

## MALARIAL INFECTION IN THE PLACENTA AND TRANSMISSION TO THE FŒTUS

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DR. C. STRICKLAND kindly gave the writer a blood film which was taken from a 15-hour old baby of a mother who had been suffering from *Plasmodium vivax* infection during pregnancy. The smear showed a large number of parasites (benign tertian) in various stages of development, from the ring stage up to maturity, including some aberrant forms. This finding has

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proportions. The evidence in support of the value of active immunization of those susceptible is so strong that there can be no reasonable doubt as to its effectiveness in protecting an individual against diphtheria.

### Summary

(1) A series of 241 residents in Calcutta have been tested for susceptibility or immunity to diphtheria by the Schick test; 91 or 37.8 per cent of these were Schick-positive reactors.

(2) Of the 137 Anglo-Indians tested 49.6 per cent possessed no immunity to diphtheria whereas of the 104 Indians tested 22.1 per cent were non-immune. The greater immunity amongst the Indians is better seen in the different age groups. It is suggested that the differences in immunity seen in Indians and Anglo-Indians is not based on racial peculiarities but on differences in environmental conditions.

(3) The importance of Schick test followed by active immunization of susceptible nurses and other staff of fever hospitals or diphtheria wards, where risk of infection is unusually high, is stressed. That there is a need for this is shown by the finding of a high percentage (39 per cent) of nurses who possessed no natural antitoxic immunity to diphtheria.

(4) Schick-test toxin can be imported without any loss of potency either in a cooled thermos flask by air mail or in cool storage by steamer. It can be stored in any domestic type of refrigerator without showing deterioration. The test itself is so simple to perform and economical of time as to permit of its widespread application to large samples of the population in different parts of India.

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already been reported (Das Gupta, 1939). The occurrence of mature schizonts in the blood of the infant 15 hours after birth proves beyond doubt that the infection was acquired *in utero* at least 33 hours before birth.

It is now generally believed that, although a rare condition, congenital malaria does occur when there is failure of the protective effect of the placenta. The protective action fails when there is any injury (during pregnancy) resulting in placental hæmorrhage. Dr. Baird, who was in charge of the patient mentioned above, informed the writer that the mother gave no history of even slight injury at any time during pregnancy.

With a view to studying the effect of malarial infection on pregnant monkeys with reference to the possibility of transmission to the fœtus, we inoculated a pregnant *rhesus* monkey with *Plasmodium knowlesi*, a species of simian malaria parasites that produces a very virulent infection in *rhesus* monkeys, causing the death of the animal if prompt treatment is not accorded.

### Experimental

A recently trapped well-nourished specimen of *Silenus rhesus* weighing 11 kilogrammes was purchased from a local dealer. The animal was in advanced stage of pregnancy as verified by skiagraphy. It was inoculated intravenously with 0.5 c.cm. of monkey's blood showing a heavy infection with *P. knowlesi*.

Six days (usual incubation period) later, its blood was examined daily for eight days. As there was no evidence of infection, it was re-inoculated with approximately four times the original dose. On the third day of the second inoculation, scanty ring forms were detected in the thick film. Gradually the parasite count increased and the animal became more and more anæmic. On the ninth day, it became severely ill, unable to sit up and refused all food. Quite a number of parasites, chiefly developing schizonts, and pigmented mononuclears were found in the blood smears. The red cell count fell to 1,600,000 per c.mm. Other evidence of anæmia such as punctate basophilia, anisocytosis, polychromasia were present. Lest the animal should not survive till the next morning, it was chloroformed at 5 o'clock in the afternoon and complete autopsy was done. The maternal organs gave evidence of acute malarial infection. The endothelial cells of the spleen and liver were found packed with large masses of pigment. The fetal blood was rich in hæmoglobin. The red cell count was high (8,200,000 per c.mm.) as compared with that of the newly-born human baby. There were a good number of nucleated red cells. Anisocytosis was marked. Smears of the spleen, liver and bone marrow of the fœtus were carefully examined. Neither parasites nor hæmozoin pigment was found.

