Changes in Haemoglobin Values and Hepatosplenomegaly Produced by Control of Holoendemic Malaria

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In many parts of the tropics the mean haemoglobin values of rural populations are very much lower than the values accepted as normal elsewhere. For example, among Bougainville Islanders Cotter *et al.* (1958) found means of 13.09 and 11.97 g./100 ml. for adult males and females respectively. They suggested controlled experiments were needed to assess the relative importance of each individual factor that could be contributing to such low levels. This paper describes an experiment to determine the effects on haemoglobin values of three years' malaria control in part of the Sepik District, New Guinea. The concomitant changes in clinical hepatosplenomegaly are also described.

Draper (1960) has quoted conflicting findings on the importance of malaria as a cause of anaemia in African infants, and he noted that little was known about its effect on adults who had acquired some immunity. In Taveta-Pare, a hyperendemic malarious area of Tanganyika, he found that malaria control for three years was accompanied by great improvement in the mean haemoglobin values of all age-groups. However, he reported that there had also been a general rise in living standards in the area during the same period. There are considerable malariological differences, especially in malarial-species ratios and adult palpable spleen rates, between New Guinea and East Africa.

Methods

Areas Studied

In the Maprik subdistrict malaria was holoendemic before residual spraying was started in 1957 (Peters, 1960 ; Peters and Standfast, 1960)—that is, transmission was stable and very intense. In 1959 we chose two as yet unsprayed areas in this subdistrict, one of which, the Wingei census division, could be conveniently included in the malaria-control programme ; the other, the Wam division, was left outside it. These areas have been described in another paper (Schofield and Parkinson, 1963).

In 1959 the Wingei division was just beyond the eastern border of the Maprik malaria-control project, until malaria control was extended over it in December of that year, immediately after the first stage of this investigation had been completed. (Since 1961 the control project has spread still further eastwards.) The Wam division has remained beyond the western boundary of the Maprik project up to the present time. Because proximity to a malaria-control boundary might complicate the malariological picture, the findings relate only to the centrally placed villages of these two census divisions.

People Selected

The haemoglobin estimations, clinical examinations, and thick blood spots for malarial parasitaemia were made by the same workers each year, by methods previously described (Schofield, 1962). In both areas they were done during December and January, starting in December 1959, and January 1960, until 1962–3. These yearly dates are hereafter called 1959, 1960, 1961, 1962 for convenience. In Wingei these visits immediately preceded the first of the two spray rounds in each year. The results shown in Tables I, III, and IV are always from the same individuals each year. Any person who was not present in both 1959 and 1962 or who had died has been excluded. Individuals absent in 1960 or 1961 have been included if they were present in both 1959 and 1962. Thus, in each age and sex group, numbers in these Tables are always equal in 1959 and 1962 but are slightly smaller in 1960 and 1961, owing to the temporary absence of a few people. Women found to have a palpable uterus on abdominal palpation (gestations of 16 weeks or more) are studied as a separate group, and all patients treated at hospital during the three years have been excluded, including a few with severe non-malarial anaemia.

The individuals selected for haemoglobin estimations were approximately the first 100 to be examined on each day, but everybody was examined clinically. The people attended for medical examination in family groups in an order predetermined by the village census books, and their record cards were numbered in that order. Thus it was easy to ensure that the findings, on four occasions for each individual, could be compared over the three-year period. However, to get meaningful results on infants born during this period, and on women who were pregnant in any of these years, the haemoglobin levels of different individuals have had to be compared from one year to another. These two groups were small in numbers, so haemoglobin estimations were done on all newborn infants and all women advanced in pregnancy in the central villages.

The ages of infants born since 1959 were known, often to the day and always to the month. The years of birth of children born since 1950 were obtained from the village census books, which government officers had kept up to date at yearly intervals. The method of estimating the ages of older people has been described elsewhere (Schofield, 1962).

