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SOME FACTORS AFFECTING THE DETECTION OF RESIDUAL TRANSMISSION
IN MALARIA ERADICATION SCHEMES IN AFRICA

by

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During a malaria eradication programme, the most effective method must be adopted for the detection of residual foci of malaria transmission. In most regions of the world, by the time that the consolidation phase of such a programme is entered, residual transmission can be detected with some reliability through the prompt examination of all new fever cases. Workers with experience of campaigns in tropical hyperendemic communities have, however, often questioned whether the relationship between malaria infection and fever is sufficiently frequent there to warrant dependence on this method. While no absolute rule can be suggested, the relationship between a malaria infection and subsequent fever is lost, or greatly diminished, when the infected individual has survived through childhood in an area where malaria risk is regularly and consistently extreme; when the individual has continued to experience this high level of malaria risk with no prolonged and recent period of absence from the malarious zone, or of protection from malaria by drugs or other means; and, finally, when the individual belongs to a racial group with a seemingly enhanced capacity to produce antibodies effective against the malaria parasite. As these requirements are fulfilled in the majority of the population of equatorial Africa, detection of casual transmission during the early years of a malaria eradication scheme in the region is not simple. It is the author's intention to consider the problem in this context,

In malaria, as with any disease in which superinfection is the rule, the most satisfactory expression of the intensity of transmission is the inoculation rate. For malaria this rate is defined as the average daily number of bites inflicted on one person

by mosquitos infected with sporozoites that are actually infective. By mathematical methods improved by Macdonald (1957) an estimate of this rate can conveniently be obtained on the one hand from parasite rates in children from birth to the second or third year of life (Macdonald, 1950) or from purely entomological data. In areas of high endemicity the rate calculated from the sporozoite rate, density and biting frequency of the vector mosquito is higher than that obtained by the former method. This disparity, referred to by numerous authors, has been attributed either to failure of a frank infection to follow the inoculation an insufficient number of sporozoites or to degenerative changes in them (Davidson, 1955).

During the attack phase of an eradication programme, due to the practical difficulty of examining an adequate and suitable sample of the remaining anopheline population, the vector density and infection rate will normally prove to be too low to be of assistance in the detection and delimitation of small foci of transmission. For this important investigation, therefore, attention must be directed to the detection of recent infections in the human population. For practical purposes, malaria infections found in infants can be assumed to have been acquired since birth, while those encountered in older children and adults are of uncertain age. Furthermore, each year passed in a malarious environment reinforces the individual's anti-parasitic immunity until a high proportion of the infections received may be masked. These considerations would seem to justify the general preference for the infant parasite rate as the best measure of recent levels of malaria transmission.

The problem of measuring a possible residue of malaria transmission was encountered in the later stages of the Pare-Taveta Malaria Scheme. The Scheme, described by Wilson (1960), was designed to establish the effects of a four-year programme of dieldrin residual spraying on an African community in a hyperendemic area on the Tanganyika/Kenya border. Spraying was started in 1956 and, by 1957, endemic indices in the sprayed villages had fallen sharply. The subsequent trend in the parasite rates (almost exclusively P. falciparum infections) in various age-groups is summarized in Table 1.

TABLE 1. PARASITE RATES IN PARE-TAVETA DURING ONE PERIOD BEFORE,
AND TWO PERIODS AFTER, THE START OF RESIDUAL SPRAYING IN 1956

(Exd.: number examined; P.R.: parasite rate)

Period	Age-groups													
	0-11 mths		12-23 mths		2-4 yrs		5-9 yrs		10-14 yrs		15-19 yrs		Over 20 yrs	
	Exd.	P.R.	Exd.	P.R.	Exd.	P.R.	Exd.	P.R.	Exd.	P.R.	Exd.	P.R.	Exd.	P.R.
1954/55	338	47	838	47	1147	64	2253	62	1891	52	705	39	4309	22
1957/58	394	2	714	4	889	12	2162	16	1570	17	501	7	2655	5
1958/59	270	1	541	3	608	6	1250	9	955	8	302	4	1543	3

It will be noted, from the figures in Table 1, that parasite rates in older children and adolescents persisted at a higher level than those in infants and adults. An investigation to reveal the cause of this disparity, for which no obvious reason suggested itself, was reported by Pringle et al. (1960). From this investigation, it appeared likely that the disparity in the parasite rates could best be explained if the infants were being infected less frequently than was the case in older children. Further support of this suggestion can be obtained from an analysis of the parasite rates in Pare-Taveta children over the entire period of protection, obtained partly from Draper & Draper (1960) and partly from Table 1 of this paper. These rates are set out in Table 2. In this table are calculated the highest theoretical parasite rate in the community commensurate with the parasite rate in each age-group and the corresponding communal inoculation rate.

