MALARIA IN INDIA: THE SYNTHETIC DRUGS AND THE RELAPSE RATE.

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INTRODUCTORY REMARKS.

This paper deals solely with the malaria statistics of the British troops in India. The average annual strength of these troops is maintained at about 55,000; and the actual number of admissions to hospital for malaria has varied between 18,878 in 1921, and 3,676 in 1934.

This special section of the military population has been singled out because it best lends itself to strict and continuous control, and to statistical accuracy. Its mode of living, working, hospitalization and so forth, are little liable to the influence of factors which lead to fallacies and vitiate conclusions.

Graph I shows the total number of admissions to hospital for malaria, per 1,000 of strength. Inasmuch as the figures are swollen by admissions for relapses, it is not a picture of the admission ratio of infections alone: hence the marked and fairly steady decline may be ascribed to one or both of the following causes:

(a) Decrease in the number of infections (primary and re-infections).

(b) Decrease in the number of relapses.

The object of this paper is not to prove that the incidence of fresh malaria amongst British troops in India has declined—although we have good reasons for the belief that, in all probability, such a decline is in progress. As its title indicates, the object of the paper is to show that, in recent years, a great decrease of relapsing malaria has occurred: that, in view of the progressive improvement culminating in the 1934-35 figures,
this decrease is likely to be permanent, and likely to be still more marked—up to a point—in the future; and that, for this welcome event, the greatest share of the credit is due to new methods of treatment.

For purposes of comparison, the relapse rate in the days when quinine alone was used is of importance. We are not in a position to give a strictly accurate figure, but Manifold (1931) puts the relapse rate at 42 per cent., and Dixon (1933) at about 50 per cent. Those who have had experience of malaria in India a decade ago will agree that even the latter figure is not unduly high. Sinton and Bird (1929) treating 667 patients of the type admitted to the Malaria Treatment Centre (i.e. cases which have relapsed repeatedly in the past), computed the average relapse rate to be 68 per cent.

**DECREASE IN THE NUMBER OF INFECTIONS.**

A decrease in the number of infections may be brought about by several factors of different sorts. Of these, the dominant one is weather.

*Weather* produces a direct effect on malarial incidence for the year, and may produce an indirect effect—on account of aftermath or "carry over"—on the incidence for the succeeding year.

This carry over is, of course, composed almost entirely of relapses.

In 1934, meteorological conditions were not good. For purposes of comparison, their adverse influence on malarial incidence in this year may be evaluated by allotting the empirical figure, 10.1

On this arbitrary basis, the corresponding figures for some of the years preceding 1934 may be set down thus:—

<table>
<thead>
<tr>
<th>Year</th>
<th>Figure</th>
</tr>
</thead>
<tbody>
<tr>
<td>1924</td>
<td>15</td>
</tr>
<tr>
<td>1928</td>
<td>0 (drought)</td>
</tr>
<tr>
<td>1929</td>
<td>17</td>
</tr>
<tr>
<td>1930</td>
<td>5 (about normal)</td>
</tr>
<tr>
<td>1931</td>
<td>5 ⋊</td>
</tr>
<tr>
<td>1932</td>
<td>8 ⋊</td>
</tr>
<tr>
<td>1933</td>
<td>20</td>
</tr>
<tr>
<td>1934</td>
<td>10</td>
</tr>
</tbody>
</table>

Variations in these conditions are reflected in the incidence for 1924 and 1928; but corresponding *pro rata* variations are not registered in other years, notably in 1933.

If the incidence figures on the graph be compared with the above index figures for weather, it will be seen that in later years there is little or no relationship between the two. In the year 1928, parallelism between incidence and weather conforms to type; but thereafter it is surprising how little the incidence seems to have been influenced by weather: where a marked rise in incidence might reasonably be expected, actually the rise is slight, or even absent.

1 This "evaluation figure" method is here employed solely in order to present the subject in as brief and graphic a manner as possible. The figures are based on the reports of the Government of India Meteorological Department; and the effect of weather conditions on malarial incidence in 1932-34 are fully discussed in the War Office Reports on the Health of the Army for these three years.
Taking into account meteorological conditions alone, the incidence of 1929 and 1932 is unduly low, and that of 1933 and 1934 remarkably low.

Next to weather, war and civil disturbances exercise a profound effect because, under their baleful influence, the troops are insufficiently protected and—when infected—not always in a position to receive adequate courses of treatment. Delayed attacks and relapses are rife. For these reasons, the 1921 figure of incidence is very high.

