typical acute porphyric episode and two others had had unexplained abdominal colics.

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Preliminary Communications

Studies on Antibody Levels during Vaccination of Rhesus Monkeys against *Plasmodium knowlesi*

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The fluorescent antibody technique has been applied extensively in recent years to the serology of malaria. It has been used to study the antigenic relationships between species of malaria parasites (Tobie and Coatney, 1961; Voller, 1962, 1964; Collins *et al.*, 1965), for the measurement of antibody produced during experimentally induced malaria infections (Kuvin *et al.*, 1962; Tobie and Coatney, 1961; Collins *et al.*, 1964), and for field studies in malaria-endemic regions of the world (Voller and Bray, 1962; Voller and Wilson, 1964; Gebbie *et al.*, 1964; Marsden *et al.*, 1965; McGregor *et al.*, 1965).

Serum from immune patients or animals contains antibody which by passive transfer will reduce parasitaemia and bring about clinical cure of acute infections (McGregor and Cohen, 1963). However, the relationship between protective antibody and the antibody measured by the fluorescent antibody technique is still not clear. In some cases strong serological cross-reactions may occur between different species of malaria although solid immunity to one confers no protection against the other, indicating that the antibody being measured probably has no protective function. In other cases, particularly in malaria-endemic areas, the elevation of gamma-globulin has been proved to be at least partly due to malaria (Gilles and McGregor, 1959), and the levels of antibody measured by the fluorescent antibody technique correspond closely to the classical concepts of malarial immunity (Voller and Bray, 1962; McGregor *et al.*, 1965).

The purpose of the present investigation was to try to relate the serum protein changes and the fluorescent antibody titres to the degree of protection obtained by vaccination of rhesus monkeys against *Plasmodium knowlesi*; that is, to relate these serological changes to the functional immune response.

MATERIALS AND METHODS

Rhesus monkeys were given two intramuscular injections of vaccine with an interval of six to eight weeks between injections. The formalized vaccine used was either concentrated infected monkey red blood cells or the malaria parasites freed from the host cells by means of a haemolytic antiserum (Targett and Fulton, 1965; Targett, in preparation). The first injection

was given with Freund's complete adjuvant, the second with the incomplete adjuvant. The monkeys were challenged about six weeks after the second vaccination.

Serum protein changes were measured as described earlier (Targett and Fulton, 1965). Sera were tested by the indirect fluorescent antibody technique for malaria, as described fully by Voller (1964).

RESULTS

Fig. 1 shows the parasitaemias developed after challenge in two groups of monkeys which were successfully protected.

Fig. 2 shows the serum protein changes that occurred in the four monkeys vaccinated with infected red blood cells. Antibody levels of sera from this second group of monkeys were measured by the fluorescent antibody technique, and Fig. 3 shows the relationship for two of the monkeys between gamma-globulin levels and fluorescent antibody technique titres during the vaccination period.

Further vaccination experiments were carried out with a similar procedure but with free parasites as vaccine. Groups

FIG. 1.—Parasitaemia after challenge in monkeys protected by vaccination.

of monkeys were given different quantities of antigen to determine how this would affect the subsequent response to challenge (Targett, in preparation). The results are summarized in Fig. 4.

There was in most cases an increase in gamma-globulin of 30–50% (range 8–128%) from the beginning to the end of the vaccination period. There was no correlation between the increase in gamma-globulin and the level of protective immunity. The increase was as great in monkeys which showed little or no resistance to the challenge as in those which were

successfully immunized. The fluorescent antibody titres were mostly very high, and, again, the levels were as high in animals which remained susceptible to challenge as in those which were protected.

FIG. 4.—Relationship between fluorescent antibody titres, gamma-globulin concentrations, and the protection obtained by vaccination. +++ Challenge infection did not become patent or produced only a low-grade parasitaemia. ++ Challenge infection produced a moderate-to-severe parasitaemia but the monkey survived. + Challenge infection suppressed for a time but the monkey did not survive. — No indication of resistance to the challenge.

DISCUSSION

All the experimental monkeys showed a serological response to the vaccination, evidenced by the increase in globulin, decrease in albumin, and increase in the malarial fluorescent antibody technique titre. However, this response did not result in functional immunity to challenge in every case. The vaccine consisted of a complex of antigens which presumably elicited many antibodies, and it would appear that the functional protective antibodies form only a small part of the total globulin.

