Correspondence.

ATEBRIN AND MALARIA.

TO THE EDITOR OF THE "JOURNAL OF THE ROYAL ARMY MEDICAL CORPS."

SIR.—Using four (4) cases as evidence, and a very incomplete bibliography as support, a contributor to the Journal of the Royal Army Medical Corps, Vol. LXIV, No. 6, June, 1935, summarizes his results thus :—

(1) “A small consecutive series of chronic benign tertian malaria is recorded in which the usual course of atebrin, 0·3 gramme daily for five days, failed in each case to bring about a cure.

(2) Reports are quoted indicating that the simultaneous administration of atebrin and plasmoquin, which theoretically would appear to be therapeutically sound, is not free from risk, the atebrin apparently increasing the toxicity of the plasmoquin.”

Lest some of your readers fail to notice the diminutive proportions of this trial: take for granted that the course prescribed was, in fact, “the usual course,” and accept without question the remark regarding the probable enhanced toxicity of plasmoquine when administered with atebrin ; I crave the hospitality of your columns to beg such readers to be neither misled nor afraid.

The inadvisability of basing a summary such as the above on four (4) cases need only be mentioned to be painfully obvious.

0·3 gramme atebrin daily for five days may be “the usual course” at Aldershot or Abbassia. It is certainly not the usual course at Agra, Alipore or Allahabad.

How anyone could expect to cure relapsing benign tertian with such a course, passes the comprehension of anyone who knows anything about malaria—in India, at any rate.

In itself, plasmoquine is a poison.

No scientific proof has yet been brought forward to show that atebrin enhances the toxic properties of plasmoquine; and opinion in India is far from unanimous that such enhancement actually occurs. Indeed, the supporters of the increased toxicity theory, although at times voluble, are in a minority. They are “inclined to opine,” they “rather think,” etc.; but of proof of any kind, they have none.

A communication issued by Army Headquarters, India, on June 25, 1934, contains the following information :—

(1) “A compilation of the results of the atebrin-plasmoquin treatment of malaria, which has been on trial since April 1, 1933, has now been made with a view to ascertaining the percentage of relapses. In all cases the patient’s history has been very carefully followed up, and any attack of malaria subsequent to the original one for which he was treated by atebrin-plasmoquine has been recorded as a relapse. It will be obvious
that a considerable proportion of these must have been reinfections and not relapses, and the true relapse rate is therefore lower than the figures make it to appear.

(2) Two courses of treatment have been tried, viz. atebrin 0.3 gramme for five days followed by plasmoquine for five days (A course) and atebrin 0.3 gramme for seven days, followed by plasmoquine for five days (B course). In the case of British troops, the daily dosage of plasmoquine was 0.03 gramme. Indian troops were given this dosage until September, 1933, when it was reduced to 0.02 gramme and 0.01 gramme on alternate days.

(3) The results have been compiled under a variety of headings which will be published in due course. The following are some of the principal figures:

<table>
<thead>
<tr>
<th></th>
<th>Cases</th>
<th>Relapses</th>
<th>Per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td>All cases, British and Indian</td>
<td>2,303</td>
<td>294</td>
<td>13.7</td>
</tr>
<tr>
<td>All cases, ‘A’ course</td>
<td>1,376</td>
<td>182</td>
<td>13.2</td>
</tr>
<tr>
<td>‘B’ course</td>
<td>927</td>
<td>112</td>
<td>12.1</td>
</tr>
<tr>
<td>All cases, B.T. malaria</td>
<td>1,603</td>
<td>218</td>
<td>13.6</td>
</tr>
<tr>
<td>M.T. malaria</td>
<td>638</td>
<td>71</td>
<td>11.3</td>
</tr>
<tr>
<td>B.T. cases, ‘A’ course</td>
<td>973</td>
<td>138</td>
<td>14.2</td>
</tr>
<tr>
<td>‘B’ course</td>
<td>628</td>
<td>80</td>
<td>12.8</td>
</tr>
<tr>
<td>M.T. cases ‘A’ course</td>
<td>352</td>
<td>40</td>
<td>11.4</td>
</tr>
<tr>
<td>‘B’ course</td>
<td>276</td>
<td>31</td>
<td>11.2</td>
</tr>
</tbody>
</table>

Certain variations exist between the results in British and in Indian troops, but these are of minor significance and need not be quoted here.

(4) Taking into consideration the fact that reinfections are included in the relapse percentage (and 1933 was a year of high infectivity and high primary incidence in many localities) and that the figures are taken from a large number of hospitals, and not from one or two specially selected hospitals in which conditions are unduly favourable, it is considered that the results are on the whole good. More satisfactory results, especially as far as benign tertian malaria is concerned, have been obtained from the employment of ‘B’ course.