In more recent years, war and civil disturbances—separately or together—broke out in 1930-33: an aftermath from the Mohmand-Bajaur operations was to be expected in 1934; and the Mohmand campaign was conducted in the malaria season of 1935.

It therefore follows that a comparison of the 1919-21 incidence with that of the period 1930-35 is of great interest and importance. It is profitable to speculate on the comparatively low admission rates for malaria in these later years, despite the Service conditions attendant on civil disorders and wars.

The incidence of infections is also more or less influenced by various antimalaria measures, the chief of which is field work.

There is no doubt that from the end of the Great War until about 1931, the quality of minor field work has steadily improved; but since the latter date (when various stringent economies made further progress difficult) a comparatively level standard has been maintained.

In 1928 the Ross Field Experimental Station at Karnal, in the Punjab, began to train, annually, a few selected military medical officers in antimalaria field work. By 1931 the beneficial effects of this special training became evident. They also became stabilized, because officers of the Royal Army Medical Corps left the country on expiry of their tours, while those of the Indian Medical Service were claimed by "civil" from time to time. The supply from Karnal was steady; but it was (and is) insufficient adequately to meet the demand.

Thus it cannot be said that, during the past three or four years, the decline in incidence has resulted from improved field measures of a minor type.

The same remarks apply to major engineering antimalaria works because, in the autumn of 1931, a "cut" of 65,000 rupees (nearly £5,000) in the antimalaria grant all but brought this form of activity to an end; and since then the "cut" has not been restored.

From 1928 to 1931 a certain amount of progress was made with the mosquito-proofing of barracks; but when the economy axe fell it was decided that, in view of financial stringency, no further new works in the direction of the mosquito-proofing of buildings should be undertaken until the situation became more normal.

By 1931, a few of the worst malaria stations had been proofed, with
marked drops in the local incidence of the disease; but the effect of this on
general malarial incidence was small; and, since then, this state of affairs
has remained unchanged.

In 1925, the measure known as "cold storage"—the move of the bulk
of the troops to the hills during the malaria season—was introduced, and
there is little doubt that this was to a large extent responsible for the
decline in malaria which occurred in the ensuing few years. If it were
possible to apply this measure universally, it would of course provide a
complete solution to the malaria problem. Unfortunately it presents
serious administrative difficulties, tends to interfere with training, and has
to take second place to more pressing considerations such as imminent
frontier hostilities. In the last few years, for various reasons, fewer troops
have enjoyed complete protection under this scheme, so that the fall in
admissions seen from 1932 onwards is not to be explained in this way.

It comes to this, then, that while we believe that some decline in the
incidence of infections has occurred in recent years, an examination of the
factors influencing such a decline clearly indicates that the decrease in
the malaria admission rate demands some other, and more convincing,
explanation. This decrease is so great and so steady that, in view of what
has been said above, it cannot be accounted for by a decline in the incidence
of infections alone.

Those who are interested in this subject will find the foregoing
introductory remarks substantiated, and elaborated in greater detail, in the
War Office Reports on the Health of the Army (Section: India); and in
the Annual Reports (Vol. II)1 of the Public Health Commissioner with the
Government of India.

DECREASE IN THE NUMBER OF RELAPSES.

From time to time this question has been the subject of considerable
controversy, and is of much interest because of the claim first made by
Sinton and Bird (1928), and elaborated by Sinton, Smith and Pottinger
(1930), that plasmoquine in combination with quinine exercises a specific
action in reducing the relapse rate of benign tertian malaria. This claim
has been challenged by the Malaria Commission of the Health Organization
of the League of Nations (1933) on theoretical grounds, and also on the
strength of certain results obtained (it would appear) in the treatment of
artificially induced malaria in patients suffering from general paralysis of
the insane.

STAGES IN THE INTRODUCTION OF THE SYNTHETIC DRUGS.

Table I gives in chronological order the various stages which have been
gone through in the adoption of these drugs for use in the Army.

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1 This volume is prepared annually, for publication by the Public Health Commissioner
with the Government of India, by the Hygiene and Pathology Section, Medical Directorate,
Army Headquarters.
### Malaria in India: Synthetic Drugs and the Relapse Rate

