

Reports

Natural Occurrence of Malaria in Rhesus Monkeys

Abstract. A relatively high incidence of malarial infections has been noted in recent importations of rhesus monkeys from Pakistan. This finding, contraverting the widely held belief that rhesus monkeys are free of natively acquired malaria, is of substantial significance to those employing Pakistani rhesus monkeys in their investigations.

This laboratory has pursued studies on the biology and therapy of primate malarias since 1945. Between this date and July 1960, some 5600 rhesus monkeys (*Macaca mulatta*) have been used in these investigations without evidence of the natural occurrence of malaria in any subject. In July 1960, one animal imported in December 1959 was found to be infected. With unwavering conviction that rhesus monkeys are not natively infected, we attributed the disease in this subject to an undefined "laboratory accident." Events of the past 2 months have made it necessary to re-evaluate this conclusion.

On 19 October 1960, 100 monkeys recently imported from Pakistan were introduced into the colony for conditioning purposes. In January 1961, prior to initiation of a malaria experiment, thick blood films were prepared on 79 of these animals, stained with Giemsa, and examined for the presence of blood parasites—a routine practice despite years of negative results. To our amazement, seven of these stock animals had positive thick films. This finding led immediately to examination of the animals of three later shipments, also imported from Pakistan. This resulted

in findings of positive films for 13 of 65 animals imported on 23 November 1960, for one of 55 of a 15 December shipment, and for one of 29 in a 22 December shipment. In all, 22 of 228 monkeys from these four shipments were found to be naturally infected. The density of infection ranged from one to two parasites per entire thick film to 2×10^7 parasites per milliliter of blood. In the majority of subjects a single plasmodium appeared to be involved. In two cases there were evidences of multiple infections.

Identification of the plasmodial species is still in progress. Data acquired to date from thin-film studies, both on monkeys with naturally acquired infections and on others in whom disease was induced through inoculation of infected blood, suggest that the parasite found in the majority of cases is the morphologic counterpart of our stock strains of *Plasmodium inui*. In the two cases suggestive of multiple infections, a plasmodium morphologically similar to *P. cynomolgi* also appears to be involved. In both natural and induced infections the disease appears to follow a rather benign course. In the induced disease the parasitemia is intensified by splenectomy.

The observations reported here (1) are at variance with the widely held belief that the rhesus monkey is free of malaria in its native habitat. This belief cannot be dismissed lightly, since it is supported by some 30 years of careful study by investigators who have employed the rhesus monkey in work on the biology and therapy of simian malarias. It appears likely to us that the conflict between findings in earlier investigations, in which we participated, and the current observations is related to the area from which the animals were obtained. For many years the great majority of rhesus monkeys have come from areas adjacent to Lucknow. Monkeys in recent shipments from this region, like those of shipments in former years, have been free of malaria. On the other hand, the infected animals originated in East Pakistan, having been exported from Dacca. Although there is no absolute certainty in this matter, it is possible that they were

obtained near the Burma-Assam border. If this is the case, the animals could have been in contact with *Macaca cynomolgus* or *M. nemestrina*, simian subjects frequently infected with *Plasmodium knowlesi*, *P. cynomolgi*, or *P. inui*. It is not too difficult to believe that the same vectors which transmit these plasmodia to the crab-eating and pig-tailed macaques could also transmit them to the rhesus monkey. There is evidence in the old literature on malaria that such an event does occur. Thus, in 1911, Mathis and Leger (2) found quartan infections (probably *P. inui*) in five of 40 rhesus monkeys collected in Tonkin. *Plasmodium inui* infections of *M. cynomolgus* are relatively common in this area.

The importance of these observations on the natural occurrence of malaria in Pakistani rhesus monkeys to investigators of plasmodial diseases needs no comment. It is equally apparent that workers employing rhesus monkeys in other investigations should be alert to the existence and potential liabilities of concurrent malarial infections.

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Reference and Note

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2. C. Mathis and M. Leger, *Ann. inst. Pasteur* 25, 593 (1911).

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Stimulus Generalization of Conditioned Suppression

Abstract. A tone ending in unavoidable electric shock was periodically presented to pigeons while they pecked a key for food. When pecking was completely disrupted by tone, shock was disconnected, and the training tone and tones having new frequencies were presented. Initially the gradient of generalization was broad; as testing proceeded, however, the gradient narrowed severely.

When a stimulus has typically preceded a noxious event, subsequent presentation of that stimulus will often cause a reduction in the frequency of ongoing responses. This reduction is referred to as conditioned suppression. In the present research we sought to investigate the degree to which conditioned suppression could be mediated by stimuli which were like, but not identical to, the stimulus that was used in the original training. This latter phenomenon, the stimulus generalization of conditioned suppression, is of particular importance, for it represents

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Type manuscripts double-spaced and submit one ribbon copy and one carbon copy.

Limit the report proper to the equivalent of 1200 words. This space includes that occupied by illustrative material as well as by the references and notes.

Limit illustrative material to one 2-column figure (that is, a figure whose width equals two columns of text) or to one 2-column table or to two 1-column illustrations, which may consist of two figures or two tables or one of each.

For further details see "Suggestions to Contributors" [*Science* 125, 16 (1957)].