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NOTES
ON
THE TREATMENT OF MALARIA OCCURRING IN INDIVIDUALS RETURNING FROM SERVICE IN MALARIOUS AREAS, 1944

By Command of the Army Council,

H. Pownall.

THE WAR OFFICE,
29th February, 1944.

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I.—Introductory.

Cases of malaria are likely to occur among officers and soldiers who have returned to this country from service overseas in a malarious country. Attacks may be relapses of a previous recognised infection or they may be primary, especially in those in whom infection may have been kept in abeyance by prophylactic treatment while in the endemic area. In the latter instances a history of a previous attack may not be obtained, and the onset of the attack may be delayed for months after the cessation of prophylactic treatment.

The necessity for early recognition and adequate treatment of cases of malaria is very great, and the possibility of malarial infection should be remembered in cases of pyrexia without obvious cause, especially if associated with shivering, vomiting and subsequent sweating, where there is a history of recent service in a malarious area.

A high percentage of cases may be of the malignant tertian variety, in which severe symptoms may suddenly supervene at the onset or later in the attack.

Exact diagnosis of malaria can be made only by the microscopical demonstration of the parasites in the blood, but, in the presence of clinical symptoms, the lack of facilities for microscopical examination should never cause delay in treatment. Before the exhibition of anti-malarial remedies, blood-slides (thick drop and film) should be made for subsequent confirmation of diagnosis by microscopy.

The notes which follow detail lines of treatment based on army experience, and they have been framed for the guidance of all those who may be concerned in the treatment of cases. Alternative lines of treatment are given to meet circumstances where certain remedies are not available, but it is to be remembered that the Standard Treatment detailed below is that found to be best in the alleviation of symptoms *and* in prevention of relapse, and is the line recommended whenever possible.

II.—Anti-malarial remedies.

Drugs employed fall into two groups :—

Group A.—Anti-symptomatic, anti-pyretic and for treatment of the acute attack.

1. Certain salts of Quinine.
2. Mepacrine hydrochloride, B.P. or Quinacrine hydrochloride, U.S.P. (Proprietary names include Atabrin, Atebrin, Quinacrine, Chinacrine, etc.).

Group B.—Anti-infective and anti-relapse, for treatment *after* the acute attack.

1. Pamaquin, the British equivalent of Plasmoquine (German).

Exhibition of Group B should *follow* exhibition of Group A.

Mepacrine and Pamaquin should *never* be administered *concurrently*.

In Group A, Quinine and Mepacrine are practically alternatives. Quinine may aggravate or cause vomiting, rarely, quinine idiosyncracy is encountered, but it has a more rapid anti-pyretic action than Mepacrine. Mepacrine may cause unimportant yellow staining of the skin and urine, acts more slowly on the pyrexia than Quinine, but does not cause vomiting, and idiosyncracy is not encountered.

III.—Standard Army Treatment of Malaria.

Days 1 and 2:—
Quinine bisulphate *or* Quinine hydrochloride, grains 10, in solution, in one fluid ounce of water, by mouth, three times in 24 hours.

Days 3, 4, 5, 6 and 7:—
Mepacrine hydrochloride, 0·1 gramme tablet, three times a day, swallowed whole with a draught of water, after food.

Days 8 and 9:—
No anti-malarial drug treatment.

Days 10, 11, 12, 13 and 14:—
Pamaquin, 0·01 gramme tablet, three times a day, after food.

Note.—Quinine dihydrochloride (acid hydrochloride of quinine), or Quinine sulphate, in dosage of 10 grains, may be used in place of the salts mentioned above, but the dihydrochloride is more unpleasant to taste and the sulphate requires the addition of one minim of Dilute Sulphuric Acid (B.P.) or of 3 grains of Citric Acid per grain of the quinine salt in order to effect solution.

IV.—General Treatment.

(1) The diet should be fluid until two days after the fever has subsided. Dehydration from excessive sweating calls for extra fluid by mouth or, in severe cases, saline by the rectum or intravenously.

(2) The patient should be kept in bed during the febrile period and for three or four days after pyrexia has subsided. He should remain in bed during the exhibition of Pamaquin.

(3) After the first dose of Quinine, Calomel, 2 grains, followed by a dose of sodium sulphate clears the bowel and aids the absorption of Quinine. Throughout the course of treatment a regular action of the bowel should be maintained by the daily administration of a moderate dose of sodium sulphate.

V.—Special Symptoms.

