TABLE III

Degree of Neurological Deficit Before Operation	No.	Degree of Recovery		
		None	Partial	Complete
None or slight	4	—	—	4
Moderate	4	—	2	2
Complete or very severe ..	7	4	3	—

One case in which disability was mainly due to severe trauma of the cauda has been excluded.

Summary

The results in 25 cases of spinal epidural suppuration, with illustrative case histories, are presented. The importance of recognition of the urgency and potential gravity of these cases is emphasized.

The survey indicates that, with early recognition and treatment prior to the onset of gross neurological abnormalities, satisfactory recovery can be anticipated in most cases; while delay until signs of severe cord damage become apparent usually results in permanent, crippling disability.

The most important factor in early diagnosis is an awareness of the possibility of the condition, and an appreciation of the rapidity with which the pathological process advances to an irreversible state.

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LOW GAMETOCYTE THRESHOLDS OF INFECTION OF ANOPHELES WITH PLASMODIUM FALCIPARUM, A SIGNIFICANT FACTOR IN MALARIA EPIDEMIOLOGY

BY

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Malariologists have long been familiar with the inconsistencies experienced when trying to infect anopheles with malaria parasites by feeding them on patients showing falciparum gametocytes—crescents—in the blood. Those subjects with the heaviest infections have not necessarily been the most infectious—in fact, they have sometimes proved completely non-infective. Many of these discrepancies have been attributed to the great disparity in the sex ratio of the crescents, to the possibility that the gametocytes are not “ripe,” and so on. Up till a few years ago, however, it was fairly generally assumed that, as the number of crescents in the blood decreased, a point was eventually reached when low density alone became a limiting factor, the subject becoming non-infective at a time when crescents could still be detected in the blood film without too much difficulty (Boyd, 1949). Those ideas seem to have been so firmly implanted that carriers with very scanty

crescent infections were almost automatically rejected as a possible means of infecting anopheles in the laboratory or in the field.

Martin Young and his colleagues (1948), working with a negro population in South Carolina, showed, however, that those ideas would have to be revised considerably. They were able to infect 10 lots of *Anopheles quadrimaculatus* (nearly half of the total infective lots) at a time when falciparum gametocyte counts were less than 5 per c.mm. Of these, five cases had fewer than one gametocyte per c.mm.; and finally a few mosquitoes became infected at a time when parasites were too scanty to be detected in the ordinary microscopical examination.

Similar observations, although on a much smaller scale, were made with *Anopheles albimanus* and a negro population in Jamaica during 1950 (Muirhead-Thomson and Mercier, 1952). These observations made a particularly deep impression on us, as at that time we were unaware of the findings in South Carolina. After feeding a batch of *A. albimanus* on a 3-year-old subject who had previously been a good carrier and infector, routine examination of the thick film taken at the time of feeding failed to reveal a single crescent, and it was dismissed as negative. The mosquito batch was kept as a matter of curiosity, and one-third of them (12 out of 37) eventually developed gland infections. Later, another subject was found to be infective at a time when only a single crescent was present in over 200 thick-film fields—0.12 crescents per 1,000 leucocytes, or less than 1 per c.mm.

Present Investigation

In the Gold Coast recently this work has been continued more intensively, using laboratory-bred *Anopheles gambiae* and working in an area west of Accra where malaria is hyperendemic. In order to find out the crescent carriers and to determine the gametocyte rate of the village population—that is, the proportion showing falciparum gametocytes in first examination—thick blood films were examined rather more thoroughly than usual, no slide being dismissed as negative until at least 200, and usually more, oil-immersion fields had been examined. The gametocyte rate—or rather crescent rate—of the population examined is shown in Table I.

