Malaria Transmission and Fetal Growth

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Summary

In view of the known relation between infection of the maternal circulation of the placenta with Plasmodium falciparum and impaired fetal growth a study was made of the effect on birth weights of a malaria eradication campaign in the British Solomon Islands. Mean birth weights rose substantially within months of starting antimalarial operations. The increases between 1969 and 1971 averaged 252 g in babies of primigravidae and 165 g in all babies. The proportion of babies with birth weights of less than 2,500 g fell by 8% overall and by 20% among babies of primigravidae. The adverse effect of malaria transmission on fetal growth was apparently reversible if transmission of infection in the community was interrupted up to as late as the third trimester of pregnancy. The beneficial effects of malaria eradication operations on infant survival, child development, and social attitudes in developing countries are discussed.

Introduction

Child mortality in the British Solomon Islands in the past, in the absence of any form of malaria control, was high. Wrightson (1951) reported that 50 of the 111 children born in the island of Savo during the period 1948 to 1950 died at birth or in very early childhood and that the average number of living children per family was only 2.15 despite a fertility rate of the order of 175 per 1,000 women of child-bearing age yearly. Malaria must have contributed substantially to this mortality because before the start of antimalarial operations in 1962 the prevalence of malarial infection in the Savo Island population as a whole was 39.1%—Plasmodium falciparum infections constituting 47% of the total—and of the infants no fewer than 3% had simultaneous triple infections with P. falciparum, P. vivax, and P. malariae (Macgregor, 1966).

A pilot project in 1962-4 had shown that it was technically feasible to eradicate malaria from the British Solomon Islands. It seemed to us therefore that a most important field for study in relation to eradication operations would be their effect on infant and child survival and, as an aspect of that, on birth weights. This was not only because of the known predilection of P. falciparum for placental tissue (Clark, 1915; Blacklock and Gordon, 1925; Garnham, 1938) but also because of the associated low birth weight, first recognized by Bruce-Chwatt (1952), and the general prevalence of low birth weights among babies in malarious countries (Lawson and Stewart, 1967). An intensive malaria eradication campaign extended in 1970 to the island of Malaita enabled us to observe whether a reduction in malaria transmission led to an increase in birth weights, and this paper reports our findings.

Methods

BIRTH WEIGHTS

In 1965 there was no centrally organized system of birth-notification in the British Solomon Islands and records of birth weights were very incomplete. A procedure was therefore established whereby all births under medical or nursing care were notified to the central health authority. Baby scales, mostly provided by Unicef, were issued and staff were trained to use them and to complete the birth notification forms. Much help was freely given by Professor W. Brass in redesigning the project and in improving the notification procedures with a view to computer analysis.

Not until 1968, however, was the standard of notifications—from some 80 hospitals and clinics throughout the country—deemed good enough for computer analysis of birth weights. This showed a highly significant difference, averaging 147 g, between the birth weights of babies born on the island of Malaita, where malaria was both endemic and uncontrolled, and those born on islands which had been subjected to antimalarial spraying for several years. The difference was most notable in babies born to primigravidae. In 1969 the presentation of data was slightly modified to show also the number and proportion
of babies with birth weights under 2,500 g. While in other respects very similar to the findings in 1968, the 1969 data showed that there was a significant excess (P < 0.001) of low birth weights among babies born on Malaita Island. Moreover, no fewer than two out of every five babies born to primigravidae weighed less than 2,500 g compared with one out of every five in malaria-controlled areas.

Since there are many ethnic differences among the Melanesian inhabitants of the Solomon Islands archipelago that could conceivably have affected the findings, it was clearly essential to continue the investigation and to observe the effect on birth weights of interrupting malaria transmission on Malaita Island. Fortunately, the first round of insecticidal measures was not scheduled to begin there until the second half of 1970. With a population of 50,659 Malaita is the most densely populated of the major islands within the British Solomon Islands Protectorate (total population, 1970 census, 160,998). Moreover, the people of Malaita, despite 14 distinct linguistic groups, are ethnically homogeneous.

