IMMUNOLOGICAL ASPECTS OF A POPULATION UNDER PROPHYLAXIS AGAINST MALARIA

by

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The earliest reference to the possibility of congenitally transmitted immunity to malaria was made by Stephens & Christophers (1900). The epidemiological and other aspects of this problem were reviewed by Bruce-Chwatt (1963).

Since the demonstration by Cohen et al. (1961) of the therapeutic effect of malaria-immune gamma-globulin, there has been growing interest in the part played by humoral immunity in malaria. Tobie et al. (1962) showed that the course of antibody production could be measured, using the fluorescent-antibody technique, in subjects experimentally infected with malaria. Similarly, Vollrath & Bray (1962) were able to assess the antibody levels in residents of a malaria hyperendemic area of West Africa. These authors noted high malarial antibody titres in cord-blood. Their inference that there was a passive transfer of maternal antibody across the placenta was borne out by the demonstration of Edosien et al. (1962) that the gamma-globulin from cord-blood had a therapeutic effect on acute malarial infections.

The present preliminary study was undertaken in order to investigate the effects of drug treatment on malarial antibody production in infants and their mothers.

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Methods and results

The study was carried out at Sukuta, Gambia, West Africa, an area of hyperendemic *P. falciparum* malaria.

A group of pregnant women was kept under observation at the weekly clinic at Sukuta. From the time of birth of their children or a few months later (see Table 1) these women and their infants were regularly given once weekly oral pyrimethamine (Group 1: mothers 25 mg weekly, children 12.5 mg weekly) or placebo (Group 2). There were seven mothers and children in each group.

Blood films were examined at weekly intervals for malaria parasites. None of the women and only one child, Boobacar Bojung, of Group 1 showed parasitaemia. All the children, except Sanna Chan, and all the women in Group 2 showed parasites at some time during the study period of four to seven months.

In December 1963 finger-prick blood samples were taken into microhaematocrit tubes and the serum separated and made up to an initial dilution of 1:25 (McGregor & Coller, unpublished observations). The indirect fluorescent-antibody test was then used to measure the levels of malarial antibody in the sera (Voller & Bray, 1962).

Slide antigens used in these tests were thin blood smears taken from children with heavy infection of *P. falciparum*. The slides were stored at -70°C until the day when they were used.

The results of the antibody determinations are given in Table 1.

Discussion

Malarial antibody was demonstrated in all of the unprotected children except one, in this study. In contrast, malarial antibody was not found in any of the infants who had been on antimalarial drug prophylaxis since birth. The average titre of the protected mothers was much lower than that of the unprotected group.

The unprotected children had an average antibody level which was considerably lower than that of their mothers. This is in agreement with the findings of Voller & Bray (1962), who showed that, although children in an endemic area are born with high malarial antibody levels, these drop over the first few months of life. Thus it would appear that the passively transferred maternal gamma-globulin is only short-lived.
This latter point is emphasized by the fact that some of the protected children had detectable antibody, although every mother in this group did have. In this group, then, all the malarial antibody passively transferred from the mother had disappeared after a few months. The drug prophylaxis was obviously effective in that no antibody was developed in the protected children. It can be concluded that sporozoite challenge at this level does not elicit the production of malarial antibody.

These results would suggest that in some circumstances the fluorescent antibody test could be a valuable addition to the examination of thick blood films for parasites.

It is of interest to note that the average malarial antibody titre of the women protected for about seven months was considerably lower than that of the unprotected group. In a study on West Africans resident in Britain, Kevin & Voller (1963) detected malarial antibody in subjects who had left the endemic area as long as seven years previously. Of course, in these cases the possibility of subpatent infection cannot be ruled out. The same possibility applies to the volunteers experimentally infected with malaria (Collins et al. 1964) in whom antibody was found a year later.

The present results suggest that repeated and frequent infection is necessary to maintain antibody at its highest level.

