

Zoonotic Malaria in Malaysia

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In this issue of the Medical Journal of Malaysia, we publish a report of a fatal case of *Plasmodium knowlesi* malaria infection¹. This is not the first case. Four fatal cases were first reported in Sarawak by Cox-Singh *et al* in 2008². Furthermore, the same team of workers who submitted this case report have noted at least six previous fatal cases in Sabah³. The report however is a reminder to the medical profession that malaria is alive in Malaysia.

Malaria was once THE greatest scourge weighing upon human habitation in Malaysia. Forty years after the British post in Penang was founded in 1786, one-third of all deaths there were attributed to malaria. Settlement of the town of Jurga was at one time abandoned by the British on account of malaria. Port Swettenham (Port Klang) was almost going the same way in 1901 when Malcolm Watson's intervention saved the situation. Remembering the work of Ronald Ross, he obtained \$30,000 from the Sanitary Board to drain the swamps around the port to control mosquito breeding and that pioneering experimental effort worked. Even when rubber estates were first economically viable, the human toll from malaria was staggering, despite the control measures that followed Watson's work. In 1911, when the Health Branch of the Medical Department was put in charge of estate health, there were 9,040 deaths among 143,614 Indian estate workers, a mortality rate of 62.9 per 1,000. A mortality rate nationwide in Malaysia today would mean a staggering disaster involving 1.8 million deaths!

Further progress in health care, resulted in a lowering of the mortality rate to 18.2 per 1,000 in 1921, which fell further to 11.4 per 1,000 in 1925 and it continued to drop in subsequent years until malaria eradication was considered an achievable goal. Even though malaria eradication has not been achieved, as hoped when the Malaria Eradication Programme was launched by the WHO in 1955, control measures reduced the incidence rate of malaria in Malaysia to between 0.20-0.27 per 1,000 between 2006-2010, numbering only between 5,297 to 7,390 cases annually⁴.

One important question that was asked by the WHO before the Malaria Eradication Campaign was launched, was whether malaria was a zoonosis⁵. It would change the paradigm if that were so. Simian forms of malaria, like *P. cynomolgi* were found in the early 1960's to accidentally infect humans in laboratories in the USA and an American army surveyor had acquired *P. knowlesi* while working in Pahang in 1965⁶. A team from America, working in collaboration with colleagues at the Institute for Medical Research in Kuala Lumpur, therefore investigated whether malaria was a

zoonosis. They collected blood from almost 1,200 villagers in Pahang, pooled the samples and injected them into rhesus macaques that were susceptible to malaria parasites, none of the monkeys acquired malaria, so the conclusion reached was that zoonotic malaria was extremely rare.

The widely-held view that malaria was not a zoonosis changed when a large number of human *P. knowlesi* infections were described in the Kapit Division of Sarawak in 2004⁵. *P. knowlesi* malaria is now recognized as the fifth cause of human malaria. Microscopically, the parasite resembles the benign *P. malariae*, but it can cause severe disease and death. It is now the most common form of malaria in many areas in Sarawak⁷ and Sabah⁸. It has been found to cause more severe malaria than *P. falciparum* and *P. vivax* in Sabah⁹. Cases have been reported in Southeast Asia from the southern borders of China with Myanmar and Vietnam down to Peninsular Malaysia and across to Borneo and the Philippines. Even urbanized Singapore has not been spared¹⁰.

Monkeys, chiefly the long-tailed macaque (*Macaca fascicularis*) and the pig-tailed macaque (*Macaca nemestrina*), found widely in Southeast Asia are the two principal natural hosts⁵. *P. knowlesi* has also been detected in banded leaf monkeys. Recent studies in both Peninsular Malaysia and Sarawak have found that wild macaques harbour the parasite^{11,12}. In its natural hosts, *P. knowlesi* generally induces a mild and transient disease, with chronic low-grade parasitemia. In the 1960s studies in Selangor identified *Anopheles hackeri* as the vector of *P. knowlesi*⁵. Since this mosquito is not attracted to humans and feeds mainly on monkeys deep in the jungle, it was believed that *P. knowlesi* malaria would not be a serious human problem. But after the recognition of the importance of human *P. knowlesi* malaria in Sarawak, vector studies have identified *A. latens* as the main natural vector of *P. knowlesi* in Sarawak and *A. cracens* as the vector in Pahang¹⁰. Other members of the *Anopheles leucosphyrus* group of mosquitoes have been found to be vectors in Vietnam. These vectors are mainly forest dwelling mosquitoes that predominantly feed outdoors after dusk.