**TABLE I.**—Adoption of the Synthetic Drugs in the Army in India, shown in Chronological Sequence.

<table>
<thead>
<tr>
<th>Year</th>
<th>Plasmoquine</th>
<th>Atebrin</th>
</tr>
</thead>
<tbody>
<tr>
<td>1927 onwards</td>
<td>Used experimentally at the Malaria Treatment Centre</td>
<td>Atebrin used experimentally in certain selected hospitals</td>
</tr>
<tr>
<td>1930-31</td>
<td>Used experimentally in certain selected hospitals</td>
<td>Plasmoquine purchased and distributed for general use on an &quot;as required&quot; scale</td>
</tr>
<tr>
<td>1931</td>
<td>A limited quantity of plasmoquine purchased and distributed for general use</td>
<td>Plasmoquine authorised and available on an “as required” scale</td>
</tr>
<tr>
<td>1932</td>
<td>Plasmoquine authorised and available on an “as required” scale</td>
<td>Atebrin used experimentally at the Malaria Treatment Centre</td>
</tr>
<tr>
<td>1933-35</td>
<td>Standard courses of treatment laid down for use in all uncomplicated cases</td>
<td>Limited quantity purchased for use in selected hospitals</td>
</tr>
</tbody>
</table>

**STANDARD COURSES OF TREATMENT.**

The standard courses of treatment adopted for general use in 1933 and slightly modified in 1934 are as follows:—

**Benign Tertian Malaria.**

(1) Atebrin-plasmoquine, consisting of atebrin 0.3 gramme daily, given to alternate cases for five and seven days respectively, and in each case followed by plasmoquine 0.03 gramme daily for five days.

A subsequent instruction—based on certain reports to the effect that atebrin was occasionally slow in controlling the febrile paroxysms—laid down that, if considered necessary, these courses could be preceded by one or two days of quinine treatment.

The year’s experience showed a balance of evidence in favour of the seven-day course of atebrin, which consequently was adopted in 1934.

(2) Quinine-plasmoquine, consisting of quinine 20 grains and plasmoquine 0.03 gramme daily for twenty-one days. This course of treatment was originally recommended by Manifold (1931).

In 1934, a shorter course of fourteen days’ treatment was tried out in Southern Command and Waziristan District.

**Malignant Tertian Malaria.**

(1) Atebrin-plasmoquine as above.

(2) Quinine as considered necessary, followed by a course of plasmoquine: a five-day course of 0.03 gramme daily was recommended, to be repeated at a later date if gametocytes were still present.

**Quartan Malaria.**

Atebrin-plasmoquine as above.

**Mixed Infections.**

According to the special circumstances of the case.
ANALYSIS OF MALARIA STATISTICS FROM JULY, 1934, TO JUNE, 1935 (INCLUSIVE).

(a) Procedure Adopted.—The period from July 1 of one year to June 30 of the next has been arbitrarily selected as representing a malaria year. We recognize that this is open to criticism. Undoubtedly primary cases of malaria occur in some parts of India in June, and to a lesser extent in May. On the other hand, it is equally certain that relapses carried over from the previous year are of relatively common occurrence in May and June; and as it is the object of this investigation to determine relapse rates, and in doing so to avoid anything which might produce an unduly favourable result, it is considered that the above period is, in this respect, the fairest.

It was our first intention to compile tables from reports furnished by hospitals, as was done in previous years. Such tables were actually prepared; but, in checking them, it became obvious that it would be impossible, short of conducting a voluminous correspondence on numerous details, to produce figures of unimpeachable accuracy.

The problem was therefore approached in another way, by means of the statistical cards (A.F. I-1220); and in the tables which follow it is possible to claim accuracy—as far as compilation is concerned—approaching as near to 100 per cent. as is humanly possible. A few details of the methods adopted may be of interest, and will serve to substantiate this claim.

Everyone is familiar with the "Admission and Discharge Book" maintained by each hospital, with its all-important serial number for each patient admitted; and with the statistical card (A.F. I-1220) which is prepared for every entry in the Admission and Discharge Book, and which, among other entries, bears the vital serial number. These cards are sent to Army Headquarters, and are used to prepare the tables embodied in the annual report on the health of the Army. From the monthly returns rendered by hospitals (A.F. A-31) a running review of current happenings is maintained, but this can never have the statistical accuracy of returns prepared from case-cards, nor do the two ever exactly tally.

At Army Headquarters one specially trained statistical clerk has, as his principal duty, the checking of the submission of A.F's. I-1220. For every hospital he maintains a check-sheet, on which are printed serial numbers in the different categories (distinguished alphabetically). As each card is received and verified, the serial number is struck off on the check-sheet. In this way missing and duplicate serial numbers (errors difficult to explain, but of common occurrence) are immediately detected, and hospitals are requested to set matters right. At the end of each year hospitals submit a return showing the last serial number used, from which it can be determined with certainty that a card has been received for every admission to hospital.