Comparability of Two Areas

Differences

The Wingei and Wam people differ linguistically and have minor differences in customs (Schofield and Parkinson, 1963). Wingei is about 500 ft. (152m.), Wam about 800 ft. (244m.), above sea-level. Since 1956 there have been two aid posts and a mission in Wingei which dispense treatment, including antimalarials, but, on our instructions, no haematinic or anthelmintic drugs were available, except at hospitals. In Wam no treatment is available locally.

Similarities

The areas are 40 miles (64 km.) apart, both being in the foothills of the Torricelli mountains. They are close enough and similar enough to be subject to the same vagaries of climate and agricultural conditions. Economic development is minimal in both areas. The diets are the same, and adults, grouped by age and sex, had exactly the same mean weights and heights in 1959. Female fertility rates, estimated from histories, were equal in 1959 (Schofield *et al.*, 1963). We have been the only

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medical personnel to visit either group of people, except for vaccinators against smallpox in 1962. Every six months a day was spent in each village, and treatment, including antimalarials, was given as needed.

In 1959 100 Wingei adults had a hookworm infection rate of 27% and 100 comparable Wam adults a rate of 34% on a single stool examination by the formol-ether concentration method (Ridley and Hawgood, 1956). No infections were found among children under 3 years of age, and the incidence among older children gradually rose to the adult rate by 15 years of age. In all positive cases infections were light, and they were not associated with haemoglobin levels lower than average.

In spite of the availability of antimalarial drugs in Wingei, the malariological indices of both groups were very similar in 1959 (Schofield, 1962); apart from the malaria control in Wingei, no observed changes had taken place in either area by 1962. Therefore the changes in mean haemoglobin values, and in splenic and hepatic enlargement, which developed in Wam should be minimal, and they provide a standard against which changes in Wingei values can be compared. Any differences that have appeared between the Wam mean values in 1959 and those in 1962, in the same individuals, can be ascribed to: (*a*) differences in the colorimeter in each year; (*b*) differences due to the age of each group rising by 3 years; (*c*) differences produced by factors affecting health. The experiment was designed to keep these variables, except malaria, the same for Wingei as for Wam. Therefore, subtraction of the changes in Wam values between 1959 and 1962 from the changes in the corresponding Wingei values should result in figures which express the effect of malaria control in Wingei. (Residual spraying might also affect the transmission of bancroftian filariasis, arboviruses, and flyborne diseases, but these infections can have only very slight influence, if any, on haemoglobin values and hepatosplenomegaly.)

Haemoglobin Estimations

A portable E.E.L. colorimeter containing an Ilford 625 yellow-green filter was used throughout all these investigations. It was calibrated, just before each yearly visit to the villages, against samples of known haemoglobin value supplied by the Red Cross Laboratories, Brisbane. Fresh solutions of a chemical colorimetric standard were taken into the villages each year and used to check the machine daily. Very consistent readings were obtained with these standards.

Blood for the malarial thick spot was taken from a finger-prick. After this had been wiped clean, 20 c.mm. of blood was measured by the standard method in a haemoglobin pipette and mixed in a numbered test-tube with 8 ml. of 0.04% ammonia solution previously dispensed from a burette. The tube was resealed with a cotton-wool plug and the colorimeter reading taken later in the day. This reading was converted into grammes of haemoglobin per 100 ml. from a graph prepared at the time of the colorimeter's calibration. A repeatability test in one village showed that variations of not more than 0.4 g./100 ml. might occur between two readings in one day from the same individuals.

For comparison with the mean haemoglobin values of the villagers, the values of 100 healthy adult Europeans—50 men and 50 women volunteer blood-transfusion donors in Port Moresby—were determined by the same method during 1959 and 1960.

Malaria Control

Routine spray rounds with residual D.D.T. have been conducted in Wingei by the Maprik Malaria Control Unit six-monthly since December, 1959. At these times a chloroquine-pyrimethamine mixture was also given by mouth to the whole population.

