

Naturally Acquired Human *Plasmodium cynomolgi* and *P. knowlesi* Infections, Malaysian Borneo

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To monitor the incidence of *Plasmodium knowlesi* infections and determine whether other simian malaria parasites are being transmitted to humans, we examined 1,047 blood samples from patients with malaria at Kapit Hospital in Kapit, Malaysia, during June 24, 2013–December 31, 2017. Using nested PCR assays, we found 845 (80.6%) patients had either *P. knowlesi* mono-infection (n = 815) or co-infection with other *Plasmodium* species (n = 30). We noted the annual number of these zoonotic infections increased greatly in 2017 (n = 284). We identified 6 patients, 17–65 years of age, with *P. cynomolgi* and *P. knowlesi* co-infections, confirmed by phylogenetic analyses of the *Plasmodium* cytochrome c oxidase subunit 1 gene sequences. *P. knowlesi* continues to be a public health concern in the Kapit Division of Sarawak, Malaysian Borneo. In addition, another simian malaria parasite, *P. cynomolgi*, also is an emerging cause of malaria in humans.

Plasmodium spp. were identified in the late 1800s, and ≥ 30 species have been described in primates, including humans, apes, and monkeys (1,2). Of these, humans are natural hosts to 4 species: *P. falciparum*, *P. malariae*, *P. vivax*, and *P. ovale*. Human infections with simian malaria parasites were thought to be extremely rare until *P. knowlesi* was identified as a major cause of malaria in humans in Kapit, Malaysian Borneo (3). Subsequent human cases of infection with *P. knowlesi* have been reported across Southeast Asia (4–9). Most cases are reported in the Malaysian Borneo states of Sarawak and Sabah (4,10,11). The zoonotic capability of this parasite was confirmed with the aid of molecular techniques because *P. knowlesi* is morphologically

similar to *P. malariae* (12). Molecular detection methods also were used to identify other zoonotic malaria parasites infecting humans, such as *P. simium* (13,14) and *P. brasilianum* (15) in South America and *P. cynomolgi* (16,17) in Southeast Asia.

After the large focus on human *P. knowlesi* infections in the Kapit Division of Sarawak state in 2004 (3), extended studies on wild long-tailed macaques (*Macaca fascicularis*) and pig-tailed macaques (*M. nemestrina*) in the area found these species harbor 6 simian malaria parasites: *P. inui*, *P. knowlesi*, *P. cynomolgi*, *P. coatneyi*, *P. fieldi*, and *P. simiovale* (12,18). Among 108 macaques examined, *P. inui* was the most prevalent parasite (82%), along with *P. knowlesi* (78%) and *P. cynomolgi* (56%). Besides *P. knowlesi*, 2 other simian parasites, *P. inui* and *P. cynomolgi*, have zoonotic capabilities that have been proven through accidental and experimental infections (1,19–21). *P. inui* was experimentally reported to infect humans in 1938, with a subsequent report in 1966 (20,21). *P. cynomolgi* was reported to infect humans during an accidental transmission in a laboratory in the United States in 1956 and later by experimental trials (1,19). A single infection of naturally acquired *P. cynomolgi* in a human was described in Peninsular Malaysia in 2014 (16) and was confirmed through molecular characterization.

Successful transmission of zoonotic malaria is highly dependent on the bionomics and distribution of competent vectors (22). After the 2004 report on human *P. knowlesi* cases in Kapit, *Anopheles latens* mosquitoes were incriminated as the only vector for *P. knowlesi* in the area and were found to harbor sporozoites of other species of simian malaria parasites (23). Because wild macaques in Kapit harbored potentially zoonotic malaria parasites and vectors were transmitting *P. knowlesi* to humans, we aimed to

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