TABLE I.—Incidence of *P. falciparum* Gametocytes in African Population. Weija, Gold Coast, 1952

Age Group (Years)	No. Examined	No. with Crescents	% Positive (Gametocyte Rate)
0-1	52	21	40.4
2-4	62	16	25.8
5-9	148	22	14.8
10-14	78	9	11.5
15 and over	151	9	5.9

Although the gametocyte rates are rather higher than usual, the general trend is similar to that found by other workers in West Africa (Barber and Olinger, 1931; Young and Johnson, 1949; Bruce-Chwatt, 1951), the higher age groups, 15 years and over, having low gametocyte rates as well as low gametocyte densities. Heavy gametocyte infections were comparatively rare, only 1 out of 491 people examined showing over 200 crescents per c.mm. Shute and Maryon (1951), in a thin-film survey in Lagos, had the same experience, only 2 out of 800 children showing 200 or more crescents per c.mm. Higher figures have been recorded elsewhere (Barber and Olinger, 1931; Robertson, 1945; Bruce-Chwatt, 1951), but they are evidently exceptional.

The actual infectiousness of as many of these crescent carriers as possible was tested by feeding batches of 40–50 laboratory-bred *A. gambiae* on them, blood films being taken at the time of feeding. The mosquitoes were dissected four to seven days after feeding, when falciparum oocysts with their characteristic pigment (Shute and Maryon, 1952) could best be detected in the mosquito stomach. In a few of the more heavily infected batches some of the mosquitoes were kept until salivary gland infections developed.

In all, 73 batches of *A. gambiae* were fed on 32 crescent carriers of all ages from 4 months upward. Of these, 24 batches became infected from 14 carriers.

In previous work in West Africa the lowest thresholds of infection were recorded by Robertson (1945), who found four infections at thresholds below 3 crescents per 1,000 leucocytes; in one batch 1 out of 13 *A. gambiae* being infected when the crescent density was 0.7 per 1,000 leucocytes—that is, less than 5 per c.mm.

In the present investigation, of the total number of batches infected, nearly half (46%) were recorded at crescent densities below 3 per 1,000 leucocytes. On six occasions—that is, 25% of total infected batches—the crescent density at the time of feeding was below 1 per 1,000 leucocytes (Table II).

TABLE II.—Particulars of Mosquito Infections Obtained at Falciparum Gametocyte Thresholds Below 1 Crescent per 1,000 Leucocytes

Age and Sex of Subjects	Crescents per 1,000 Leucocytes	Mosquitoes Dissected	Positive		Mean No. Oocysts per Positive Stomach
			No.	%	
F, 2½ years	0.52	13	3	23	1.7
F, 5 "	0.20	21	2	9	1.5
M, 5½ "	0.27	20	1	5	3.0
F, 9 "	0.26	12	1	8	1.0
	0.10	10	1	10	1.0
M, 10 "	0.16	18	1	6	1.0

The two lowest figures recorded correspond to a density at or below one crescent per c.mm., the first crescent being found only after examination of 300–400 oil-immersion thick-film fields. Those slides would normally have been dismissed as negative for crescents, and it was only the knowledge that the subjects were actually infective to mosquitoes which made the search so prolonged and persistent.

From Table II it will be seen that of the total number of mosquitoes feeding on those subjects with low crescent counts the proportion infected is usually about 10% or less, and that the intensity of infection is also low—from 1–3 oocysts in each positive stomach. These figures will be seen in their right perspective if we compare them with what happens with the most infectious subjects found in this African village survey. In the four most efficient infectors found—whose crescent densities covered a wide range from 1.2 to 24.0 crescents per 1,000 leucocytes (roughly 8 to 150 per c.mm.)—it will be seen from Table III that the number of oocysts per positive stomach remains fairly low.

Of the 87 positive mosquito stomachs in this series, 76 (89%) had fewer than 10 oocysts per stomach, and only 4

TABLE III.—Record of Experimental Feeds on Four Most Infectious Crescent Carriers in Gold Coast Village Survey

Age and Sex of Subjects	No. of Mosquito Batches Fed	Range of Crescent Density during Most Infective Periods (per 1,000 Leucocytes)	Total <i>A. gambiae</i> Dissected	No. with Oocysts	Intensity of Infection. Oocysts per Positive Stomach		
					Max.	Min.	Mean
M, 2 yrs.	1	6.0	18	7	26	1	9.1
M, 3 "	3	1.2–4.1	50	23	28	1	5.7
M, 5 "	7	7.9–24.0	107	39	28	1	5.0
F, 9 "	5	1.7–8.2	97	18	10	1	3.4
			272	87			

(5%) had more than 20. Higher oocyst densities have been recorded elsewhere (Barber and Olinger, 1931; Robertson, 1945), but our own experience is that they are unusual, particularly after a single infective feed.

