N Engl J Med* 2012; **367**: 834–841.
- 42 Yu XJ, Liang MF, Zhang SY, *et al*. Fever with thrombocytopenia associated with a novel bunyavirus in China. *N Engl J Med* 2011; **364**: 1523–1532.
- 43 Pritt BS, Sloan LM, Johnson DK *et al*. Emergence of a new pathogenic Ehrlichia species, Wisconsin and Minnesota, 2009. *N Engl J Med* 2011; **365**: 422–429.



This work is licensed under a Creative Commons Attribution-NonCommercial-NoDerivative Works 3.0 Unported License. To view a copy of this license, visit <http://creativecommons.org/licenses/by-nc-nd/3.0>