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Malaria in Infancy

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To the epidemiologist malaria in the infant is of two-fold interest. In highly malarious areas it is the first attacks, occurring during the early years of life, which build up a relative immunity at the cost of considerable death and disability. Secondly, the rate of infection in the infant serves as a useful yardstick of transmission and is widely used as a measure of the success of control.

The effects of malaria are extremely variable and are often more obvious in the areas where transmission is less intense. A rational explanation has been provided by the concept of "stable" and "unstable" malaria (Macdonald, 1952). In stable areas transmission is steady and usually intense, spleen and parasite rates are high, particularly in children; the effects of the disease are not obvious, as the deaths and disability that it causes are limited to childhood, a period when other disabling diseases are common. In unstable areas the "malaria season" causes incapacitating disease in adults, which may reach epidemic proportions, disrupting the life of whole communities. Although the present article is meant to be general in its approach, it cannot avoid being biased by the writer's experience, which is limited to Ghana and the hinterland of Sarawak, where malaria is predominantly stable.

EFFECTS OF MALARIA

Schoolchildren and adults living in areas where malaria is highly endemic appear to suffer little from constant and heavy infections. In Ghana it was found that seven-year-old schoolchildren, kept free from parasitaemia by means of chemotherapy, were saved from five or six days of sickness every year; for adolescents the figure was about three days (Colbourne, 1955a). This relative immunity is acquired at the cost of deaths in early childhood; their number and the extent of permanent organic damage caused by malaria infection remain obscure.

(i) *Infant Mortality.*—There is no doubt that infants die from malaria. In countries where malaria attacks 100 per cent. of the children before they are three years old it is not easy to distinguish, even at autopsy, deaths due to malaria, deaths to which malaria contributed and deaths in those suffering from coincident malaria. Deaths from cerebral malaria give definite *post-mortem* signs and are steadily reported from areas where malaria is hyperendemic (Edington, 1954; Rothe, 1956).

Estimates of the number of deaths caused by malaria have been made in the Belgian Congo by Duren (1951), in Lagos, Nigeria, by Bruce-Chwatt (1952), and in Accra, Ghana, by Colbourne and Edington (1954). These results were obtained from death registrations and checked against the results of *post-mortem* examinations. It appeared that about 5 per cent. died from malaria, the great majority before they reached the age of five years. In Accra it was possible further to confirm the accuracy of the cause of death by showing a seasonal variation with the rainfall and with the prevalence of anophelines. In the suburbs of Accra, where transmission is intense, most of the deaths occurred in the first two years. In the less malarious centre of the town they were more evenly spread over the first five years. The total number of deaths was about the same in the two areas.

It is of interest to compare the death rates in childhood in Victorian Britain with those in Accra, Lagos and England and Wales to-day.

The improvement in England and Wales is largely due to the elimination of the infectious diseases of childhood in a cold climate. In West Africa malaria appears to be a similarly preventable cause of death.

(ii) *Morbidity Due to Malaria.*—Garnham (1949) and Bruce-Chwatt (1952) have stressed the great individual variation in the reaction to the first attack of malaria. The latter showed that, judging from body-weight increase, there were three patterns. About a third of the infants became infected without obvious disease and without any slowing of the rate of weight increase. In about a third there was some slowing, but after a few months the lost ground was regained. In the remainder the first infection was accompanied by a clinical disease and a severe interference with growth. It is presumably in the last group that the deaths due to malaria occur. In a group of 46 infants observed in Accra from birth to the age of six months, 28 became infected; in two the reaction was severe and it is considered that without treatment they would have died (Colbourne, 1956b).

Macgregor *et al.* (1956) observed 52 Gambian infants from June, 1951; half were protected from malaria infection by the administration of

Table

DEATH RATES PER 1,000 IN WEST AFRICA AND BRITAIN

Age in Years	Accra 1948-52 (Average)	Lagos 1950	England and Wales	
			1850-61	1949
Under 1	119	138	149	33
1— 2	31	69	50	2
3— 4		18	21	1
5—10	5	5	8	1
11—15		3	5	1

chloroquine. By October, 1952, five of the controls and one of the treated children had died. This intensive investigation of a small number of infants could not reveal the death rate caused by malaria, but the results are consistent with the extensive investigations referred to above.

At the end of three years 20 treated children and 13 controls were still under observation; all the controls had large spleens and were infected with malaria. The nutritional and general condition of all the children was satisfactory. There was then no difference in weight; the control children had fallen behind when they were first infected, but the lost ground had been regained. The control children were slightly shorter. They had a very definitely lower haemoglobin. Their serum proteins were higher, mainly due to increased gamma globulin. One child infected with *Plasmodium malariae* had protein and casts in the urine; there was no proof of a causal relationship. Thirteen of the controls and only one of the treated children had enlarged livers. This confirmed that malaria is a cause of enlargement of the liver.