Up to this point, i.e. as far as obtaining accurate records from hospitals is concerned, there are two possible sources of error capable of affecting the present investigation.
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The first is the outpatient treatment of cases of malaria, because outpatients are not, of course, shown as admissions to hospital. As far as British troops are concerned (and this paper relates only to them) we have no hesitation in saying that this practice is virtually non-existent. Nowadays it would no more be attempted by the medical officer than it would be accepted by his patients. Further, treatment along these lines would sooner or later produce chronic relapsing cases whose admission to hospital could not be evaded. The fact that cases of this kind are conspicuous by their absence—which will be made clear in the following tables—is in itself proof that this practice does not exist.

The second source of error is the concealment of malaria under such diagnoses as sandfly fever, dengue, intestinal toxæmia, etc. The arguments given above apply equally to this fallacy. Normally, malaria does not undergo spontaneous cure; and subsequent relapses, which could not be overlooked, would sooner or later make the true diagnosis unmistakable. As a matter of fact, perusal of the cards leaves little doubt that the shoe is on the other foot, and that a considerable number of the illnesses diagnosed “clinical malaria” are attributable to wholly different causes.

To return to the question of statistical methods, the checked cards are “coded” and, for purposes of the annual report, “sorted” in a variety of ways which have no bearing on the present inquiry. Ultimately, however, they are arranged in drawers by regiments, corps, or similar formations. As before, this procedure is carried out by a specially trained clerk, and is to all intents and purposes foolproof.

For the purpose of the present investigation all malaria cards appertaining to the selected period were separated from these groups, and arranged, still by regiments or corps, etc., in strict alphabetical order. By this means, all cards relating to the same man were brought together, and were then attached to each other. Up to this stage the sorting and arranging of the cards was carried out, under supervision, by clerks of the statistical section; from here onwards all the work was carried out personally by one of us. Each card was read through and coded to permit of subsequent sorting under the various heads. Each item has been repeatedly checked, and the margin of possible error is believed to be negligible.

As a preliminary step, cards relating to all units which left India in the trooping season 1934-35 were excluded, as the curtailed “follow-up” possible in such cases is not considered adequate. A similar step is not practicable in the case of those men who left India, not in complete units, but in drafts; nor is it possible, without making a heavy imposition on the time and goodwill of other departments, to trace the whereabouts of each individual; but, working on the average turnover, it may be taken that the number leaving India in drafts is approximately 10 per cent. of those remaining. If, therefore, the relapse percentages which are given later be increased by one-tenth, this error will be adequately covered.

In twenty-eight cases the same individual was admitted on two
separate occasions for different types of malaria, i.e. benign tertian on one occasion, and malignant tertian on another. As these admissions occurred at a time when re-infection was possible, they have been treated as separate infections and, for statistical purposes, appear as separate cases in the following compilations.

With this exception, the first admissions to hospital for malaria during the selected twelve months have been taken as the starting point of the observations. All subsequent admissions of the same individual are regarded as relapses. It is beyond question that this procedure worsens the true relapse rate, for it is obvious from the form of parasite found (scanty rings or trophozoites, but no gametocytes) that many second attacks were reinfections and not relapses; but, as selection of cases in this way would inevitably introduce the possibility of error of the "personal" type, the less flattering but uncontroversial method described above has been adopted.

No account is taken of the result of treatment of any admission except the first for each case in this selected period. By disregarding the "cures" which followed the treatment of subsequent attacks, an artificial increase of cases showing no relapse has been avoided. Had the second attack, for purposes of treatment and observation, been regarded as another "case," the relapse rate would have been still further (but fallaciously) decreased. Each individual (except as regards reinfection with a different type of parasite, as mentioned above) appears only as a single case in the tables.

(b) Details of Findings.—The total number of British "Other Ranks" who were admitted for malaria during the period was 2,795. Of these, 323 relapsed, giving a relapse rate of 11.6 per cent. This is a crude figure which embodies several fallacies, and it is given merely for purposes of comparison. It includes cases of "clinical" malaria, a diagnosis which, in an analysis of this kind, is obviously unsatisfactory. It also includes cases admitted and treated for the first time in 1935, some of them "delayed" cases appearing in the early months, others primary cases occurring in May and June. In neither type is a sufficiently long period of observation possible. Finally, it includes three fatal cases, none of whom, it may be mentioned, had been treated with plasmoquine.

All these cases have been excluded from the subjoined tables, which deal exclusively with microscopically confirmed cases of malaria admitted to hospital during the last six months of 1934, and observed until the end of June, 1935. There is thus a minimum period of observation of six months; but, as most cases occurred from July to October, the average period of observation is approximately nine months.