Results

Mean Haemoglobin Values

Main Groups.—In Table I the mean values for each age and sex group are shown for each year. The right-hand column shows the changes in mean values which had developed in each group in each area between 1959 and 1962. Each Wam figure in this column was then subtracted from the corresponding Wingei figure just above it, and the standard error of the difference between these two figures was calculated. Where this was less than half the difference ($P<0.05$), the Wingei figure has been marked by an asterisk, thus indicating the age and sex groups in which changes in Wingei levels were significantly greater than those in Wam. In Wam, considerable rises in mean haemoglobin values have occurred in children who were under 6 years of age in 1959, presumably due to their being three years older in 1962, and there were also rises with age in the cases of youths and girls aged 16 to 20. It is against such changes in Wam that the changes in Wingei must be evaluated.

TABLE I.—*Yearly Mean Haemoglobin Values in Wingei and Wam of Same Individuals in Each Year*

Age in 1959	No.	Hb (g./100 ml.) 1959	1960	1961	1962	Difference 1959–62
Both sexes:						
Born 1961 ..	48				11·6	
	33				9·3	
„ 1960 ..	49			11·6	12·3	
	34			9·4	10·1	
„ 1959 ..	45		10·6	11·6	12·3	
	32		9·2	10·0	10·4	
13–36 months ..	45	9·2	11·0	11·1	11·9	+2·7*
	31	9·2	9·9	10·4	10·6	+1·4
37–72 „ ..	58	10·3	11·1	11·6	12·3	+2·0*
	36	10·6	10·6	10·8	11·2	+0·6
6–10 years ..	110	11·3	11·4	12·0	12·4	+1·1*
	94	11·4	11·6	11·4	11·7	+0·3
11–15 „ ..	72	12·1	12·2	13·2	13·4	+1·3*
	47	12·0	12·1	12·0	12·1	+0·1
Males:						
16–20 years ..	37	13·3	13·0	14·6	14·5	+1·2
	29	12·9	12·9	13·1	13·4	+0·5
21–30 „ ..	63	14·2	14·2	14·5	14·4	+0·2
	44	13·7	13·5	13·5	13·4	−0·3
31–40 „ ..	57	14·1	14·1	14·1	14·1	0
	38	13·1	13·1	13·0	13·0	−0·1
41–50 „ ..	50	14·1	14·1	14·2	14·0	−0·1
	45	13·0	12·9	12·8	13·0	0
Over 50 years ..	36	13·8	13·7	13·7	13·7	−0·1
	19	13·1	12·7	12·7	12·8	−0·3
Females:						
16–20 years ..	44	12·8	12·7	13·3	13·4	+0·6
	41	12·1	12·1	12·3	12·4	+0·3
21–30 „ ..	88	12·4	12·4	13·0	13·1	+0·7*
	63	12·3	12·0	11·9	12·2	−0·1
31–40 „ ..	66	12·4	12·3	13·3	13·3	+0·9*
	51	12·3	11·9	11·9	12·0	−0·3
41–50 „ ..	53	12·7	12·7	13·3	13·4	+0·7*
	42	12·1	11·9	11·7	11·8	−0·3
Over 50 years	28	12·7	12·5	13·1	13·0	+0·3
	16	12·4	12·3	12·1	12·2	−0·2

In each group, Wingei figures are shown above those of Wam.
* Indicates a significant difference between changes in Wingei and Wam figures.

Europeans in Port Moresby.—Fifty men and 50 women had mean haemoglobin values of 15.6 and 14.3 g./100 ml. respectively (standard deviations were much smaller than among the villagers.) Wintrobe (1961) gives the normal values for men as 16 ± 2.0, and for women as 14.0 ± 2.0.

Infants.—The mean haemoglobin values for infants under 12 months of age are not shown in Table I, because their normal range is very wide (19.5 ± 5.0 at birth, 12.2 ± 2.3 at 3 months, and 11.2 g./100 ml. at 12 months). The values in both areas, before malaria control, appear to fall into two subgroups—under and over 3 months of age. Infants under 3 months of age all had haemoglobin levels which fell into the normal range even though 44% of this group had overt malarial parasitaemia and 33% had palpable spleens. As in other areas where women have much premunition, no cases of congenital infection were discovered. From 3 to 12 months of age mean haemoglobin levels before malaria control were very low—9.1 g./100 ml. in both areas—but 85% of the infants in this group who were born in Wingei under malaria control had levels within the normal range (Wintrobe) for their age, and none of these had overt parasitaemia. The remainder who had anaemia also had overt parasitaemia in every case in spite of the malaria control.