PARASTOLOGY

The prespraying malariometric survey of Malaita, though not strictly on a random basis, covered enough villages in coastal, lagoon, and hill areas for the island reliably to be classified as mesoendemic. Overall, the survey showed in the 2-9 year age group a P. falciparum species rate of 7-3% and a parasite formula of P. falciparum 23-3%, P. vivax 71-3%, P. malariae 5-4%. Though P. vivax predominated P. falciparum made a substantial contribution to the parasite load.

Spleen rates were not routinely measured but the rates in the 2-9 year age group in a sample of several coastal village populations were in the range of 60-80%. Had these surveys been carried out more extensively the island as a whole would probably have been classifiable as hyperendemic. In general we can say that high spleen and parasite rates were common in villages at low altitude and on the coast while lower rates prevailed in villages at higher altitude and also in those on artificial islands in the offshore lagoons.

The parasite rates in pregnant women were not recorded in the survey, but it may reasonably be assumed that many if not already malarious must have been exposed to infection during the course of their pregnancies. The fact that placental infections can occur from the fourth month of gestation onwards (Garnham, 1938) is noteworthy.

ENTOMOLOGY

The principal vector of malaria in Malaita Island, as in the Solomons generally, was found to be Anopheles farauti, subsidiary vectors being A. punctulatus and A. koliensis. Before residual insecticidal spraying these vectors were found in abundance at many sites, but after spraying A. punctulatus and A. koliensis disappeared completely and A. farauti became scarce.

<table>
<thead>
<tr>
<th>Date of Survey</th>
<th>No. of Months</th>
<th>No. of Examinations</th>
<th>Total Parasites†</th>
<th>P. falciparum</th>
<th>P. vivax</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>After First C.S.O.*</td>
<td></td>
<td>No. Positive</td>
<td>Rate (%)</td>
<td>No. Positive</td>
</tr>
<tr>
<td>Before spraying:</td>
<td>1970</td>
<td>2,174</td>
<td>646</td>
<td>29-7</td>
<td>159</td>
</tr>
<tr>
<td>After spraying:</td>
<td>1971</td>
<td>6</td>
<td>970</td>
<td>325</td>
<td>35-5</td>
</tr>
<tr>
<td>April</td>
<td>1971</td>
<td>12</td>
<td>920</td>
<td>242</td>
<td>26-3</td>
</tr>
<tr>
<td>July</td>
<td>1971</td>
<td>24</td>
<td>1,278</td>
<td>163</td>
<td>12-0</td>
</tr>
<tr>
<td>October</td>
<td>1971</td>
<td>24</td>
<td>1,278</td>
<td>163</td>
<td>12-0</td>
</tr>
</tbody>
</table>

* C.S.O. = Cyclical spraying operations
† Total Parasites includes P. malariae infections, which are not shown separately.

Results

MALARIOLOGIC

Malariometric parasite surveys of the 2-9 year age group carried out every six months after the start of spraying in villages selected randomly throughout the island clearly showed a steady and rapid initial fall in the P. falciparum parasite rate together with an initial rise and subsequent slower fall in the P. vivax rate (table 1). The fall in the P. falciparum rate satisfied the first standard for the interruption of malaria transmission as defined by the World Health Organization Expert Committee on Malaria (World Health Organization, 1966). While not quite coming within the expected slope for zero reproduction (fig. 1) it nevertheless met the minimum acceptable rate of fall, corresponding to a reproduction rate of 0-2 (Macdonald and Göckel, 1964).

The initial rise in the P. vivax rate was probably associated with the apparent suppressive effect of P. falciparum infections on P. vivax parasitaemia, as described by Shute and Maryon (1954), while the subsequent very slow fall in the P. vivax rate was typical of happenings in the Solomon Islands. This was probably a characteristic of the fast-relapsing Chesson strain of P. vivax, which can persist in the body for up to four years or more (Hill and Amazuzio, 1949). Though Macdonald and Göckel (1964) postulated that the declination rate representing zero reproduction of P. falciparum was generally valid whichever parasite might predominate Macgregor (1966) showed that the Solomon Islands strain of P. vivax does not conform to expectations in this respect.