Further and final trials in which atebrin was used on an all-India scale were made during the malaria season of 1934. The experimental-statistical period, open on July 1, 1934, and the “follow-up” did not expire until June 30, 1935.

The results have been received at Army Headquarters, but they have not yet been fully tabulated and analysed. Already, however, it is evident that these results are as good as those of the 1933 trial quoted above.

The War Office Annual Report on the Health of the Army is available to all. Those of your readers (including, I hope, your Aldershot contributor) who are interested in this subject are referred to the report for 1932, pp. 108 and 109; and to the report for 1933, pp. 110 to 112.
Correspondence

It will be found that the report for 1934, when published, confirms India's previous experience of, and results with, the use of atebrin in malaria.

The following extracts contrast violently with your contributor's results:

(a) From the Annual Report of the D.A.D.P.—1934, Madras District:

"It seems clear that fresh cases of malaria are very rarely, if ever, contracted in the military cantonments of the Madras District. *A. subpictus* and *A. fuliginosus* have been identified in Madras and Bangalore, but none of the anophelines usually recognized as carriers.

Analysis of all the cases in the Q.V.O. Madras Sappers and Miners, Bangalore, the largest source of our malaria figures, shows that every case except one was admitted to hospital within a week of returning to Bangalore either from leave to his home, camp duty, or duty in frontier stations.

The treatment of these cases by plasmoquine and quinine or plasmoquine and atebrin, as per D.M.S. Circulars, has been so successful that there has been no relapse for two years in a total of 112 cases. The absence of any possibility of local reinfection makes Bangalore very suitable for judging the results of treatment."

(b) From the Annual Report of the Medical Transactions, 1934, Indian Military Hospital, Quetta:

"All cases this year treated with atebrin-plasmoquine course, as laid down by Army Headquarters No. Z-10453/43 (D.M.S.3).

The results of this treatment have been most satisfactory. The relapses after completing the course have been as follows:

<table>
<thead>
<tr>
<th>M.T.</th>
<th>B.T.</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>14</td>
</tr>
<tr>
<td></td>
<td></td>
<td>20</td>
</tr>
</tbody>
</table>

It would appear, therefore, that only 2 per cent relapsed after the atebrin-plasmoquine course. These are astonishing figures but have been carefully checked."

Dozens of similar reports could be quoted, and the temptation to bombard your contributor with them is great; but perhaps enough has been said to preface the following summary of opinion in military medical circles in India, regarding atebrin:

(1) In therapeutic effects, there is not much to choose between atebrin and quinine. It is probable that, in some cases, the initial action of the former administered *per oram* is slower than that of the latter; but that is a minor and still debated point.

(2) Is atebrin a more efficient sterilizer than quinine? Does atebrin treatment result in a lower relapse rate than treatment by quinine?

Although it is believed that atebrin is as effectual in practice as is quinine, we cannot say that it is a better drug in either of the above respects.
Correspondence

(3) In itself, atebrin is not toxic; and so far, absolutely no proof has been produced to show that it enhances the toxicity of plasmoquine.

(4) A course of atebrin-plasmoquine treatment is considerably shorter than an equally efficacious course of quinine-plasmoquine. In the interests of the patient, his attendants and the State, this is a point of major importance.


I am, etc.,

A. C. Amy,
Colonel.

Simla,
July 15, 1935.

CHRONIC RELAPSING MALARIA.

TO THE EDITOR OF THE "JOURNAL OF THE ROYAL ARMY MEDICAL CORPS."

SIR,—In the British Medical Journal of July 27 there is a report of a conference of consultants on ex-Service cases. The consulting physician to the British Army, in his remarks, referred to the common occurrence of officers and men reporting that they were suffering from malaria contracted ten or fifteen years ago, when they were really suffering from a cold or influenza.

Colonel Heatly-Spencer further remarked that he believed there was no such thing as chronic relapsing malaria lasting for many years after the person had left the tropics. I should like to comment on this remark:

(1) Why the tropics? The greater part of India is outside the tropics. But it is, perhaps, unfair to criticize an apparent slip of the tongue.

(2) What period does Colonel Heatly-Spencer mean by the term "many years"? Would seven or eight years be included in the term? If the answer to the latter question is "Yes," my experience is at variance with Colonel Heatly-Spencer’s dictum.

During about five years, from the summer of 1922 onwards, when I was pathologist to the Ministry of Pensions Hospital, Bath (including the whole of the South-Western Pensions Area), there was a very considerable number of cases of relapsing malaria, gradually getting less, it is true, but still to me a surprising number in the first three years (1922-24).

Unfortunately I have no records, but my recollection is that most of the cases were infected in Macedonia, Palestine, Irak or India. Certainly all of these cases were relapses after at least five years, and more probably after seven or eight years.

44, Combe Park,
Bath.
July 28, 1935.

I am, etc.,

J. Cowan,
Lt.-Col. (Retired).