Children Aged 13 to 24 Months.—By following diagonally the figures for these groups at the top of Table I it can be seen that the yearly cohorts born in Wingei in 1960 and 1961, after malaria control had started, had a normal mean value. (This is 11.5 g./100 ml. at 24 months.)

Pregnant Women.—Only the haemoglobin values of women with gestations of 24 weeks or more, judged by the height of the uterine fundus, are considered. As the numbers were not large in either area in any one year, the values among pregnant women in each area in the years 1959 and 1960 have been taken together, and the resulting means compared with the means of values in 1961 and 1962 taken together. This seems justified, as Table I shows that, among non-pregnant adult women in Wingei, one year's malaria control was not enough to produce any apparent effect on haemoglobin levels. The mean values of pregnant women, as g./100 ml. were:

1959+1960: Wingei 10.2 (42) ; Wam 9.9 (34)
1961+1962: Wingei 11.6 (67) ; Wam 9.8 (49)

The figures in parentheses indicate the number of pregnant women in each group. The difference between the two Wingei groups is statistically significant at the 5% level.

Malariological Findings

Parasitaemia

Malaria parasite rates and the various splenic indices in each age-group did not differ appreciably between Wingei and Wam in 1959, and in both areas they were very similar to those found in 1957 around Maprik by Peters (1960), which he considered characteristic of holoendemic malaria. In Table II are given the Wingei parasite rates for each age-group in December, 1959, followed by the parasite rates for the same age-groups—not necessarily the same individuals—in December, 1962. (Children aged 0 to 12 months in 1959 were in the 37 to 72 months age-group in 1962, and so on.) Under malaria control there are unmeasured differential changes in premunition at various ages as well as in the risks of new infection. Therefore the efficacy of malaria control, when measured by parasite rates, is shown better by serial cross-sections at the same age in each year than by the method of longitudinal study which has been used for the haemoglobin values. In both years more than 50 blood slides from each age and sex group were examined.

TABLE II.—*Wingei Parasite Rates in 1959 and 1962: At Same Ages in Both Years*

Age-group in 1959 and 1962	Parasite Rate (%) 1959	1962
Both sexes:		
0–12 months	90·2	9·4
13–36 „	96·2	34·6
37–72 „	92·4	29·4
6–10 years	82·1	30·9
11–15 „	66·6	23·1
Males:		
16–20 years	54·9	5·5
21–30 „	30·6	14·0
31–40 „	18·3	12·6
41–50 „	18·3	6·6
Over 50 „	16·4	10·3
Females:		
16–20 years	53·2	5·1
21–30 „	25·8	6·9
31–40 „	23·6	8·7
41–50 „	26·6	8·7
Over 50 „	18·9	7·6

The figures show that malarial transmission was greatly reduced, but not halted, by the malaria control. In 1962 9.4% of infants born that year and 34.6% of children aged 13–36 months who had been born in the first two years of the project were overtly infected. Comparisons of Wingei parasite rates, including mixed infections, by species were as follows:

0–12 months in 1959, *P. falciparum* 60%, *P. vivax* 70%, *P. malariae* 35% ; in 1962 a ratio of 1:4:0
13–36 months in 1959, 1:1:0.6 ; in 1962, 1:17:2
Older children in 1959, 1:2:1 ; in 1962, 1:8:1
Over 15 years in 1959, 1:3:1 ; in 1962 1:8:0.5

Total and species parasite rates in Wam were stable over the three years, and very similar to those of Wingei in 1959.

Correlations were sought in Wingei in 1962 between overt parasitaemia and the presence of symptoms or of haemoglobin levels lower than average. None was found among men, adolescents, or non-pregnant non-lactating women. There was some correlation, with low haemoglobin values only, among pregnant women and those who had been lactating for less than six months, and a marked correlation, with both fever and anaemia, in children under 6 years of age.