In the tables cases are divided into three categories according to the treatment employed: namely, those which received the standard atebrin-plasmoquine course, those which received the standard quinine-plasmoquine course, and those which were treated by other methods.
In modification of the atebrin-plasmoquine course, quinine was frequently given for a few days prior to beginning atebrin, or for two or three days along with atebrin, the object being to control the fever more rapidly.

The routine quinine-plasmoquine treatment in cases of benign tertian malaria was of fourteen or twenty-one days' duration, in accordance with the experiment which was being made. In malignant tertian malaria any form of quinine treatment combined with, or followed by, plasmoquine is accepted in this category.

Under the third heading are grouped together cases treated by other methods. Of the 188 cases of benign tertian malaria in this group, 101 were treated by one of two special courses which will be detailed later. The remaining 87 cases received various courses of treatment, the majority receiving quinine alone. In most of these cases this treatment was given, not because of any undue severity or peculiarity of the case, but mainly, it would appear, because the medical officer in question lacked faith in the standard treatments. Most of these cases came from stations where malaria is rare, and experience in its treatment slight. The malignant tertian cases in this category were not given plasmoquine.

**BENIGN TERTIAN MALARIA.**

Table II gives the total figures relating to cases of benign tertian malaria.

**Table II.—Relapse Percentages in Benign Tertian Malaria.**

<table>
<thead>
<tr>
<th>Total cases</th>
<th>Atebrin-plasmoquine</th>
<th>Quinine-plasmoquine 14 days</th>
<th>Quinine-plasmoquine 21 days</th>
<th>Quinine-plasmoquine (total cases)</th>
<th>Other forms of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>Rel.</td>
<td>Per cent</td>
<td>Cases</td>
<td>Rel.</td>
<td>Per cent</td>
</tr>
<tr>
<td>1,905</td>
<td>254</td>
<td>13.3</td>
<td>944</td>
<td>106</td>
<td>11.2</td>
</tr>
<tr>
<td>97</td>
<td>12.5</td>
<td>188</td>
<td>51</td>
<td>27.1</td>
<td></td>
</tr>
</tbody>
</table>

The figures shown under the heading "Cases" are those of the total number of individuals admitted to hospital. The relapses comprise those individuals in this group who had one or more subsequent attacks.

The ratio of relapses would be even lower were it not for the very bad results given by two units: the 2nd Royal Scots in Quetta, and the 2nd Green Howards who spent the first part of the year in Poona and thereafter moved to Meerut. For purposes of comparison and discussion, the details of these units, and of certain others stationed in malarious cantonments, are embodied in Table III.

The figures of the Royal Scots and of the West Yorks are in striking contrast. These units lived in barracks which were only a short distance apart, both in an area described in the recent Malaria Survey of Quetta as...
TABLE III.—RELAPSE PERCENTAGES, BENIGN TERTIAN MALARIA, IN CERTAIN SELECTED UNITS.

<table>
<thead>
<tr>
<th>Unit</th>
<th>Station</th>
<th>Atebrin-plasmoquin treatment</th>
<th>Quinine-plasmoquin treatment</th>
<th>Other forms of treatment</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Cases</td>
<td>Rel</td>
<td>Per cent</td>
<td>Cases</td>
</tr>
<tr>
<td>2nd Royal Scots</td>
<td>Quetta</td>
<td>28</td>
<td>8</td>
<td>28.6</td>
<td>63</td>
</tr>
<tr>
<td>1st West Yorks</td>
<td>Quetta</td>
<td>17</td>
<td>0</td>
<td>0</td>
<td>31</td>
</tr>
<tr>
<td>2nd Green Howards</td>
<td>Poona-Meerut</td>
<td>25</td>
<td>13</td>
<td>52.0</td>
<td>3</td>
</tr>
<tr>
<td>1st Royal Warwicks</td>
<td>Poona</td>
<td>12</td>
<td>3</td>
<td>25.0</td>
<td>3</td>
</tr>
<tr>
<td>2nd Essex</td>
<td>Nasirabad</td>
<td>39</td>
<td>4</td>
<td>10.3</td>
<td>43</td>
</tr>
<tr>
<td>1st King’s</td>
<td>Jubbulpore</td>
<td>27</td>
<td>1</td>
<td>3.7</td>
<td>25</td>
</tr>
<tr>
<td>1st K.S.L.I.</td>
<td>Delhi</td>
<td>59</td>
<td>5</td>
<td>8.6</td>
<td>8</td>
</tr>
<tr>
<td>2nd P.W. Vols.</td>
<td>Allahabad</td>
<td>47</td>
<td>3</td>
<td>6.4</td>
<td>40</td>
</tr>
<tr>
<td>2nd H.L.I.</td>
<td>Peshawar</td>
<td>6</td>
<td>1</td>
<td>16.7</td>
<td>0</td>
</tr>
<tr>
<td>1st Hampbieres</td>
<td>Rawalpindi</td>
<td>38</td>
<td>3</td>
<td>7.9</td>
<td>2</td>
</tr>
<tr>
<td>Royal Artillery</td>
<td>Various</td>
<td>249</td>
<td>30</td>
<td>12.0</td>
<td>201</td>
</tr>
</tbody>
</table>