It must not be thought that the demonstration of malarial antibody implies the existence of an effective functional immunity. The unprotected children in the present study showed evidence of antibody production, but this age-group frequently carries a heavy load of malaria parasites. A finding of malarial antibody indicates past or present infection with malaria. However, the early antibody production, together with maternal antibody, may account for the relatively mild first malaria infections as noted by Bruce-Chwatt (1952) and by McGregor (1960).

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RESUME

Grâce à la méthode des anticorps fluorescents, on a montré la présence d'antigènes du paludisme chez tous les enfants non protégés, sauf un. Par contre, il n'y avait pas d'anticorps chez les enfants à qui l'on avait administré des médicaments antipaludiques à titre prophylactique depuis leur naissance. Le titre moyen était beaucoup plus faible chez les mères protégées que chez celles du groupe non protégé.

Chez les enfants non protégés, le taux moyen d'anticorps était beaucoup plus bas que chez leurs mères. Les enfants des régions où le paludisme est endémique ont un titre élevé d'anticorps à la naissance, mais ce titre diminue au cours des premiers mois de vie. Il semblerait donc que la gamma-globuline maternelle, qui est transmise passivement à l'enfant, ne soit active que pendant peu de temps.

Le titre moyen d'anticorps des femmes protégées depuis sept mois environ était beaucoup plus faible que celui du groupe non protégé. Les résultats actuels amènent à penser que les anticorps ne se maintiennent que si l'individu est victime d'infections fréquentes et répétées.

Il ne faut pas croire que la découverte d'anticorps du paludisme chez un individu implique l'existence d'une immunité fonctionnelle affective. On a constaté que l'organisme des enfants non protégés examinés au cours de cette étude produisait des anticorps, mais les enfants de ce groupe d'âge sont fréquemment porteurs d'un grand nombre de parasites du paludisme. Lorsqu'on trouve des anticorps chez un individu cela signifie qu'il a été ou est infecté. Cependant, le caractère relativement bénin des premières infections peut s'expliquer par la production précoce d'anticorps et par la présence d'anticorps maternels.
REFERENCES


Stephens, J. W. W. & Christophers, S. R. (1900) Reports to the Malaria Committee of the Royal Society, 3, 4


# TABLE 1. MALARIAL ANTIBODY ANALYSIS OF PROTECTED AND UNPROTECTED MOTHERS AND CHILDREN IN GAMBIA

## Group 1. Protected Individuals

<table>
<thead>
<tr>
<th>Child</th>
<th>Mother</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name</td>
<td>Protection period in months</td>
</tr>
<tr>
<td>Lamin Colley</td>
<td>7</td>
</tr>
<tr>
<td>Boobacar Bojang</td>
<td>10</td>
</tr>
<tr>
<td>Adams M’Boob</td>
<td>12</td>
</tr>
<tr>
<td>Ousman Cham</td>
<td>4-1/2</td>
</tr>
<tr>
<td>Abdouli Sanyang</td>
<td>9</td>
</tr>
<tr>
<td>Bakari Kammara</td>
<td>12</td>
</tr>
<tr>
<td>Saku Sanko</td>
<td>7</td>
</tr>
<tr>
<td><strong>Average</strong></td>
<td>8-1/2</td>
</tr>
</tbody>
</table>

## Group 2. Unprotected Individuals

<table>
<thead>
<tr>
<th>Child</th>
<th>Mother</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name</td>
<td>F.A. titre</td>
</tr>
<tr>
<td>Momadu Cham</td>
<td>11</td>
</tr>
<tr>
<td>Lamin Bojang</td>
<td>9</td>
</tr>
<tr>
<td>Isatou Jallow</td>
<td>11</td>
</tr>
<tr>
<td>Ibraima Colley</td>
<td>7</td>
</tr>
<tr>
<td>Kuley Cham</td>
<td>9</td>
</tr>
<tr>
<td>Bass Jatta</td>
<td>10-1/2</td>
</tr>
<tr>
<td>Sanna Cham</td>
<td>6-1/2</td>
</tr>
<tr>
<td><strong>Average</strong></td>
<td>9</td>
</tr>
</tbody>
</table>
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