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MALARIA AS A ZOONOSIS
(Addendum)

by

Dr L. J. Bruce-Chwatt, Chief
Research and Technical Intelligence
Division of Malaria Eradication
World Health Organization, Geneva

The paper under the above title released in the WHO/Zoon and WHO/Mal series of cyclostyled documents was intended to summarize as briefly as possible the up-to-date information on problems of simian malaria related to both malariology and comparative medicine.

In the attempt at concise presentation some points of undoubted importance were omitted and a few recent developments were not included.

The following additional remarks may fill some of the more obvious gaps in the over-all picture of a field of research developing so rapidly that its annual reviews may soon become necessary.

1. Malaria in anthropoid apes

1.1 In addition to *P. hylobati* exhibiting quartan periodicity, found in a gibbon (Hylobates sp.) from Java and described by Rodhain (1941), three other plasmodia have recently been isolated from Malayan gibbons. They are as follows:

P. youngi (Eyles et al., 1964)

P. eylesi (Warren et al., 1965)

P. jefferyi (Warren et al., 1966)

While P. youngi and P. eylesi show an undoubted tertian periodicity, the tertian periodicity of P. jefferyi is less certain and there is the possibility that it is quotidian. The schizogony of this parasite takes place mainly in the internal organs and mature asexual forms are very rare in the peripheral orientation (Warren et al., 1966)

2. Malaria parasites of lower monkeys

2.1 P. cynomolgi was originally described by Mayer in 1907 and redescribed by Mulligan in 1935. A subspecies of P. cynomolgi was described by Garnham in 1959 and given the name bastianellii. Following a study by Warren (1963), Bennett et al. (1966a) have recently shown that there are several morphologically similar but biologically different forms of P. cynomolgi sensu lato.

It is recognized today that P. cynomolgi is a species complex which comprises the following forms variously designated as species, subspecies or strains (Garnham, 1966).

Name	Area	Host
P. cynomolgi cynomolgi	Malaya	M. irus, M. nemestrina
P. cynomolgi bastianellii	Malaya	M. irus
P. cynomolgi (Gomba strain)	Malaya	M. irus
P. cynomolgi (langur strain)	Malaya	Presbytis cristatus
P. cynomolgi cyclopis	Taiwan	M. cyclopis
P. cynomolgi (Cambodia strain)	Cambodia	M. irus
P. cynomolgi ceylonensis	South India	M. sinica M. radiata
P. cynomolgi (langur strain)	Ceylon	P. entellus

2.2 A brave attempt at recovering strains of simian malaria parasites from a selected sample of a population living in an area of Malaysia, where natural transmission of plasmodia between the human and simian hosts is very likely, was made recently by Warren (in print) and reported at the Annual Meeting of the American Society of Tropical Medicine and Hygiene (Puerto Rico, November 1966). A natural transmission of P. knowlesi briefly reported by Chin et al. (1965) took place probably in the area of Malaya where A. letifer and A. leucosphyrus introlatus (jungle mosquitos) bite man and monkeys more or less indiscriminately and where it may be a common vector. Blood samples collected from nearly 1200 people in this area were inoculated into rhesus monkeys and no simian parasites were recovered (Warren et al., in print).

2.3 The evolution of P. cynomolgi infection in various species of lower monkeys has been carefully studied by Rossan & Schmidt (in print) by inoculation of sporozoites of infected A. freeborni or by blood infection. The differences in response were striking and this opens a new chapter in the study of the host-parasite relationship in primate malaria.

2.4 The asexual cycle of P. knowlesi has been recently studied by Hawking (1966). This study revealed that the parasites come to schizogony at approximately the same time and that this depends on factors related to the circadian rhythm of the host. The infectivity of this plasmodium to A. stephensi follows a 48-hour cycle and seems to be synchronized with the nocturnal feeding time of the vector. Continuous antigenic variation occurs in chronic P. knowlesi infections according to Brown & Brown (1965).

3. Infection of man by simian plasmodia

3.1 Following the first report on the transmission of P. cynomolgi to man (Eyles, 1960), other forms of this species complex were transmitted by Coatney et al. (1961), Schmidt et al. (1961) and Bennett & Warren (1965).

The latter authors isolated a strain of P. cynomolgi from Macaca irus from Cambodia and transmitted it to man by bites of A. maculatus. The infection was transmitted back to monkey by inoculation of parasitized blood.