*Placenta.*—Smears prepared with the tissue snipped off the maternal surface shows a

stupendous number of parasites in different stages of schizogony and a good number of macrophages with ingested parasites and pigment. No gametocytes are seen. In sections the intervillous space is found packed with parasitized red cells and some pigmented phagocytes, the number of the infected red cells being estimated at more than 95 per cent, while the vessels of the chorionic villi are entirely free from infection.

*Comment.*—Although some observers have noted that congenital malaria is a common occurrence in localities where the disease is endemic; for example, Ziemann records that Weselko (Mense, 1924) in Albania attributed to congenital malaria the death in the first week of 144 children of mothers infected with *Plasmodium falciparum*. Swellengrebel (1925) records 48 cases of congenital malaria in the Near East in each of which a microscopical diagnosis was made at periods varying in time from one to five days, yet the trend of current opinion is to accept the view that the transmission of malaria from the mother to the foetus is an unusual phenomenon. This opinion has been particularly emphasized by Blacklock and Gordon (1925). These workers after a study of a large series of cases have concluded that transplacental infection of the foetus is of great rarity and may be acquired when there is a failure of the barrier action of the placenta. Lately, Garnham (1938) investigated over 400 cases to see if congenital malaria occurred. In no case could placental transmission of the malaria parasite be detected. The tremendous infection of the maternal organs especially the intervillous spaces of the placenta in the experimental monkey (plate XII, fig. 3, and plate XIII) and the total absence of the parasites or any evidence of infection in the foetus (plate XII, fig. 4) show very clearly that the protective function of the placenta is very efficient. This finding is in complete agreement with the observation of Blacklock and Gordon (1925). The protective effect of the placenta sometimes however fails, allowing the parasites to pass through and produce an infection of the offspring. This failure on the part of the placenta has been attributed to injury resulting in placental hæmorrhage, by Clark (1915), Jean (1927) and Thonnard-Neumann (1931) and others. To the present writer it seems rather more likely that the efficiency of the placenta with regard to its protective action is interfered with as a result of damage caused by prolonged parasitic invasion.

Dr. Baird's case, referred to above, may be cited as an example of the failure of the protective action of the placenta as a result of chronic infection. The patient was suffering off and on from fever (malaria) during the entire period of pregnancy with no history of injury.

That duration of infection and not so much the intensity plays an important part is also

borne out by the following facts. While investigating the possibility of placental transmission of leptospira in guinea-pigs it was often noticed that if the infected mother died at a very early stage of the disease the foetus invariably escaped infection; that if it lived a few days more very scanty foetal infection could be demonstrated by the inoculation of the foetal tissues (liver and kidneys) into young guinea-pigs, the smears of these organs being usually negative; that should the animal survive still longer, leptospiræ in fair number were found present in the sections of the liver and kidneys of the foetus. It thus follows that the longer the infected mother survived, the greater was the chance of the infection of the foetus, although the placenta showed an extraordinarily heavy infection even during the early stage of the disease. Furthermore, it has been shown that syphilis is not transmissible to the offspring if the mother acquires the infection during the last few weeks of pregnancy.

It is remarkable that the viscera of the foetus were full of blood, in marked contrast to the great anæmia of the maternal organs. Although there were a fair number of parasites in the peripheral blood, the placental sinuses were crammed with parasitized red cells. The localization of the parasites in these situations was first pointed out by Clark (1915) and later noted by Blacklock and Gordon (1925) and others, and is probably the result of partial stasis in the sinuses.

#### Summary

An experimental infection in a pregnant rhesus monkey with *P. knowlesi* was studied from the view-point of the possibility of the intra-uterine infection of the foetus. It is noted that the foetus is entirely free from parasitic invasion even when the maternal sinuses of the placenta are crammed with parasitized red cells, more than 95 per cent of the cells being infected. The blood of the mother shows extreme anæmia as a result of terrific blood destruction owing to massive infection with the parasite, in marked contrast to the florid blood of the foetus.