Splenic Indices

Wam indices in 1959 have been tabulated in another paper (Schofield, 1962), and they had not changed in 1962. Table III gives the Wingei indices in 1959 and 1962 ; in both years each group consisted of the same individuals, and no group contained fewer than 50. (The average spleen is the sum of all spleen sizes—as measured by Hackett's method (W.H.O., 1951)—divided by the total number of people examined. The average enlarged spleen is the sum of the sizes of the palpable spleens only, divided by the total number of individuals who had such spleens.)

TABLE III.—*Wingei Splenic Indices in 1959 and 1962: In the Same Individuals Both Years*

Age in 1959	Spleen Rate (%) 1959	Spleen Rate (%) 1962	Average Spleen 1959	Average Spleen 1962	Average Enlarged Spleen 1959	Average Enlarged Spleen 1962
Both sexes:						
Born 1960–2	—	14·9	—	0·30	—	2·03
0–36 months	65·5	26·4	1·80	0·54	2·62	2·06
37–72 „	96·7	52·9	2·74	1·15	2·87	2·16
6–10 years	91·8	38·6	2·21	0·75	2·39	1·95
11–15 „	86·1	35·0	1·91	0·74	2·30	2·12
Males:						
16–20 years	54·2	21·2	1·37	0·45	2·15	2·10
21–30 „	34·8	12·6	0·56	0·27	1·81	2·13
31–40 „	35·0	18·0	0·75	0·42	2·00	2·35
41–50 „	30·0	9·6	0·66	0·18	1·85	1·85
Over 50 „	26·3	7·1	0·52	0·21	1·91	3·00
Females:						
16–20 years	66·1	11·1	1·51	0·22	2·28	2·00
21–30 „	67·0	30·1	1·42	0·71	2·11	2·36
31–40 „	64·7	40·0	1·51	1·02	2·34	2·55
41–50 „	74·2	48·7	1·71	1·10	2·30	2·26
Over 50 „	55·9	35·8	1·46	0·74	2·61	2·05

Hepatomegaly

The criteria of hepatomegaly and the method of clinical examination have also been described in the other paper, and the palpable-liver rates for each age and sex group more than 24 months old in 1959 were given for both areas. The patterns in each area were in that year very similar, and Wam rates had shown very little change by 1962. Therefore Table IV gives Wingei figures only ; these apply to the same individuals in both years and no group contained fewer than 50.

A repeatability test, on the results of one of us (F. D. S.) who made all the clinical examinations, showed a consistency of over 90% for splenomegaly in all age-groups and over 85% for hepatomegaly—except among children under 2 years of age, where consistency in measuring liver enlargement was only 60%.

TABLE IV.—*Wingei Palpable Liver Rates, 1959 and 1962: In Same Individuals Both Years*

Age in 1959	Palpable-liver Rate (%)	
	1959	1962
Both sexes:		
Born 1960–2	—	13·3
25–36 months	34·0	20·6
37–72 "	65·9	33·3
6–10 years	59·8	20·6
11–15 "	51·4	16·2
Males:		
16–20 years	38·2	9·1
21–30 "	13·3	4·1
31–40 "	20·8	13·5
41–50 "	9·1	8·5
Over 50 "	3·2	8·5
Females:		
16–20 years	36·9	17·3
21–30 "	46·2	39·1
31–40 "	44·8	53·4
41–50 "	70·4	63·6
Over 50 "	39·0	57·4

Anaemia in Relation to Residual Hepatosplenomegaly

The haemoglobin values of the women in Wingei in 1962 have been analysed statistically to discover whether residual enlargement of the liver or spleen after three years of malaria control could be correlated with anaemia. (Among men hepatosplenomegaly had become too rare for this to be done.) Mean haemoglobin values in each age-group were very similar in three categories of women—those without palpable livers or spleens, those with palpable livers only, and those with palpable spleens only (Even these means were 1 g. below those of the European women.) However, Wingei women who had hepatomegaly and splenomegaly together—27% of the total—had mean values significantly lower still.