Note.—Multiple relapses, and cases having a first admission in 1935 are shown in this table, the totals in which therefore disagree with Table III.

(F. = fresh infection. R. = relapse.)
20 had malaria in 1933. It might be suggested that most of these cases were relapses from 1933 infections; but against this is the fact that only 7 of the 34 cases suffered from malaria in the January to June period of 1934, which is the season when benign tertian relapses may be expected.

A possible solution emerges when these relapses are classified according to the months in which they occurred. This is shown in Table IV where, for convenience, the Poona figures, which will be discussed later, are also included.

It will be seen that in the case of the West Yorks, the Green Howards, and the Royal Warwicks, relapses occurred mainly in the second half of the period, which is as would be expected. In the case of the Royal Scots, however, most of the so-called relapses were in the first half, and in the following June, i.e. in those months when fresh infections occur. When the state of affairs elsewhere is considered, it is difficult to avoid the conclusion that most of these cases were reinfections, and not relapses; but whether due to some local condition favouring a high carrier rate in the mosquito population, or to lowered resistance resulting from previous infections, it is not possible to say. If these July to December cases are accepted as reinfections and not as relapses, the relapse rate declines to the average level elsewhere.

The Royal Scots' figures are the cause of the high relapse rate for the twenty-one-day course of quinine-plasmoquine shown in Table II. Excluding the Royal Scots, the percentage under this heading for the rest of India is 10.3.

As regards the Green Howards, we have searched in vain for a satisfactory explanation of this unusually large number of relapses. In the January to June period there are not only numerous relapses, but also numerous fresh cases, of which the January ones, at least, must be "delayed" attacks. The picture corresponds exactly with that which commonly follows the liberal use of "prophylactic" quinine, but inquiry has failed to elicit any information to the effect that this measure was employed. The local authorities incline to the opinion that these were reinfections; and certainly climatic conditions in the second half of the period were abnormal, and, for part of the time, within the limits of temperature and humidity in which fresh infection can occur. Further, gametocytes were found in the slides of only 8 of the 22 cases occurring in January to May, inclusive. Nevertheless, we are diffident about accepting this explanation, especially as, in this period, the British cavalry in Meerut had no cases at all; and the Royal Warwicks, who remained in Poona, had results shaping in the same way as the Green Howards.

It is of interest that none of the Green Howards' cases which relapsed

1 We are aware that this is not in conformity with the views expressed by the Malaria Commission, Health Organization, League of Nations, on the subject of immunity in malaria.
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between January and June, 1935, have had any further attacks up to the end of 1935.

The other units from Southern, Eastern and Northern Commands, whose figures are included in Table III, are selected because they have the highest malaria incidence in these Commands. The relapse rates indicate the results which may be expected with these standard courses of treatment under normal Indian conditions. The Burma figures are too small to be worth recording.

In eighteen out of forty-four regiments of British infantry, no cases treated by these standard courses had a second admission for malaria within the period of observation.

The figures of the Royal Artillery are of particular interest, representing as they do the sum of the results in a number of stations throughout the country. The average gunner leads a much more exposed and strenuous life than his comrade in the infantry; he works harder and longer in all weathers and he is largely deprived of the benefits of the move to the hills during the malaria season. These disabilities are reflected in the higher incidence of malaria per 1,000 in the artillery. The infantry and gunner average admission ratios (malaria all types) calculated on official strength returns, are 43.4 and 76 per 1,000 respectively. The slightly higher relapse rate in the artillery is possibly associated: (a) a higher proportion of reinfections; and (b) difficulty in carrying out post-hospital treatment. Even so, the close correspondence between these figures and the all-India average is very striking.

Other Courses of Treatment.

At the request of certain officers who were interested, two special courses of treatment were tried out. The figures which are now given relate only to cases of benign tertian malaria whose first attack in the prescribed period received these special treatments. It is hoped that full details of the experiments will be published in due course by the officers concerned.