It is suggested that the duration of infection and not so much the acuteness is responsible for the failure of the protective function of the placenta.

I wish to express my indebtedness to Dr. C. M. Wenyon, F.R.S., who very kindly examined the materials on which these observations are based and drew my attention to the work of Garnham in this connection. I am also grateful to Professor C. Strickland for his helpful suggestions.

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PLATE XII

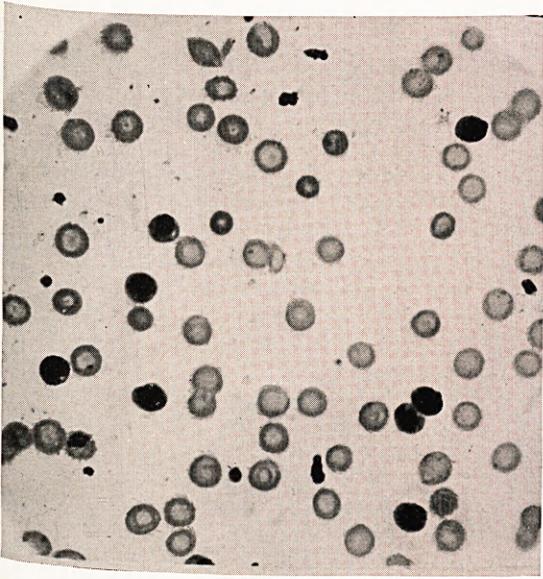


Fig. 1.—Maternal blood smear (stained with combined Leishman and Giemsa's stains). Fair number of parasites present.  
(Photomicrograph  $\times 580$  approx.).



Fig. 3.—Section of placenta (stained with Mallory's iron-haematoxylin and eosin) shows that the intervillous space (a) is packed with infected red cells, while the cells in a blood vessel of a chorionic villus (b) is entirely free from infection.  
(Photomicrograph  $\times 580$  approx.).

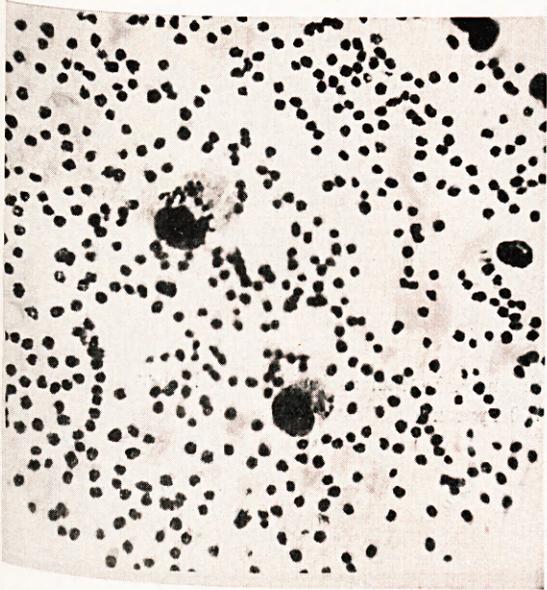


Fig. 2.—Smear of tissue snipped from the maternal surface of the placenta (Giemsa's stain), showing innumerable parasites (growing trophozoites and early schizonts) and some pigmented phagocytes. Most of the parasite-containing red cells are hemolysed.  
(Photomicrograph  $\times 580$  approx.).