Discussion

Haemoglobin Values

As parasitaemia decreases, the resulting reduction in malarial haemolysis and bone-marrow depression (Fairley, 1934; Fairley and Bromfield, 1933) should lead to rises in haemoglobin levels unless other factors contributing to anaemia are also present. Inadequate body stores of iron (not attributable to ancylostomiasis in these populations) or chronic protein deficiency, which has been shown by Woodruff (1951, 1955) to be associated with a relatively intractable anaemia in a malarious area of Africa, could be factors limiting the haematological response of the older age-groups in Wingei. It is also possible that intense malarial parasitaemia in early life may produce long-term pathological changes with the same effect.

Malaria control, although it had not completely interrupted transmission in Wingei over three years, had produced significant improvements in haemoglobin values among children of 3 months to 15 years of age. The greatest improvement occurred in the younger children born before malaria control, who, presumably because they had least premunition, had originally suffered from the greatest degree of anaemia. Uninfected children born after the beginning of malaria control had mean values which were normal for their age, but children born before the first spray round had rises every year which had not yet reached normal values after three years. It is quite possible that normal values for their ages will be reached in the fourth or subsequent years.

Falls in parasite rates among children are roughly correlatable with rises in their haemoglobin values, and among infants aged 3 to 12 months in 1962 every case of anaemia was found to show overt parasitaemia. Evidence of other anaemias, such as iron-deficiency (suckling) anaemia, has not been found among these breast-fed infants. Infants less than 3 months of age were not found to be anaemic even when suffering from parasitaemia, probably because of their maternal antibody, their foetal haemoglobin, or the short time they had been infected.

Women in Wingei aged 21–50 years had statistically significant but suboptimal improvement in haemoglobin values during their second year under malaria control, but no further improvement in the third year. It had been found previously (Schofield, 1962) that the stress of pregnancy and lactation among women of this region reduced their malarial premunition, as judged by parasite rates. Bruce-Chwatt (1952) found the same phenomenon in Africa. The beneficial though partial effect on their haemoglobin values of reduction in malarial parasitaemia is quite evident in Table I, and among the pregnant women. This effect on adult women has also been reported by McGregor (1960).

In the case of men and adolescents, either their malarial premunition had reached such a high level before the control programme started that this programme could not materially improve their haemoglobin values, even though it greatly reduced parasite rates, or else these values remained low because of factors other than parasitaemia. It is concluded that malarial parasitaemia among these two groups of people was not the cause of their subnormal haemoglobin levels, which remain about 1.5 g./100 ml. below those of the Europeans. It could be that in the past malaria produced pathological changes which are still contributing to these low values, but, if so, these changes do not appear to be quickly reversible.

Other Effects of Malaria Control

Among Wingei men in 1962 overt parasitaemia did not produce symptoms or lower haemoglobin levels. They cannot, therefore, have lost much clinical premunition in the three years, but their economic capacity, in so far as it is affected by their haemoglobin levels, is unlikely to have been improved by malaria control. This may alter when the boys reach working age.

There is no evidence that individual malarial infections persist for more than three years, except in some cases of *P. malariae* (Black, 1960). Therefore the Wingei parasite rates in 1962 must preponderantly represent new infections acquired during malaria control. As in other control projects in this country, transmission of *P. vivax* has been least affected, possibly because of its comparatively short extrinsic incubation period. The Wingei species ratios for 1962 suggest that few of the new infections had been acquired on journeys beyond the limits of the control project.

Hepatosplenomegaly

Study of Wingei spleen rates shows much smaller falls among women over the age of 30 than among the rest of the population, even though the parasite rates of these women fell rather more than those of the men in the same age-groups. Also, study of the sizes of the average enlarged spleen in Wingei reveals that, although the percentage of adults with enlarged spleens has fallen as a result of malaria control, the average size of all their spleens which were still palpable was no smaller in 1962 than in 1959. It appears that a large proportion of Wingei adults suffer from a splenomegaly which is comparatively irreversible when parasitaemia is reduced. The figures for spleen rates in 1962 show that this type of irreversible splenomegaly is more common among women than among men, the ratio being 2.5 : 1 at 21–30 years and 5 : 1 over 40 years. As a result of the previous study (Schofield, 1962), it is thought these sex ratios are explained by the stresses of multiparity in females.