In comparing the infectiousness of these village subjects showing the lowest crescent densities (Table II) with the infectiousness of the most efficient carriers found in the survey (Table III), we can say roughly that while the best infectors will infect about 30–40% of the mosquitoes feeding on them, and produce on the average about 5 oocysts per stomach, the carriers with the lowest threshold may infect up to 10% of the mosquitoes, and produce about 1–2 oocysts per stomach. The low-threshold carriers are therefore relatively much more infective than we would imagine from their very low gametocyte densities. There is some evidence to show that such a carrier may retain a very scanty crescent infection and at the same time remain infective for long periods.

In discussing these very low gametocyte densities it must be pointed out that, as many of the figures have to be based on the finding of only one or two crescents in several hundred thick-film fields, they may possibly give a misleading idea of the true density not only in the blood film itself but also in the mosquitoes' blood meal. In fact, our findings would be altogether easier to understand if we assumed that at these low densities the distribution of crescents throughout the blood stream is very uneven.

In contrast to these low-threshold, or "cryptic," infectors, our routine tests revealed several striking examples of subjects being non-infective at a time when crescents were abundant in the blood. The most outstanding examples are shown in Table IV.

TABLE IV.—Particulars of Non-infective Feeds at Gametocyte Densities Greater than 3 per 1,000 Leucocytes

Age and Sex of Subjects	Crescents per 1,000 Leucocytes	No. of <i>A. gambiae</i> Found Non-infective
F, 4 months	3.3	22
F, 6 "	4.8	16
M, 2 years	7.7	13
F, 3 "	2.8	15
F, 7 "	3.9	17
F, 7 "	3.1	19

In our investigation in Jamaica (Muirhead-Thomson and Mercier, 1952), the subject with the heaviest infection remained non-infective for several weeks, while Martin Young and his colleagues (1948) report a similar failure with the two patients showing the highest gametocyte count. In this connexion it is interesting to note that in the Gold Coast village survey the highest proportion of non-infective carriers occurred in infants—0–1 year age group—only 2 out of 13 crescent carriers proving infective to mosquitoes. Whether this figure is really representative of that group or whether it is just a sampling error is obviously a point which will require further investigation.

Discussion

The first conclusion from all these findings is that the presence or apparent absence of falciparum gametocytes in routine blood-film examination may really give a very misleading idea of the infective status of the subject. Until further improvements in technique occur, actual infectiousness can be determined accurately only by test feeds with anopheles. In fact, one might go so far as to say that in trying to determine the proportion of malaria infectors in the African or native village community a more accurate picture might be obtained if test feeds were carried out on a large scale, at random, quite irrespective of the blood picture. Obviously, too, in implicating cryptic infectors, the larger the batch of mosquitoes used in the test the better. Even with batches of 40–50 anopheles one might still miss the occasional carrier who infects only 2 to 3% of the mosquitoes feeding on him. How fruitful a line of inquiry this random testing

might be is already indicated by the first tentative tests in the Gold Coast. Out of 28 adults, two young men aged about 20-25 proved infective. In view of the low gametocyte rate of this group, and the low gametocyte densities encountered under hyperendemic conditions, adults have usually been regarded as of negligible importance as a source of malaria infection. As crescent infections may occur at all ages, including the very oldest inhabitants in the community, the usual blood picture may be giving quite an erroneous impression of the infective status of this group.