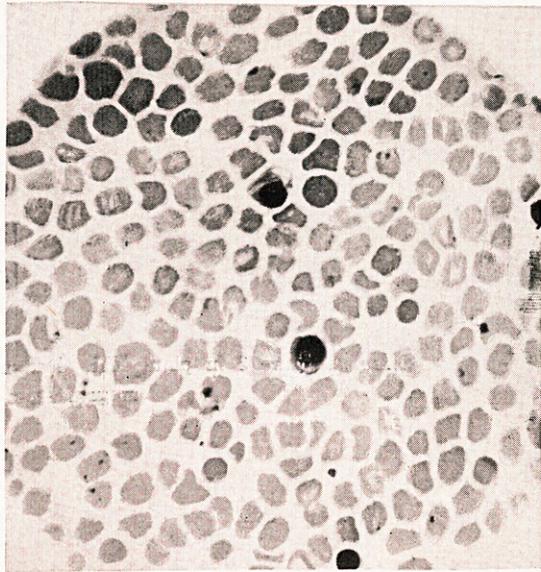
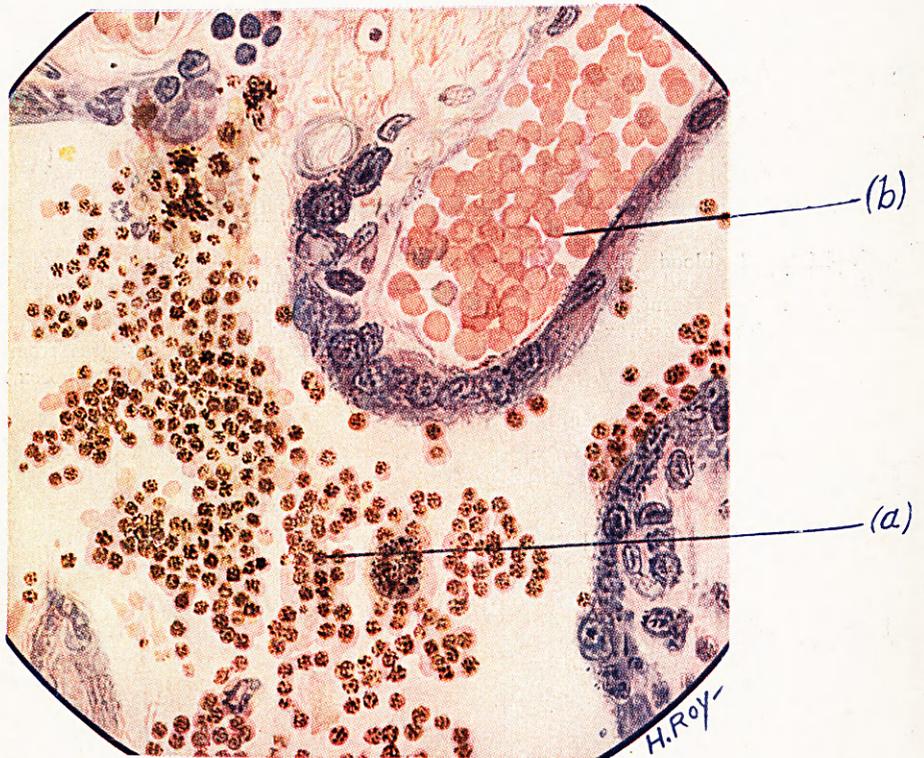


Fig. 4.—Smear of heart blood of the fetus (Giemsa's stain). No parasite or any evidence of malarial infection is present. Nucleated red cells and anisocytosis characteristic of embryonic blood are seen.  
(Photomicrograph  $\times 580$  approx.).

PLATE XIII



Same as figure 3 in plate XII. Drawn with an Abbe camera lucida at a higher magnification ( $\times 790$  approx.).