TABLE 2. CALCULATION OF THE COMMUNAL MALARIA RISK IN PARE-TAVETA ON THE BASIS OF THE PARASITE RATES IN CHILDREN OF DIFFERENT AGES OVER A PERIOD OF THREE YEARS AFTER THE INSTITUTION OF RESIDUAL INSECTICIDE SPRAYING

Age-group	Total exd. 1957-59	Average parasite rate ¹	Highest theoretical parasite rate (L)	Communal inoculation rate (<u>h</u>)
0-3 mths	707	0.010	0.036	0.00018
3-5 mths	1097	0.025	0.052	0.00026
6-8 mths	863	0.033	0.050	0.00025
9-11 mths	630	0.054	0.068	0.00034
12-17 mths	478	0.068	0.072	0.00036
18-23 mths	172	0.087	0.089	0.00044
2-4 yrs	1497	0.095	0.096	0.00048
5-9 yrs	3412	0.137	0.137	0.00068
10-14 yrs	2525	0.036	0.136	0.00068

These data suggest that the malaria risk during infancy was only a fraction of that to which older children had been exposed. The only alternative possibility is that there had been a progressive retardation with age of the recovery rate of infections from infancy to the middle years of childhood. The recovery rate in experimental falciparum infections varies with the previous infection history of the individual: patent parasitaemias becoming shorter-lived and scantier with each re-infection by a homologous strain. It is difficult to believe that the falciparum infections in the Pare-Taveta children were not behaving in a similar fashion. If this was so, however, and the period of patency was indeed diminishing with age, the increase in infection risk after infancy must have been even more marked than the figures in Table 2 suggest.

It can only be concluded, under the circumstances then prevailing, that the infants were acting as relatively poor indicators of the intensity of the residual malaria transmission. This could be so only if the infants were relatively insusceptible to infection or were being bitten relatively infrequently by vector mosquitos. It can be accepted that infants born to a mother who has been living in

¹ Expressed as a proportion.

a hyperendemic area are born with passively-acquired antibodies and thus are protected against severe infections, and that this protection diminishes gradually over the first half of infancy. Other suggestions have also been put forward to explain the apparent insusceptibility of young African infants: Gilles (1957) has pointed out the possible importance of the persistence of foetal haemoglobin into infancy; Maegraith et al. (1952) suggested that a purely milk diet might provide some protective action against the malaria parasite. While the dietary in human infants appears to have little significance in this respect, Gilles (loc. cit.) has drawn attention to the possible bearing on parasitism of changes in the intestinal flora during infancy. Nevertheless, none of these influences, which are mainly operative in early infancy, would appear to explain the apparently steady increase in infection risk over the early years of childhood. One important possibility remains: that the infant is bitten relatively infrequently. Muirhead Thompson (1951) demonstrated that A. albimanus does not feed on infants as freely as it does on older members of the family, while observations reported by Thomas (1951) and Clyde & Shute (1958) suggest that, in Africa, A. gambiae may show a similar preference for feeding on the older, as opposed to the younger, members of a household. Freyvogel (1961) reported that caged Aedes aegypti fed reluctantly on an infant less than three months old but attacked the same child freely some eight months later. The same author (loc. cit.) reported an increase in the attraction of male baits at puberty and postulated that this might be associated with the physiological skin changes occurring at this age.

Davidson & Draper (1953), in a mathematical study of the epidemiology of hyperendemic malaria in coastal East Africa, discussed possible reasons for the disparity between the mosquito-derived inoculation rate and that calculated from the infection rates during infancy. These authors questioned whether this difference could be attributed to a reduced vector attack rate on infants on the grounds that the sporozoite rate could be accounted for only by assuming that an appreciable proportion of the blood meals were being obtained from young children - the group with the greatest incidence of effective gametocyte carriers. These authors divided the falciparum gametocyte carriers in their population into those with over 100 crescents per mm³ and those with a lesser density. Their data have been re-arranged in Table 3, where the number of

individual crescent carriers of high and low density in a standard lowland East African population have been calculated. In the last column of the table is an estimate of the number of individuals per thousand population with potentially significant numbers of crescents in their blood.