Walters (1957) carried out liver biopsies on the children and showed that the enlargement was due to vascular congestion and to deposition of malaria pigment. There was no constant increase in the fibrous stroma in the untreated children. He concluded that in this group of well-nourished children there was no evidence that malaria was a factor in the production of liver fibrosis. This does not necessarily invalidate his previous conclusion (Walters and Waterlow, 1954) that malnutrition and malaria together may be responsible for the liver fibrosis so common in adult Africans.

(iii) *Miscellaneous.*—Only brief mention will be made of the problem of congenital malaria, which is considered to be rare in hyperendemic areas. Bruce-Chwatt (1952) found one doubtful case in a group of 551 women, with a parasite rate of 27 per cent. In Accra, in 126 deliveries by women with a parasite rate of 20 per cent., no congenital malaria was found. The reported incidence of 44 per cent. in Southern Nigeria by Atkins (1957) is difficult to understand.

Archibald (1956) has shown that malaria may have an indirect effect on the survival of African infants by increasing the number of premature births.

The treatment of infants suffering from malaria is outside the scope of this paper, but some of the deaths ascribed to malaria may be due to over-dosage with such drugs as mepacrine (Bruce-Chwatt, 1950a).

Towards the end of infancy, when the parasite rate is nearly 100 per cent. and the spleen rate is very high, the diagnosis of a disease as due to malaria is extremely difficult. Parasitaemia in a child admitted to hospital on account of fever is of little significance; a child whose symptoms are really due to malaria may have had the parasitaemia cleared by an antimalarial administered by the parent of the patient.

It is not known whether it is an advantage to delay the first attack of malaria from the first year with its many other hazards to health to later childhood, when some of the factors that may be responsible for the relative immunity of the infant have disappeared. Schoolchildren treated for a year in Accra by Colbourne (1955a) and for two years in Lagos by Archibald and Bruce-Chwatt (1956) showed no loss of immunity when reinfected.

Infection suppressed by drugs may still maintain a developed immunity. African students on their return to Ghana after several years

in Europe seemed to have lost some, but not all, of their immunity (Colbourne, 1955b).

(iv) *Conclusion.* — In hyperendemic areas malaria causes the death of about 5 per cent. of all children before they reach the age of five years. After that age a considerable degree of immunity has been won. The amount of permanent damage suffered by the survivors is obscure. Malaria definitely causes enlargement of the liver. There is no clear evidence that it causes fibrosis. Malaria causes a degree of anaemia and a change in the serum proteins. The effect of these changes on health has not yet been measured.

THE INFANT PARASITE RATE

The infant parasite rate is one of the recognised measures of the degree of transmission existing before and after attempts at control (Clark, 1935). It would seem obvious that it must give a clear indication of the intensity of transmission during the previous 12 months. It has, however, several disadvantages (apart from the term itself, which suggests infection with a tiny trophozoite, scarcely weaned from the schizont).

(i) *Availability of Infants.*—Infants are not particularly common; 30 per 1,000 of the population is a high figure. In many small rural communities, where the intensity of transmission is low, the number of infants may not be sufficient to ensure that a zero rate means that transmission is not occurring.

In thinly populated areas it is difficult to find sufficient infants to be able to work out the number of effective infections according to the methods of Macdonald (1950). This is unfortunate, as the concept is most useful to those engaged on control schemes. In some areas a reasonably reliable figure can be obtained from the parasite rate in older children.

The practical difficulty of collecting bloodfilms should not be overlooked. It needs considerable tact on the part of the technicians to persuade as many mothers as possible to agree to the examination of their children. Co-operation may depend largely on medico-religious beliefs; in Sarawak the Dayaks like to see a free flow of blood, as it is said to indicate good health. The Chinese, on the other hand, consider blood to have an essential value of its own and grudge the loss of even a few drops.

(ii) *Assessment of Age.*—In many countries malaria control has preceded the efficient registration of births; the parents are seldom sure of the age of their children, although they may know at what stage of the farming cycle the last child was born. Where technicians are responsible for collecting bloodfilms it is essential to provide a firm set of rules for the assessment of age. In Sarawak we are measuring the parasite rate of children with less than five teeth and calling it the infant parasite rate.

However difficult it may be to assess the age of the very young child under field conditions, there is no other age group in which a comparable degree of accuracy can be achieved.

(iii) *Exposure to Infection.*—The infant may not be exposed to the same risk of infection as the adult. In West Africa he is usually unprotected from mosquito bites. In Sarawak the majority of women sleep in a tent-like structure, called in Malay a *kelambu*. The derivation of this word shows that, although it usually translated mosquito net, the real object of the structure is to provide privacy in the communal rooms of a longhouse. In fact, observations made while catching mosquitoes at night show that the *kelambu* provides very poor protection, as many engorged female anophelines have been caught, as they bite through the cloth into an arm or leg applied to its inside surface. However, the infants are asleep in the *kelambu* earlier than the adults and may be partially protected.