The first of these courses was identical with the official atebrin-plasmoquine course, expect that the atebrin was replaced by quinine, either 20 or 30 grains per day being given according to the circumstances of the case. This experiment was carried out with the greatest care. In all, 57 "first attacks of the year" were treated between July and December, 1934. Of these 12, or 21 per cent, had relapsed before July, 1935. In one regiment, where conditions of treatment, etc., were alike for all, 52 cases were treated by atebrin-plasmoquine, and 48 by the above special treatment: of the former only 5, or 9 per cent, relapsed, but of the latter 11, or 22.9 per cent.

The second special treatment was that advocated by Knowles (1931) namely, alkaline mixture followed by quinine ten grains, twice daily for ten days, with plasmoquine 0.01 gramme daily for the last six days.
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In the period under analysis 44 cases were treated in this way, of whom 11 or 25 per cent relapsed.

In both instances, therefore, although the treatment included plasmoquine, the results fall short of those given by the standard courses recommended by Army headquarters.

**Number of Relapses.**

The number of relapses suffered by the 254 cases who had more than one attack is shown in Table V.

<table>
<thead>
<tr>
<th>Number of cases having:</th>
<th>Atabrin-plasmoquine treatment</th>
<th>Quinine-plasmoquine treatment</th>
<th>Other forms of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 relapse</td>
<td>87</td>
<td>81</td>
<td>41</td>
</tr>
<tr>
<td>2 relapses</td>
<td>17</td>
<td>11</td>
<td>8</td>
</tr>
<tr>
<td>3 relapses</td>
<td>2</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>4 relapses</td>
<td></td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

To put this in another way: over 82 per cent of the cases which were not cured by a first course of treatment had only one relapse during a period of observation averaging nine months.

**Seasonal Incidence of Relapses.**

The number of relapses occurring in different months is shown in Table VI.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign tertian</td>
<td>8</td>
<td>29</td>
<td>34</td>
<td>35</td>
<td>29</td>
<td>32</td>
<td>17</td>
<td>21</td>
<td>26</td>
<td>31</td>
<td>25</td>
<td>39</td>
</tr>
<tr>
<td>Malignant tertian</td>
<td>0</td>
<td>4</td>
<td>8</td>
<td>9</td>
<td>8</td>
<td>8</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

Both first and all subsequent relapses which occurred are shown in this table. The significant feature is the absence of any wave of "spring fever." There is no doubt that a proportion of the autumn, May and June cases are reinfections but, with the details at our disposal, this is not capable of proof.

**MALIGNANT TERTIAN MALARIA.**

Malignant tertian malaria is normally less liable to relapse than benign tertian, particularly as far as "long-term" relapses are concerned.
Nevertheless, with only quinine treatment, relapses occurring soon after the primary attack are by no means uncommon. Table VII shows the results obtained by the standard courses of treatment.

Where the number of cases is sufficiently high, the figures of individual regiments—from which this table is compiled—correspond fairly closely with the average in Table VII. The only exception is provided by the 1st Gloucestershire Regiment at Mhow, where seventeen cases occurred with six relapses. It is difficult to discover the exact cause of this but, in view of the uniformly good results obtained elsewhere, it seems probable that it is referable to some local circumstance which is of no general importance.

Table VII.—Relapse Percentages in Malignant Tertian Malaria.

<table>
<thead>
<tr>
<th></th>
<th>Atebrin-plasmoquine</th>
<th>Quinine-plasmoquine</th>
<th>Other forms of treatment</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>216</td>
<td>185</td>
<td>41</td>
<td>442</td>
</tr>
<tr>
<td>Relapses</td>
<td>21</td>
<td>14</td>
<td>4</td>
<td>39</td>
</tr>
<tr>
<td>Per cent</td>
<td>9.7</td>
<td>7.6</td>
<td>9.8</td>
<td>8.8</td>
</tr>
</tbody>
</table>

As previously mentioned, no hard and fast quinine-plasmoquine course for malignant tertian malaria was laid down. The general recommendation made from time to time by Army Headquarters was that, where this form of treatment was adopted, quinine should be given as indicated by the individual circumstances of the case; and should be followed by 0.03 gramme of plasmoquine daily for five days, to be repeated after an interval if gametocytes were still present. This was carried out in a number of cases; in others, either the standard fourteen-day or twenty-one-day course was given; and others were treated by Knowles' method. All patients who were treated with quinine, accompanied or followed by plasmoquine, are shown under this heading.