TABLE 3. DATA FROM DAVIDSON & DRAPER (1953) ILLUSTRATING THE DISTRIBUTION OF GAMETOCYTE CARRIERS IN VARIOUS AGE-GROUPS OF A STANDARD EAST AFRICAN LOWLAND POPULATION

Age-group	Number per thousand standard population	High density crescent carriers (>100 per cu.mm.) (a)	Low density crescent carriers (<100 per cu.mm.) (b)	Numbers likely to be infective (a) + (b)/2
2 wks - 2 mths	8	0.06	0.42	0.27
3-5 mths	14	0.84	4.62	3.15
6-11 mths	19	1.14	6.27	4.27
12-23 mths	34	1.70	11.56	7.48
2-4 yrs	95	2.85	26.60	16.15
5-10 yrs	103	0.0	14.42	7.21
11-14 yrs	95	0.0	9.50	4.75
15 yrs and over	632	0.0	7.60	3.80
Totals per thousand population:		6.59	80.99	47.08

The valley investigated by Davidson & Draper is immediately adjacent to an area that has been under intensive study by the Entomology Section of the East African Malaria Institute since 1950. The local biology of A. gambiae and A. funestus is now more fully understood than it was at the time of Davidson & Draper's investigation. For instance, it seems that, in this locality, A. gambiae sometimes departs from a rigid feeding cycle; on the other hand, A. funestus apparently feeds consistently, at all seasons, at intervals of 72 hours. Thus, only the latter species can be used reliably for exercises in mathematical epidemiology. Over many thousands of dissections in this area the sporozoite rate in funestus is 2.2 per cent. and the average daily mortality is 9.5 per cent. (Gillies, 1963). By extrapolation from a

figure drawn by Macdonald (loc. cit.), it would appear that funestus acquires infections here 0.008 times daily, or once in every 125 days. Given that the mosquito feeds every 72 hours, it seems that every 42nd blood meal is followed by a mosquito infection, or that 24 individuals per 1000 bitten are epidemiologically potent gametocyte carriers. Referring to Table 3, however, we can note that if funestus were feeding at random on all ages of this population the local sporozoite rate in this species would be 10 per cent. It follows therefore that there must be a significant feeding bias on the part of this mosquito towards that section of the population with a relatively low incidence of gametocyte carriers.

It is reasonable to suppose that a mosquito entering a room in which a family is sleeping will be attracted more readily to a larger person or to a larger, rather than a smaller, area of skin. The evidence discussed above, though by no means conclusive, does suggest that this may well be so. From the point of view of the malariologist attempting to discover foci of transmission, this matter is of some concern. It implies that infant infection rates will be relatively uninformative and that greater attention should be paid to the pattern of infections in older children.

While the frequency of mosquito attack, and so the liability to contract infection, may well increase with body size, or skin area, the value of the individual as an indicator of transmission is affected by his, or her, level of immunity. Immunity, of course, tends to increase with age and renders the adult population relatively refractory to infection and of proportionately little value for this purpose. What is needed, therefore, is a preliminary indication of the age-group that is most "sensitive" to the existence of sporadic infections. It is thought that this can be ascertained within a year or so of the initiation of active eradication measures by determining the age at which there is the greatest incidence of falciparum parasitaemias.

Having found the most "sensitive" age-group, the child population of this group can then be used as indicators of transmission. The first task would be to register as many as possible of the children in and around this age-group and to administer antimalarials in a sufficient dosage to bring about a radical cure of falciparum malaria in each child. The children can then be re-examined, and re-treated, at intervals of two to three months. It is worth recalling that the age of optimal sensitivity will advance progressively as protection continues and it should then be

possible to depend, within a fairly short time, on primary schoolchildren for the bulk of this work. The author has used this method to measure transmission in the Pare-Taveta area since the suspension of residual spraying operations in 1959.

Summary

1. Evidence is adduced suggesting that, under East African conditions, infants may be relatively insensitive indicators of malaria transmission.
2. Under these circumstances, it is reasonable to concentrate the search for sporadic foci of transmission on somewhat older children and a method for doing so is outlined.

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