Again, out of 1,452 children in the age group 0-23 months examined during the period March to September 1971 only 10 were found to have P. falciparum infections. Unfortunately it is not recorded whether the older infants in this group
could have contracted the infection before spraying operations began. Nevertheless, since four of these 10 infections were discovered only during the last quarter of 1971 transmission of the disease must almost certainly have continued in some areas until then, albeit at a very low level.

As in many other malaria eradication programmes (World Health Organization, 1971) the third W.H.O. standard concerning the ratio of heavy to light infections regrettably could not be applied as evidence of the interruption of malaria transmission owing to a shortage of the special laboratory skills needed for this assessment. On the whole, however, we considered that our findings indicated that there was a very substantial if not entirely complete interruption of malaria transmission in Malaita Island during the latter part of 1970, 1971, and the first two-thirds of 1972.

BIRTH WEIGHTS AND PREMATURITY RATES

The returns under the voluntary birth notification scheme steadily increased from year to year. In 1971 an estimated 69% of all births were notified, with Malaita Island ahead of this average by an additional 4%.

Birth weights in Malaita increased dramatically between 1969 and 1971, the increases averaging 252 g in babies of primigravidae and 165 g in all babies (tables II and III). The number of low birth weights (< 2,500 g) fell to levels virtually identical with those in the malaria-controlled area. These findings prompted a re-examination of the 1970 data to see how closely they could be linked to the initial application of insecticide.

The low birth weight rate for the third quarter of 1970 proved to be 16% (50 out of 308) and for the last quarter 14% (34 out of 246), while the average weight of the 246 babies born in the last quarter of the year was 104 g heavier than the 1969 mean birth weight for all babies. Caution is of course necessary in interpreting these figures, because of the fairly small numbers. Nevertheless, the latter figure represents some 63% of the overall gain in Malaita birth weights from 1969 to 1971 and can be correlated with the percentage spraying coverage of the Malaita population attained at mid-October 1970. The lag period between the interruption of malaria transmission and release of fetal growth potential may therefore be not much more than a month.

The decline in the Malaita Island low birth weight rates year by year over the period is also compared graphically with the corresponding rates in the malaria-controlled areas of Malaita Island. We think the slight deterioration in 1972 reflected the disruption of the supply of insecticide and the consequent less-than-adequate interruption of malaria transmission.

We considered whether these findings might have been affected by a large increase in specific medication. We think this may be discounted. The consumption of antimalarial drugs in Malaita hospitals and clinics did not increase during the period—in fact, it decreased from 1971 onwards. The issue of such drugs prophylactically to pregnant women was not encouraged as an act of policy and no retail drug outlets or private medical practitioners existed on Malaita Island at the material time.

Table III—Birth Weights of all Babies born in Malaita Island 1969-72

<table>
<thead>
<tr>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of babies</td>
<td>191</td>
<td>232</td>
<td>263</td>
<td>337</td>
</tr>
<tr>
<td>Mean birth weight (g)</td>
<td>2,577 ± 526.9</td>
<td>2,671 ± 516.9</td>
<td>2,830 ± 473.9</td>
<td>2,829 ± 460.7</td>
</tr>
<tr>
<td>No. (%) &lt; 2,500 g</td>
<td>79 (41)</td>
<td>72 (31)</td>
<td>56 (21)</td>
<td>65 (19)</td>
</tr>
</tbody>
</table>

Discussion

Jelliffe (1967) deplored the fact that despite some 15 studies since Clark's (1915) the possible relation of placental malaria to the enormous problem of infant wastage in many developing countries had been little recognized. The position has not materially changed. Authoritative documents barely mention malaria as a threat to normal fetal development. Though the global eradication campaign launched by the Eighth and Ninth World Health Assemblies has achieved the most aston-
lishing success, with over 1,000m people living in areas freed from endemic malaria (World Health Organization, 1971), malaria transmission is still unchecked in many countries, most notably in tropical Asia and Africa. It therefore seems timely to reconsider the part which malaria may play in affecting fetal development, to say nothing of perinatal morbidity or infant and child mortality.