The results with quinine-plasmoquine treatment appear the most favourable, but the numbers are too small to permit of any definite conclusions being drawn; and it will be noticed that, in the small group of cases treated without plasmoquine, almost equally good results were obtained.

Table VIII.—Number of Times Individual Cases Relapsed: Malignant Tertian Malaria.

<table>
<thead>
<tr>
<th>Number of cases having:—</th>
<th>Atebrin-plasmoquine treatment</th>
<th>Quinine-plasmoquine treatment</th>
<th>Other forms of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 relapse</td>
<td>17</td>
<td>14</td>
<td>3</td>
</tr>
<tr>
<td>2 relapses</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 relapses</td>
<td>1</td>
<td></td>
<td>1</td>
</tr>
</tbody>
</table>
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The number of relapses from which the various cases suffered is shown in Table VIII.

The monthly incidence of all relapses is shown in Table VI. It will be seen that the majority occur between August and December.

QUARTAN MALARIA.

The number of cases of quartan malaria is too small to be of significance, and the figures relating thereto are quoted merely as a matter of interest (Table IX).

<table>
<thead>
<tr>
<th>Table IX.—Quartan Malaria Relapses.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atebrin-plasmoquine treatment</td>
</tr>
<tr>
<td>-----------------------------</td>
</tr>
<tr>
<td>Cases</td>
</tr>
<tr>
<td>17</td>
</tr>
</tbody>
</table>

The three relapse cases remained apparently cured after their second course of treatment.

MIXED INFECTION.

Here also the material is scanty; but the figures, in so far as they go, show a tendency towards a higher relapse rate than occurred in simple infections (Table X).

<table>
<thead>
<tr>
<th>Table X.—Mixed Infection Relapses.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atebrin-plasmoquine treatment</td>
</tr>
<tr>
<td>-----------------------------</td>
</tr>
<tr>
<td>Cases</td>
</tr>
<tr>
<td>24</td>
</tr>
</tbody>
</table>

Of the 9 cases which relapsed, 7 remained free from attacks after their second course of treatment, and 2 were admitted in all 3 times each.

TOXIC SYMPTOMS.

The toxic signs and symptoms noted among these cases are shown in Table XI.
A. C. Amy and J. S. K. Boyd

TABLE XI.—TOXIC SIGNS AND SYMPTOMS WHICH FOLLOWED THE ADMINISTRATION OF THE SYNTHETIC DRUGS.

<table>
<thead>
<tr>
<th>Symptom</th>
<th>After atebrin alone</th>
<th>After atebrin-plasmoquine</th>
<th>After quinine-plasmoquine</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colic</td>
<td>3</td>
<td>17</td>
<td>11</td>
<td>31</td>
</tr>
<tr>
<td>Colic and vomiting</td>
<td>2</td>
<td>-</td>
<td>-</td>
<td>2</td>
</tr>
<tr>
<td>Colic and diarrhea</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Colic and cyanosis</td>
<td>-</td>
<td>3</td>
<td>-</td>
<td>3</td>
</tr>
<tr>
<td>Cyanosis</td>
<td>5</td>
<td>6</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Tachycardia</td>
<td>-</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Transitory albuminuria</td>
<td>-</td>
<td>1</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Haemoglobinuria</td>
<td>-</td>
<td>1</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>6</td>
<td>28</td>
<td>19</td>
<td>53</td>
</tr>
</tbody>
</table>

At first sight this may appear a somewhat formidable list. Actually, however, it is not. In the colic and diarrhoea group there is no evidence whatever that the symptoms were caused by the drugs and, knowing the frequency with which gastro-intestinal disturbances and other minor disorders occur in the soldier in India, it is surprising that a longer and more striking list of signs and symptoms, coincident with these malarial attacks and treatment, cannot be compiled.

In the majority the symptoms were trivial and quickly disappeared. Indeed, were it not for our desire to mention every point of possible interest and relevancy, it would not be necessary to set down any of the items in this list, except haemoglobinuria. In some cases the treatment was not interrupted: in others it was omitted for a day or two until the symptoms subsided. Details of the case of haemoglobinuria are given in the Annual Report on the Health of the Army, 1934, page 127. Of the 53 cases, this is the only one which can be regarded as in any way serious, or calling for special remark.

No cases of “cerebral excitement” of the type described in Malaya have been reported.

Yellow discoloration of varying degrees occurred in a few cases treated with atebrin, but this was not associated with any untoward symptoms.

There is nothing to suggest that the toxicity of plasmoquine was in any way enhanced by being given immediately after a course of atebrin.

*(To be continued.)*