3.2 Contacos et al. (1963) transmitted P. brazilianum (a quartan type of malaria parasites of New World monkeys) to man by bites of infected mosquitos. Although blood transmission of P. inui to man was reported some 30 years ago by Dasgupta (1938) the mosquito transmission of P. inui to man has been described only recently (Coatney et al., 1966). This quartan parasite of Old World monkeys was transmitted to two human volunteers by bites of infected A. stephensi and A. maculatus and to three volunteers by blood inoculation. A quartan fever pattern lasting for about three to four weeks was well marked in two volunteers. Their parasitized blood when injected into clean rhesus monkeys produced typical infections.

3.3 P. knowlesi the quotidian parasite of monkeys described by Sinton & Mulligan in 1933 has been used for malariatherapy by blood transmission. A successful transmission of this parasite to monkeys by inoculation of sporozoites from experimentally infected A. stephensi was obtained by Hawking & Mellanby in 1953 and by Hawking and his colleagues in 1957. A case of natural infection of man by P. knowlesi in Malaya was reported by Chin et al. (1965). Since then new studies were carried out by the group at the N.I.H. Laboratory of Parasite Chemotherapy at Chamblee, Georgia using human volunteers. A successful transmission of the H strain of P. knowlesi to man and back to monkey was obtained through A. balabacensis balabacensis. The full report is now in print.

3.4 A report on the transfer of P. falciparum to the Panamanian marmoset Saguinus geoffroyi has been presented by Young & Porter at the 1966 annual meeting of the American Society of Tropical Medicine and Hygiene in Puerto Rico.

4. Entomological aspects of transmission of simian malaria

Following on the previous studies of Warren (1963), Bennett et al. (1966b) have recently shown in a series of papers that the morphologically similar but biologically different forms of the P. cynomolgi complex may be recognized by the pattern of their sporogonic development in certain Anopheles species. Detailed study of the sporogony of five forms of the P. cynomolgi complex from south-east Asia

in A. maculatus, A. kochi and A. vagus revealed characteristic differences in the average size of the mature oocyst and in the time required for sporozoites to reach the salivary glands. These differences may be used as additional elements for better systematics of this species complex of plasmodia of primates.

5. Immunological studies on primate malaria

The staining of P. cynomolgi bastianellii parasites using the fluorescent antibody technique was carried out by Ingram (1961) and cross reaction studies between monkey and human plasmodia were reported by Tobie et al. (1962), Voller (1962), Voller & Bray (1962) and more recently by Collins et al. (1965, 1966).

Labelled P. vivax antibody was tested against P. vivax and P. cynomolgi bastianellii, P. "osmaniae" and P. gonderi. There was also a high level of cross reactivity between the antigen of P. cynomolgi bastianellii and sera of subjects from highly endemic malarious areas (Kuvin & Voller, 1963). Collins et al. (1966) tested nearly 100 sera from Malaysian and Indian monkeys against six species of simian plasmodia and over 50% of these monkeys has positive fluorescent antibody tests with the highest number of reactions against P. fieldi and P. gonderi. The results indicate either a prior malaria infection or the presence of a non-specific antibody but command some caution in using non-tested imported monkeys for studies of the host-parasite relationship of primate malaria. Recently Collins et al. (1966) tested the antisera from monkeys infected with P. inui, P. shortti, P. brazilianum, P. fieldi, P. cynomolgi, P. coatneyi, P. gonderi, P. knowlesi and what was probably P. fragile against 10 homologous and heterologous antigens.

The quartan group (P. inui, P. shortti, P. brazilianum) showed differences in their reactivity from the "tertian" group (P. fieldi, P. cynomolgi, P. coatneyi, P. gonderi and "P. fragile"). P. knowlesi differed slightly from the other groups but all the species showed some cross reaction with any of the other species. All of them gave a high level of heterologous reaction against P. fieldi antigen.

6. Corrigenda to WHO/Zoon/66.90 and WHO/Mal/66.578

6.1 On page 4 in the table of plasmodia in anthropoid apes the last row of the fifth column should read P. (L) falciparum.

6.2 Page 9, last paragraph, fourth line, read: Serial transmission through A. albimanus was successful and P. vivax has been thus transmitted from man to monkey to man (Young & Porter, in press).

6.3 Table 1, third column, first paragraph: for "P. cutellus" read P. entellus.

6.4 Page 9, last paragraph, last sentence should read: It also appears that P. vivax has been transmitted by blood infection to the Brazilian squirrel monkey (Saimiri seiureus) according to Deane et al. (in print).

6.5 Page 11, first paragraph, last sentence (This information . . . Table 1) to be omitted.

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