Freund *et al.* (1948) immunized monkeys against *P. knowlesi*, and found that there was no correlation between antibody titre (C.F.T.) and protection. Spira and Zuckerman (1962 and personal communication) have shown by immuno-electrophoresis that there are considerably more precipitating bands produced by serum obtained from rabbits after injection of a rodent malaria parasite preparation than are produced by the sera from rats which have recovered from infection with the same parasite. Recently Zuckerman *et al.* (1965) have also shown that a significant degree of protection against *Plasmodium berghei* is conferred on rats by inoculation of a non-living preparation of *P. berghei*.

The conclusion that considerable amounts of non-specific and non-protective antibody are produced is supported by the results obtained during an investigation of the rates of catabolism of gamma-globulin obtained from normal and from *P. knowlesi* immune monkeys when injected into monkeys infected with the homologous parasite. There was in fact no detectable difference in catabolic rate between the globulins, indicating that the amount of specific protective antibody in the immune globulin was very small, probably no more than 5% of the total (Freeman *et al.*, 1965). The recent elegant work by Curtin *et al.* (1964) also indicates that much of the gamma-globulin thought to be excited by malaria infections may be non-specific. They found by column techniques that only a small amount of the gamma-globulin could be removed by absorption with malaria antigenic material.

FIG. 2.—Concentrations of serum proteins in monkeys protected by immunization with infected red blood cells. ● Total protein. ▲ Albumin. ■ γ-globulins. ○ β-globulins. △ α₂-globulins. □ α₁-globulins. V₁ 1st vaccination. V₂ 2nd vaccination. C Challenge infection.

FIG. 3.—Relationship for two of the protected monkeys between fluorescent antibody titres and gamma-globulin concentrations during the vaccination period. V₁ 1st vaccination. V₂ 2nd vaccination. C Challenge infection.

Thus we must conclude that consequent on vaccination against malaria, and probably also on infection, the gamma-globulin rises, and that this is partly non-specific, is partly specific-antibody but not protective-antibody, and is partly specific-protective-antibody.

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Medical Memoranda

Transgastric Approach to Unusual Oesophageal Foreign Body

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Foreign bodies impacted in the oesophagus may be removed by oesophagoscopy, and, failing that, by oesophagotomy.

Sellers (1947) removed a razor blade by the transthoracic approach, and Grey Turner (1947) removed a tooth-plate by the same route. In the case described here a more unorthodox approach was successful in dealing with a more unusual situation.

CASE REPORT

A man aged 59, wishing to practise the art of swallowing a nasogastric tube, experimented with a leather thong one night. He found it easy to swallow but not to remove. When he arrived at the casualty department of a local hospital about 6 in. (15.2 cm.) of the thong protruded from his mouth. Attempts at removal by

Photograph of knotted leather thong swallowed by patient.

oesophagoscopy and traction were unsuccessful, and the patient was transferred to the thoracic unit.

Oesophagoscopy showed the distal part of the thong to be knotted, and the oesophageal mucosa torn and bleeding. The knot was so firmly stuck in the oesophageal wall that we were unable to pull it up. It was decided, therefore, to undertake laparotomy.

At operation, the stomach was exposed through an upper midline incision. The foreign body could not be felt by palpation at the cardia. Through an incision in the stomach the index and middle fingers of the right hand were introduced up the oesophagus, where they managed to grasp the knot, which was then disimpacted and pulled down into the stomach and out of the abdomen. A temporary gastrostomy was performed.

A barium-meal examination carried out 25 days later showed no evidence of oesophageal stricture or of ulceration. The psychiatrist found no overt psychiatric abnormality. The thong was 0.75 cm. in diameter and about 60 cm. long. The knot was 4 cm. thick in its maximum transverse dimension (see Figure).

COMMENT

It was fortunate that neither the patient's manoeuvre nor our attempts at removal resulted in a tear of the oesophagus. Whether the thong was knotted before it was swallowed or whether it knotted itself within the oesophagus remains conjectural, as the patient himself gave first one story and then another.

Oesophagotomy is perhaps less dangerous to-day than it was 20 years ago, because of the availability of a wide range of antibiotics. It still remains, however, a potent source of post-operative empyemas, sinuses, and fistulae. It is a comforting thought, however, that oesophagotomy was not needed in this case.

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