

## TRANSMISSION OF *P. INUI* TO MAN.

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(*Read at Symposium, August 27-28, 1937.*)

### INTRODUCTION.

Blacklock and Adler (1922) observed malaria parasites in the blood of a chimpanzee in West Africa, some of which resembled *P. vivax*, some the band forms of *P. malariae*, and some the crescentic gametocytes of *P. falciparum*. Attempts were made to transmit this infection to man both by blood inoculation and by mosquito-bite (*A. costalis*), but neither method proved successful.

Berenberg-Gossler (1909), and Gonder and Rodenwalt (1910) failed to infect man with a similar plasmodium subsequently classified by Sinton and Mulligan (1933) as *P. inui* var. *gonderi*. Attempts to transmit *P. brasilianum* to man were made by Clark and Dunn (1931), but it is doubtful whether these were successful. The first undoubted infection in man with a species of monkey plasmodium was obtained by Knowles and Das Gupta (1932) with *P. knowlesi*, when 3 human volunteers were infected with this parasite. In these cases, the incubation period varied from 7 to 20 days and fever lasting about a week was observed in each case. Parasites usually appeared 1 or 2 days before febrile symptoms were observed and they persisted in the blood for some time after the disappearance of fever. Although the body temperature sometime rose above 104°F. the number of parasites in the blood was never high. In all three cases recovery was spontaneous. These observations were later confirmed by Nicol (1935), by Cinca *et al.* (1935), and by Van Rooyen and Pile (1935).

### MATERIAL AND METHODS EMPLOYED.

The strain of *P. inui* used for the present experiment was received in November, 1935 through the courtesy of Lt.-Col. J. A. Sinton, I.M.S., then Director, Malaria Survey of India. This strain has since been maintained by passage through a series of four monkeys of which the first three were *S. rhesus* and the fourth *S. irus*. In order to exclude the possibility of a latent malarial infection in the latter monkey, repeated and exhaustive blood examinations were made and the results were consistently negative. In addition, 2 cc. of blood from this monkey were inoculated into a specimen of *S. rhesus* but no malarial infection subsequently developed in the latter animal. There is a strong probability, therefore, that this specimen of *S. irus* was free from natural

malarial infection. When, however, it was inoculated with *P. inui*, parasites appeared in the peripheral blood 9 days after inoculation, and a low grade infection with typical *P. inui* parasites developed.

Since it was found by Knowles and Das Gupta (1932) that a large dose of parasites was required to ensure successful transmission of *P. knowlesi* to man, it was considered desirable in the present experiment to inoculate as many *P. inui* parasites as possible. The specimen of *S. irus* which was selected as the donor animal for this experiment showed only a scanty infection and it was thought desirable to increase the prevalence of parasites by splenectomising this animal. On the third day after splenectomy about 32 per cent of the red cells were infected and the monkey was obviously ill. It was accordingly anaesthetised and 6 cc. of blood were obtained by cardiac puncture. This was defibrinated and injected intramuscularly into the human volunteer. The latter was in good health apart from a scaly skin affection of the forearms and wrists. This individual had been experimentally infected with *Spirillum minus* about eight months previously in order to determine whether there was any acquired tolerance to re-infection in rat-bite fever. With the exception of some febrile attacks induced by the inoculation with *Spirillum minus*, the volunteer gave no history of fever for several years previously.

#### RESULTS.

Twenty-three days after inoculation with *P. inui* from the splenectomised *S. irus* very scanty parasites were detected in the blood of the human volunteer. The number of parasites increased slightly during the seven days that followed and the forms encountered were rings, trophozoites and very scanty schizonts. Gametocytes were not seen at any stage of the infection. On the 28th day after inoculation the patient's temperature began to rise, but febrile symptoms were present only for three days and the maximum temperature observed was 102°F. On the 29th day after inoculation 5 cc. of the human volunteer's blood were injected intravenously into a young specimen of *S. rhesus*. A scanty infection with typical forms of *P. inui* developed in the latter animal on the eighth day after inoculation. This infection also remained a low grade one up to the time of writing (22nd day after inoculation) during which period no clinical symptoms had been observed in this animal. Owing to the small number of parasites available for study in this monkey it has not been possible to determine the duration of the schizogony cycle accurately.