From the malariological standpoint, as a number of malariologists, including Metselaar (1956), have pointed out, the picture presented by the splenomegaly of adults in holoendemic malarious areas of New Guinea appears to differ from that described from similar areas of Africa. This difference has not yet been studied histologically, nor explained aetiologically.

Black (1954) has described the relation betwen malaria and hepatomegaly in South-west Pacific islanders, and Jansen (1959) and Kariks (1960) have described an association of hepatomegaly with anaemia in New Guineans which is most evident in malarious areas. Palpable-liver rates among adult women in Wingei, which had altered even less than their spleen rates after three years of malaria control, have also been found to be associated closely with the stresses of lactation (Schofield, 1962). (Men over 40 years of age also had no decrease in liver rates, though these were much lower than the women's). These findings contrast with the great decreases in hepatomegaly among younger people, in whom it was reversible and correlatable with parasitaemia. The pathology of reversible malarial hepatomegaly has been described by Walters and McGregor (1960). They believe that chronic malaria will not produce more than a slight degree of periportal fibrosis unless "additional provocation, such as nutritional hepatocellular necrosis" is also present. The great loss of weight found in the child-bearing period of life among women in Wingei and Wam (Schofield, 1962) is evidence that they suffer from nutritional deprivation at that age.

The reversible hepatosplenomegaly which accompanies parasitaemia persists longer than the parasitaemia, and it might be thought, *per se,* to contribute to a more rapid destruction of non-parasitized red cells or to some inhibition of bone-marrow activity. However, it will be noted that Wingei youths and young men had quite large falls in palpable liver and spleen rates between 1959 and 1962 without any significant rises in haemoglobin values. In contrast, among the older women there was a considerable proportion with persisting hepatomegaly and splenomegaly, both together. This condition was significantly associated with even lower mean haemoglobin values than those of the other women, and is probably similar to that found by Woodruff (1951, 1955) in Africa. However, since all groups of Wingei men have shown no improvement at all, and since the women's improvement was limited to the second year of malaria control, it seems evident that at least one additional factor, as already discussed, is materially contributing to the residual anaemia of this population.

Summary

Estimations of mean haemoglobin values, clinical examinations, and examinations for malarial parasitaemia were made in 1959 on two groups of villagers living in similar environments in the Sepik District, New Guinea. Malaria was holoendemic in both areas; some light hookworm infections were found, but they were not significant haematologically. Immediately after the first series of examinations malaria control was extended over one group but not the other. No changes affecting health, apart from the malaria control, were observed in either area for the next three years. The examinations were repeated on the same individuals each year. The changes which were observed in the group under malaria control have been compared statistically with those in the other group. For purposes of comparison, the haemoglobin values of a group of healthy Europeans were determined by the method used in the villages.

Mean haemoglobin values showed statistically significant improvements in the malaria-control area and were inversely correlatable with parasitaemia only among children under 15 years of age and women in the child-bearing period of life. Children up to 10 years of age had steady improvements in haemoglobin levels, but the values among older children and women showed limited rises confined to the second year. Men and adolescents of both sexes had subnormal mean haemoglobin levels which were not significantly improved by reductions in parasitaemia and clinical hepatosplenomegaly.

After three years of malaria control the presence of parasitaemia was correlatable with haemoglobin levels lower than average among children and pregnant and lactating women, but not among the other groups.

Although palpable enlargement of both liver and spleen was found to be reversible and directly correlatable with malarial parasitaemia in the younger age-groups of both sexes, there was much persistent combined hepatosplenomegaly among women which had not been altered by malaria control. This condition was significantly associated with mean haemoglobin levels even lower than those of the rest of the women.

The findings are discussed in relation to malarial pathology and premunition. They suggest that other factors besides overt parasitaemia and hepatosplenomegaly contribute materially to the low haemoglobin values of adults.

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