The possible role of these cryptic infectors as reservoirs of malaria has also to be considered in the light of recent observations on the distribution of anopheles bites and feeds among different human age groups. With both *A. albimanus* in Jamaica (supported by observations on *A. aquasalis* and *A. bellator* in Trinidad) (Muirhead-Thomson, 1951) and *A. gambiae* in West Africa (Thomas, 1951) it has been shown that in general there is a tendency for mosquitoes to obtain the bulk of their blood meals from older children and adults rather than from infants and toddlers. From this it would appear that an adult with a cryptic infection might be a much more important reservoir of malaria than an equally infective baby, the low infectivity being counterbalanced in nature by the greater number of mosquitoes feeding on the adult.

In trying to understand the conditions leading up to malaria epidemics, or even to seasonal waves of malaria, malariologists have long been influenced by the changing gametocyte rate of the human population as found in routine blood-film examination. It is possible that the difficulties they have encountered in trying to explain the discrepancy between low gametocyte rates and densities in the human population on the one hand, and rapidly increasing infection rates among the anopheline mosquitoes on the other hand, might be due to a much higher proportion of the population actually being infective to mosquitoes for the reasons described above.

Frohne *et al.* (1950), for example, have shown in an area in South Carolina that, despite a remarkable reduction in the parasite rate of the negro population in the proportion of 318 to 1 between 1945 and 1948, infections in wild-caught anopheles still persisted. One of the explanations suggested by these workers was that a higher proportion of the human population is infective to anopheles than is indicated by the monthly parasitaemia rates. They were dealing with a strain of *P. falciparum* which had already been shown by Young and his colleagues to be capable of infecting *A. quadrimaculatus* at extremely low gametocyte densities.

Finally, it is interesting to note that these extremely low gametocyte thresholds of infection have been encountered in three different parts of the world, using three different species of anopheles, and probably as many different strains of *P. falciparum*. One feature common to all three investigations is that the human population experimented with has been negro or of negro origin. It might be worth considering how far these results could be influenced by racial characteristics.

Summary

Observations in Gold Coast villages where malaria is hyperendemic have confirmed previous findings in Jamaica, and by American workers in South Carolina, that some carriers can infect anopheles with *P. falciparum* at a time when the density of gametocytes in the blood is so low that they may be detected only with difficulty in routine blood-film examination.

In the Gold Coast experiments these cryptic carriers formed a significant proportion—roughly one-quarter of all infective carriers. This finding, together with the fact that many good crescent carriers are non-infective to mosquitoes, suggests that the blood-film examination may prove a very deceptive guide to the real malaria infectors in the African or native village community.

The implications of these findings are discussed in the light of recent work on the uneven distribution of anopheles bites and feeds among different human age groups.

The work briefly described above forms the first phase of a research scheme carried out under the control of the Colonial Office and the Colonial Medical Research Committee. It is hoped that a more detailed report will be produced at a later date.

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RHEUMATIC HEART DISEASE COMPLICATING PREGNANCY

BY

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Improvements in antenatal and intranatal care over the past 50 years have resulted in a great reduction in the maternal mortality rate. Advances in particular fields have altered the relative importance of many complications, because some which were formerly of the utmost gravity are now more amenable to treatment. The change is exemplified by an analysis of 328 maternal deaths occurring in 128,474 deliveries in the three Dublin maternity hospitals during the decade 1940-50 (O'Driscoll and Quinn, 1951), the chief causes of which were:

Eclampsia	43
Sepsis (usually complicated)	42
Rheumatic heart disease	35
Accidental haemorrhage	32
Post-partum haemorrhage	25
Ruptured uterus	21
Placenta praevia	17
Non-convulsive toxaeemias	15

These figures demonstrate the importance of rheumatic heart disease as a factor in maternal mortality. No reference is made to other forms of heart disease complicating pregnancy, as few cases were seen and none was fatal.

To evaluate the problem of rheumatic heart disease in pregnancy a clinical survey was begun by us in the National Maternity Hospital on January 1, 1948, and, for the purpose of this communication, was concluded on January 1, 1952. During these years 250 pregnancies in 175 patients with rheumatic heart disease were studied. The patients were graded according to the recommenda-