(1) **Vomiting.**—This may be due to the disease or to Quinine. If the first dose of Quinine is vomited, a second dose, given at once, is often retained. If the vomiting is due to the Quinine, this may be replaced by Mepacrine in dosage of 0·1 gramme tablet three times a day, but its effect on the initial pyrexia is often slow. Adrenalin hydrochloride, 10 to 20 minims of a 1/1,000 solution, in half an ounce of water, given hourly by mouth, may effectively control vomiting to permit of retention of Quinine by the mouth. If, after three or four doses, it fails to stop vomiting, recourse must be had to intramuscular or intravenous injection of Quinine as described below.

(2) **Cerebral Symptoms.**—Especially in malignant tertian malaria, severe symptoms, stupor, delirium, coma or epileptiform seizures may occur at the onset or in the early days of an attack. These require prompt and energetic treatment by either intramuscular or intravenous Quinine injections if life is to be saved.

(3) **Collapse or Algid Symptoms.**—Also in malignant tertian infections, collapse cases with symptoms of shock, and, it may be, with frequent watery purging, are met with. These, as well as cases showing dysenteric or other haemorrhagic syndromes, require urgent treatment by injection.

It is to be remembered that a patient seen during the early stages of an acute attack of malaria may feel and look very ill, may have a high temperature, be suffering from nausea and vomiting, and in a few hours be comparatively comfortable again with little or no treatment. Judgment, therefore, must be exercised in deciding to have recourse to injection therapy, but in all cases of doubt resort should be made to this method.

VI.—Intramuscular Injection of Quinine.

This route of administration is indicated in heavy infections, particularly with the small ring-forms of malignant tertian malaria, and also at the onset of the severe symptoms mentioned above. As a rule, one or at the most two or three injections are necessary. They should be given at intervals of twelve hours, and return to the oral route should be made as soon as possible.

Dosage and Technique.—Dissolve 7½ grains of Quinine dihydrochloride by boiling in 45 minims of distilled water, and after cooling, inject the solution intramuscularly into the gluteal muscles. The site of injection should be about three inches below the iliac crest and well away from the sciatic nerve. As a preliminary, the skin should be thoroughly cleansed, and the outside of the needle well dried with sterile cotton wool, and, after injection, the part should be gently massaged and the puncture sealed with collodion. Absolute asepsis is essential.

VII.—Intravenous Injection of Quinine.

This is reserved for cases of great urgency or for cases of very heavy infection with malignant tertian malaria in which it may be the only means of saving life, by reason of its powerful and rapid action. It should never be used as a routine, and there are definite dangers attendant upon its use. The most noteworthy of these are :—

(1) A fall in blood-pressure which may result in syncope or collapse in a patient already severely shocked.

(2) Fatalities most frequently follow upon too rapid injection of quinine.

(3) The quinine solution often causes thrombosis and occlusion of the vein.

Dosage and Technique.—The salt of Quinine used is again the dihydrochloride in dosage of 7½ to 10 grains, dissolved in 20 c.c. of sterile normal saline, boiled or autoclaved before use, cooled to body temperature and injected *very slowly*, at a rate of not more than 2 c.c. a minute, into the vein at the bend of the elbow. In very heavy infections and in severely ill and collapsed patients quinine usually gives the best results when administered in a large amount of fluid, say 200 to 300 c.c.

As a general rule, not more than *one* intravenous injection should be given. This may be followed by one or more intramuscular injections at 12- to 24-hour intervals, as the course of the disease may indicate. Return to the oral route should be made as soon as the patient's condition permits.

For use in both intramuscular and intravenous medication, sterile ampoules of suitable quinine solutions may be available and are more convenient than the making up of solutions as required.

VIII.—Suggested Course if Mepacrine is not available.

Give 10 grains of quinine, in solution, by mouth three times a day, after food for 7 days, combined with 0·01 gramme of pamaquin three times a day during the last 3 days of this treatment.

To conserve the supply of quinine it is, however, important that the combined quinine, mepacrine, pamaquin course as laid down in Section III should, whenever possible, be employed.

IX.—Anaemia.

Anaemia is common after an attack of Malaria and is best treated by massive doses of iron (ferrous sulphate).

Note.—As an alternative to *intramuscular* injection of Quinine, a soluble preparation of Mepacrine may be employed. A suitable preparation is Mepacrine methane sulphate B.P. (Proprietary names include Atebrin musonate and Quinacrine soluble).

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