The question now is how do we control this disease which is being acquired from a large population of monkey reservoir hosts? How extensive will it become? Will current malaria control methods involving vectors, which are designed against mosquitoes that feed indoors, be able to control these vectors that are outdoor feeders? How practical would it be to reduce the number of these forest dwelling mosquitoes? Will vector control have any impact on the animal reservoir of the disease? If that is not going to curb the spread of disease,

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what other options do we have? Should culling the host-monkey, which are a protected species, be an option? While answers to these questions are being sought, clinicians in Malaysia should be aware that there is a fifth malaria parasite, and patients with this form of malaria should be treated with a sense of urgency and should be managed appropriately.

REFERENCES

1. Rajahram GS, Barber BE, Yeo TW, Tan WW, William T. Case Report: Fatal *Plasmodium knowlesi* malaria following an atypical clinical presentation and delayed diagnosis. *Med J Malaysia* 2013; 68: 71-2.
2. Cox-Singh J, Davis TME, Lee KS, Shamsul SSG, Matusop A, Ratnam S, Rahman HA, Conway DJ, Singh B. *Plasmodium knowlesi* malaria in humans is widely distributed and potentially life threatening. *Clin. Infect. Dis* 2008; 46: 165-171.
3. Rajahram GS, Barber BE, William T, Menon J, Anstey NM, Yeo TW. Deaths due to *Plasmodium knowlesi* malaria in Sabah, Malaysia: association with reporting as *Plasmodium malariae* and delayed parenteral artesunate. *Malaria J* 2012, 11:284 doi:10.1186/1475-2875-11-284
4. Lokman H. Malaria trend in Malaysia 1995-2010 – Akademi Sains Malaysia. Akademisains.gov.my/download/tropical/Lokman.pdf
5. Garnham PCC. *Malaria Parasites and other Haemosporidia*. Oxford: Blackwell Scientific Publications, 1966.
6. Singh B, Kim Sung L, Matusop A, Radhakrishnan A, Shamsul SSG, Cox-Singh J, Thomas, AW, Conway D. A large focus of naturally acquired *Plasmodium knowlesi* infections in human beings. *Lancet*. 2004; 363: 1017-24.
7. Singh B, Daneshvar C. *Plasmodium knowlesi* malaria in Malaysia. *Med J Malaysia*. 2010; 65; 224-230.
8. Barber BE, William T, Jikal M, Jilip J, Dhararaj P, Menon J, Yeo TW, Anstey NM. *Plasmodium knowlesi* malaria in children. *Emerg Infect Dis* 2011; 17:814–820.
9. Barber BE, William T, Grigg MJ, Menon J, Auburn S, Marfurt J, Anstey NM, Yeo TW. A prospective comparative study of *knowlesi*, *falciparum* and *vivax* malaria in Sabah, Malaysia: high proportion with severe disease from *Plasmodium knowlesi* and *P. vivax* but no mortality with early referral and artesunate therapy. *Clin Inf Dis* 2013; 56:383-397.
10. World Health Organization. Meeting report of the informal consultation on the public health importance of *Plasmodium knowlesi*. World Health Organization Regional Office for the Western Pacific Press. Manila, Philippines. 2011
11. Vythilingam I, Noorazian YM, Huat TC, Jiram AI, Yusri YM, Azahari AH, NorParina I, NoorRain A, LokmanHakim S. *Plasmodium knowlesi* in humans, macaques and mosquitoes in Peninsular Malaysia. *Parasites Vectors* 2008; 1: 26.
12. Lee K-S, Divis PC, Zakaria SK, Matusop A, Julin RA, Conway DJ, Singh, B. *Plasmodium knowlesi*: reservoir hosts and tracking the emergence in humans and macaques. *PLoS Pathogens* 2011, 7: e1002015