Garnham (1938), describing the reticuloendothelial re-
action in the placenta in different forms of malaria, pointed out that in certain phases of malaria the interstitial spaces contained an almost solid mass of reticuloendothelial cells, and he found it difficult to understand how the feto was nourished. He thought that many of the abortions in malaria probably resulted from fetal death through physical inter-
ference with the placental circulation rather than to the direct effect of malaria toxins. Blacklock and Gordon (1925) also postulated that malarial infection of the mother predisposed to accidents during pregnancy or at birth, and Clark (1915) reported no fewer than 44 accidents (abortions, still-
births, premature labours) in 400 maternity cases. In seven of the 44 the placenta was infected with P. falciparum whereas the placenta was so infected in only 12 of the 356 normal deliveries. Subsequent workers (Bruce-Chwatt, 1952; Archibald, 1956; Cannon, 1958; Spitz, 1959; McLaren and Ward, 1962; Jeliffe, 1967) concentrated their atten-
tion on the difference between live birth weights associ-
ated with infected placentae and those associated with uninfected placentae. All except McLaren and Ward found significantly smaller mean birth weights in babies when the placenta was infected compared with birth weights when the placenta was uninfected. In McLaren and Ward’s cases the difference was only marginally significant.

Unfortunately there is no correlation between the presence of malaria parasites in the peripheral blood and placental infection. Hence it is impossible to identify women in an endemic area who have had a P. falciparum placcental infec-
tion. Even if it were it would hardly be possible to categorize such women as infected or uninfected for placental infections are known to occur virtually at any time after the embryonic placenta has become a functioning organ. Some of the women investigated in the studies quoted are also likely to have recovered naturally from a placental infection just before being categorized as uninfected. There must, therefore, have been at least some overlap between the categories “infected” and “uninfected” in the hyperendemic situations prevailing, and if so the fact that significant birth weight differences were recorded suggests that fetal recovery from the effects of placcental infection must have been remarkably rapid. Moreover, the wide variation in the mean birth weight differences reported by the above authors and the lack of apparent correlation with overall placental malaria positivity rates may be a function of the degree to which the “uninfected” samples were in fact “infected” before the diag-
nostic examination at term.

We hope that the present study, by comparing birth weights in an endemic area before and after interrupting malaria transmission, provides a clearer picture of the quanti-
tative effects of placental malaria. It shows a remarkably stable birth weight pattern in both the malaria-controlled areas and in the endemic area (Malaita Island) after malaria transmission was interrupted. It also shows a rapid rise in all birth weights, and especially in babies of primigravidae, after the initial application of insecticide in Malaita Island, together with an extraordinary decline in the proportion of low birth weight babies—a gain most noticeable in those of primigravidae. The special susceptibility of primigravidae to malarial infection has been commented on by Bruce-Chwatt (1952). More recently McGregor et al. (1970) have also discussed pregnancy in relation to malaria immunology.

Bearing in mind the special place the first baby—and in many cultures particularly the first-born son—has taken throughout the ages in folklore, religious testimony, and the law of inheritance no other measure is likely to have such profound implications for social attitudes in the family health field than one which seems selectively to enhance the chances of survival of the first-born child. This aspect apart, how-
ever, the interruption of malaria transmission, particularly the transmission of P. falciparum, must have materially con-
tributed to the chances both of survival and of healthy de-
velopment of some 8% of the live-born Malaita children who formerly were in the low birth weight category. Moreover, the implications do not relate only to the quantitative aspects of survival, since there is now ample evidence ( Fitzhardinge and Steven, 1972) that children whose fetal growth was im-
paired tend to be intellectually below average and to have learning difficulties. Thus, quite apart from the devastating infant mortality of up to 500 per 1,000 which malaria can cause in unprotected rural communities, countries labouring under the burden of this disease clearly may be at a sub-
stantial disadvantage educationally.

We thank the many nurses in the British Solomon Islands whose unselfed co-operation in completing many thousands of elaborate birth-notification forms made this study possible, and the staff of the Malaria Eradication Programme for their highly effective field operations. We also thank the Overseas Development Administra-
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tistical aspects of this paper.

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