Muirhead-Thomson (1951) has shown that in Jamaica anophelines are reluctant to bite infants; as the infant obviously has a smaller body surface than the adult, these two factors must mean that the individual adult is more likely to become infected than the infant.

Members of one family do not always sleep in the same house. In many parts of the world farming is carried out at some distance from the village, and temporary huts are built on the farms. Sometimes the mothers do not accompany their husbands to the farms; it is therefore most dangerous to assume that a negative infant parasite rate indicates that the adults have not been exposed to infection.

(iv) *Development of Infection in Infants.*—The relative protection of the infant from mosquito bites cannot explain the whole of the discrepancy between the rate of infection calculated from entomological data and the actual appearance of parasites in the blood of the infant. In Tanganyika infants who were probably receiving about 40 infected bites a year only developed malaria at a rate that could be produced by 3.5 bites (Davidson and Draper,

1953); in Uganda the figures were 100 and 5.5 (Davidson, 1955); in rural areas of Ghana, 24 and 1.8 (Colbourne and Wright, 1955).

It is more difficult to obtain figures from areas where transmission is less intense; there is usually more local and seasonal variation; the mosquitoes are not so heavily infected, so that very large numbers have to be dissected to produce a reliable sporozoite rate. In central Accra the number of infected bites per year was 0.1 from the entomological evidence and between 0.15 and 0.4 from the parasite rate in infants; this paradox could be explained by trips taken by the infants and their mothers to more malarious areas outside the town, but it suggests that under hypoendemic conditions more of the infected bites do develop to parasitaemia (Colbourne and Wright, 1955).

Various reasons for this discrepancy have been suggested. All the sporozoites may not be infectious (James, 1931). Cells containing foetal haemoglobin may be less susceptible to infection than those containing adult haemoglobin (Lehmann, 1953; Allison, 1954; Gilles, 1957). A purely milk diet may be deficient in a substance necessary for the development of the malarial parasite (Hawking, 1954; Colbourne, 1956; Macgregor, Gilles and Fuller, 1956). The infant may derive some immunity from its mother; such an immunity to *Plasmodium bergei* in rats was shown by Bruce-Chwatt (1954). Most of these factors are more likely to be protective during the first few months of life. All of them are unproved.

Bruce-Chwatt (1956) has examined *post-mortem* results from Nigeria and the United Kingdom and has come to the conclusion that the African infant in Nigeria is born with a larger spleen and liver than the European.

It is probable that, in highly malarious areas, infants do not develop malaria as quickly as would be expected from the density of infected mosquitoes; there is some evidence that this relative immunity is more marked in the first few months of life. However, in Kanara, India, where transmission is less intense than in West Africa, Viswanathan (1945) considered that, during the malaria season, the young infant is as susceptible to infection as the child about a year old.

It is not known whether the discrepancy between the sporozoite rate and the real infection rate still occurs in adults in hyperendemic areas, where the picture is hopelessly complicated by the development of an acquired immunity. In West Africa the newly-arrived European, in common with the African infant, is usually visiting a highly malarious country for the first time. Nowadays his reaction is obscured by drug prophylaxis, but those who are foolish enough to neglect this precaution rapidly contract the disease. This tiny minority provides almost all the non-African deaths from malaria in Nigeria (Bruce-Chwatt, 1950b); the numbers are too small to assess the proportion of infected bites that develop into the patent disease.

The European can undoubtedly develop an immunity to malaria. Hall (1926) gives an account of medical practice in West Africa at the end of the nineteenth century. The newcomer, if he survived the first six months, developed a "physiological hypertrophy of the spleen" and was much less troubled by fever. Those transferred to West Africa from Batavia, where malignant malaria was common, were much less susceptible to fever than those coming from the less malarious parts of India.

(v) *Conclusion.*—No better measure than the infant parasite rate exists for the estimation of the intensity of the transmission of malaria during the preceding 12 months, but there are many reasons why the results obtained may suggest too low a rate of transmission. Those evaluating control schemes would be most unwise to accept a negative rate as proof that transmission has been stopped, especially in the face of contrary evidence from entomological data or the *Plasmodium falciparum* rate in other age groups.

A reliable rate will not be obtained unless the bloodfilm is examined sufficiently thoroughly. In a group of 100 infants in Ghana the prolongation of the examination of the thick bloodfilm from 100 to 400 oil-immersion fields increased the infant parasite rate from 52 per cent. to 61 per cent. (Colbourne, 1956a).

SUMMARY

An assessment is made of the amount of damage caused by malaria to children in hyperendemic areas. It probably kills about 5 per cent. of all children born. It causes enlargement of the liver, but there is no clear evidence that it causes fibrosis.

The significance of the infant parasite rate is discussed. It is shown that the amount of parasitaemia in infants may underestimate the amount of transmission occurring in the community.

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