AN ABDOMINAL TUMOUR CAUSED BY  
*GNATHOSTOMA SPINIGERUM* (OWEN,  
1836)

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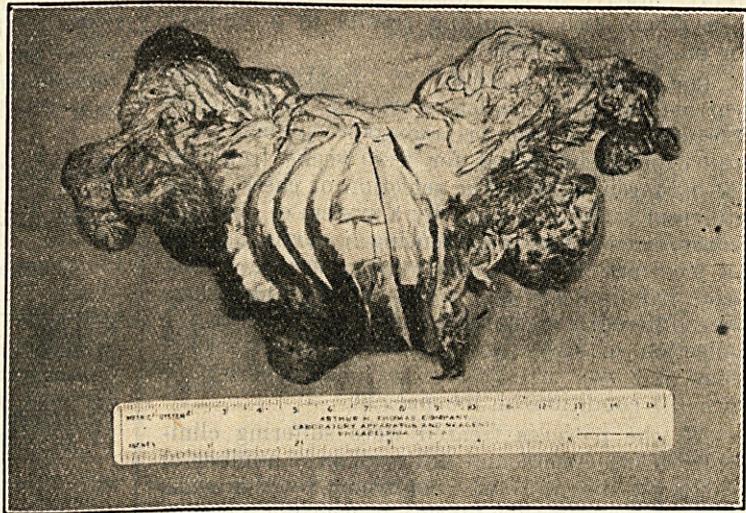
A TUMOUR and a small living round worm were removed by a surgeon from the abdominal cavity of a Siamese female, aged 27, with symptoms of intestinal obstruction and were sent to the Department of Pathology for diagnosis. The pathological examination of the tumour and morphology of the parasite are recorded as follows:—

**Macroscopic description.**—The specimen consisted of an irregular reddish-yellow firm tumour and a living round worm. The tumour measured 7.0 × 6.5 × 3.0 cm. and was situated in the great omentum below the greater curvature of the stomach. It was apparently covered with smooth dull-looking peritoneum and at one place was overlaid by a few dark-red blood clots. On serial section it was found to be composed of greyish moist firm shiny tissue marked with many small, scattered, yellow, opaque areas and it contained a long distorted channel with the diameter about the size of a pin's head. This channel was filled with brownish turbid exudates and opened to the external surface of the tumour. A few small old hæmorrhagic areas were also observed in the tissue near this channel.

**Microscopic examination of the tumour.**—The hæmatoxylin-eosin stained sections of the specimen were made up mainly of œdematous cellular-adipose fibrous tissue which was very extensively infiltrated with eosinophiles and some large and small mononuclear cells. In some sections there were a few small irregular spaces filled with degenerated and necrotic leucocytic exudates. The tissue about these spaces was necrotic and more heavily infiltrated with eosinophiles and polymorphonuclear leucocytes.

These channels looked like small abscesses. One edge of the section studied was covered with a thick layer of hæmorrhagic exudate.

**Description of the worm.**—After careful examination, the worm was identified as an immature female *Gnathostoma spinigerum* having the following structure:—It measures, after fixation, 10.80 mm. in length and 1.04 mm. in width. The anterior end is provided with a pair of trilobate lips and a cephalic bulb which measured 0.36 mm. long and 0.58 mm. wide and is furnished with eight rows of single-pointed spines pointing posteriorly. The eighth row is still in a rudimentary stage. The body is separated from the cephalic bulb by a definite constriction and is transversely striated. The anterior two-thirds of the body are covered with tridentate and simple spines and the remaining posterior third shows none of them. The posterior end of the worm is more or less pointed. The alimentary system consists of a muscular œsophagus which measured 2.6 mm. in length, and an intestine. The latter contains a great amount of dark-red blood and opens into the subterminal anus. The vulva opens on one side of the body at the anterior part of the posterior



half of the worm. A great number of presumably young unfertilized ova are also observed in the bipartite uterus which is coiled up and down inside the body.

Unquestionably, the tumour thus described was formed as the result of the infestation by this worm. It is also interesting to note that to the best of my knowledge this is the first human case of an intraperitoneal tumour caused by *Gnathostoma spinigerum* reported in the literature.

The writer wishes to thank Dr. C. Prommas, head of the Department of Pathology, for his valuable aid and suggestions and is indebted to Dr. Khun Ketudasma for the photography.

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