#### DISCUSSION.

In the writer's opinion there can be little doubt that the infection produced in the human volunteer was one with a pure strain of *P. inui*. This is borne out by the fact that the infection appeared within a reasonable incubation period, that the morphology of the parasite was typical of a pure infection with *P. inui*, and that when the infection was subsequently passed to a clean

specimen of *S. rhesus* the resultant infection was in every way typical of *P. inui* infection in this species of monkey.

There are, however, certain other possibilities which must be excluded. These include: (1) the possibility that the human volunteer had a latent malarial infection which flared up as the result of inoculation of monkey blood, (ii) that the volunteer contracted a fresh infection with a species of human plasmodium while in hospital, (iii) that the blood of the donor monkey was infected with both *P. inui* and *P. knowlesi* and that the infection which developed in the human volunteer was one with *P. knowlesi* which, as has previously been shown, is transmissible to man.

(i) It appears to the writer that the possibility of a latent infection in the human volunteer is extremely unlikely. This individual gave no history of previous malarial attacks, his blood was repeatedly negative before the monkey blood was inoculated and, if a latent infection had flared up by the injection of fresh blood, it would be expected that this would have made its appearance early in the 23-day period which elapsed before parasites were detected. The infection was morphologically identical with *P. inui* and since it was subsequently shown to be infective to *S. rhesus*, the probability is that it was not a human species of plasmodium. So far as is known, it is doubtful whether *S. rhesus* is susceptible to infection with any of the human species of plasmodium. Apart from the observation of Taliaferro and Taliaferro (1934) who produced an infection with *P. falciparum* in young howler monkeys, and the unconfirmed observation of Mesnil and Robaud (1920) who attempted to infect apes with human malaria, all other attempts to transmit human malarial infections to simian hosts have failed.

(ii) The possibility that the human volunteer contracted a fresh infection while in hospital is extremely unlikely, because malaria transmission in Calcutta at this season of the year is rarely known to occur.

(iii) There is no reason to believe that the donor monkey (*S. irus*) was suffering from a mixed infection with *P. inui* and *P. knowlesi*. Against this possibility is the fact that after splenectomy the parasitic infection in the donor animal was sufficiently intense to allow of the detection of *P. knowlesi* on morphological grounds.

In view of the fact that a clean specimen of *S. rhesus* was inoculated with the blood of the human volunteer at the time when the infection in the latter was at its height, and that this animal subsequently developed a malarial infection which both clinically and morphologically was in every respect similar to the usual type of *P. inui* infection in *S. rhesus*, there is, in the writer's opinion, little or no doubt that the infection produced in the human volunteer was one with a pure strain of *P. inui*.

The absence of gametocytes throughout the whole course of the infection in the blood of the human volunteer is an interesting observation. This may perhaps be explained by the fact that the degree of natural resistance to *P. inui* by the human host is sufficiently high to prevent the formation of

gametocytes. It is well known from epidemiological studies that the number of gametocytes in any given community or individual is in inverse proportion to the degree of immunity present.

#### SUMMARY.

*P. inui*, a quartan parasite occurring as a natural infection in *S. irus*, has been successfully transmitted to a human volunteer in whose blood the parasites appeared 23 days after inoculation and in which the infection persisted for one week. The number of parasites observed in the blood of the volunteer was never high and recovery was spontaneous. Febrile symptoms were observed for three days only. The parasites encountered were rings, trophozoites, and schizonts. Gametocytes were never encountered.

The writer wishes to express his gratitude to Lt.-Col. J. A. Sinton, I.M.S., for his kindness in supplying the strain of *P. inui* used in this experiment.

His thanks are also due to Major H. W. Mulligan, I.M.S., for kindly going through this manuscript and making some valuable suggestions.

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