A Naturally Acquired Quotidian-Type Malaria in Man Transferable to Monkeys

Abstract. *A quotidian-type parasite,* Plasmodium knowlesi, *has been found as a natural infection in man. The infection was acquired by a white male during a short visit to peninsular Malaysia. This occurrence constitutes the first proof that simian malaria is a true zoonosis.*

In 1960 the tertian-type simian parasite, *Plasmodium cynomolgi*, B strain (*1*), was accidentally transferred to man by mosquito bite (*2*). Shortly thereafter, other strains of the same species were shown to be infective to man by the same route (*3*). In 1963 the quartan-type parasite of New World monkeys, *P. brasilianum*, was also shown to be infective to man as a result of bites of infected mosquitoes (*4*). Until this present report, none of the simian malarias have been found as natural infections in man.

A 37-year-old white male, B.W., a surveyor for the U.S. Army Map Service, was admitted to the Clinical Center of the National Institutes of Health on 9 April 1965 with complaints of chills, fever, and sweating of several days' duration. His illness began 9 days prior to admission when he was in Bangkok, having returned from 4 weeks in Malaya. At this time he experienced anorexia, mild fatigue, and occasional nausea. Because his symptoms were not severe, he elected to return to the U.S. before seeking medical attention. Three days prior to his admission, the patient had arrived at Travis Air Force Base in California, where he experienced sore throat and shaking chills, associated with high fever and profuse sweating. He was seen by the base physician who treated him for an upper respiratory infection, whereupon he proceeded to his home in Silver Spring, Maryland. There he was seen by his private physician during a chill. Upon finding many ring-form parasites in a smear from the patient's peripheral blood, the physician made a tentative diagnosis of falciparum malaria. The patient was then referred to the Clinical Center at the National Institutes of Health, where the diagnosis of malaria was confirmed, but the infecting parasite was considered to be *Plasmodium malariae* rather than *P. falciparum*. Treatment was started on 10 April 1965 with the conventional regimen of chloroquine followed by primaquine. Prior to treatment, a parasitized blood sample was taken, refrigerated at 4°C, and forwarded to the Laboratory of Parasite Chemotherapy malaria project at the U.S. Penitentiary, Atlanta, Georgia. The blood was inoculated into a healthy Caucasian volunteer on 15 April 1965. Since then it has been serially subinoculated into six additional volunteers (five Caucasians and one Negro), and into rhesus monkeys from each of the first three volunteers. All of the volunteers and each of the monkeys readily became infected.

The salient features of the infection in man include an asexual cycle of approximately 24 hours, a quotidian fever pattern with temperatures as high as 104.8°F, and parasite counts as high as 20,850 per cubic millimeter of blood. The clinical manifestations were moderate to severe, with attacks terminating spontaneously after approximately 2 weeks. In three volunteers in which treatment was required, the parasite yielded readily to conventional antimalarial therapy.

The three rhesus monkeys, *Macaca mulatta*, which received parasitized blood from the volunteers, all died with overwhelming malaria infections within 5 to 7 days after the advent of patency. Virtually 100 percent of the red blood cells were parasitized just before death. No morphologic changes were apparent as a result of subpassage from man to monkey. By inoculating with sporozoites, the infection has been passed from man to monkey and from monkey to monkey each time with fatal results. The earliest prepatent period observed was 5 days. Other simians—the pig-tailed monkey (*M. nemestrina*), the long-tailed monkey (*M. irus*), the squirrel-monkey (*Saimiri sciurea*), and the gibbon (*Hylobates lar lar*)—were inoculated with parasitized blood and all except the gibbon became infected. The parasites were typical and none of the animals died as a result of the infection.

On the basis of its morphology, quotidian periodicity, and pronounced infectiousness to rhesus monkeys, the parasite has been identified as *Plasmodium knowlesi* Sinton and Mulligan, 1933.

This report of a naturally acquired malaria infection in man transferable to monkeys represents the first proof that simian malaria is a *true zoonosis*. The fact that humans can become infected with simian malaria in nature is of special significance at this time because of its possible importance to the program of worldwide malaria eradication.

WILLIAM CHIN*
PETER G. CONTACOS†
G. ROBERT COATNEY
HARRY R. KIMBALL
National Institute of Allergy and Infectious Diseases, Bethesda, Maryland 20014

References and Notes

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* Present address: Malaria Project, U.S. Penitentiary, Atlanta, Georgia.
† Present address: Cytology Section, LPC, P.O. Box 190, Chamblee, Georgia.

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Crown-Gall Tumorigenesis: Effect of Temperature on Wound Healing and Conditioning

Abstract. *Temperatures which inhibit crown-gall tumorigenesis in* Kalanchoë daigremontiana *plants also accelerate the rate of wound healing and the rate at which cells in the wound area become competent to react to the tumorigenic stimulus. The concept that the "tumor-inducing principle" is thermolabile and of high molecular weight may be invalid since it is based in part on the lack of effect of temperature on wound healing and conditioning. The rate of division of host cells may determine the success of crown-gall tumorigenesis.*

Crown-gall tumors are formed when a susceptible host plant is wounded, and the wound is infected with a virulent strain of *Agrobacterium tumefaciens* (Conn). Although the agent responsible for the tumorous change in