The Management and Treatment of Malaria

H.M. Gilles,
B.Sc., M.D., D.Sc. (Hon. Causa : Malta),
M.Sc. (Oxon.)., F.R.C.P. (Lond.), F.F.C.M. (U.K.)., F.M.C.P.H. (Nigeria)., D.Med.Sc. (Hon. Causa : Karolinska Institute, Stockholm)., D.T.M. & H.
Emeritus Professor of Tropical Medicine, University of Liverpool.
Formerly Professor of Tropical Medicine, and Dean, Liverpool School of Tropical Medicine.

The package tour holiday industry, the expansion of international trade and the speed of travel are all playing a major role in the problem of 'imported diseases', especially as tourists are becoming increasingly adventurous and travelling to more remote and exotic places year by year.

Of all the travel-associated diseases malignant tertian malaria due to *Plasmodium falciparum* is the most important. There is no other 'tropical' illness that changes so dramatically from a relatively benign infection to a catastrophic and fatal one in the space of a few days. In 1987 in Britain, 7 deaths due to *P.falciparum* were recorded and up to July 1988 already 3 deaths had occurred. All the fatalities were due either to misdiagnosis or delayed treatment. Unless practitioners become aware of this problem, however rare in their experience it may be, unnecessary deaths will continue to occur. The simple *routine* habit of eliciting a recent geographical history has yet to become accepted good medical practice in many non-endemic malarious areas of the world. *Unde Venis viator et quo vadis?*[1,2]

'Airport' malaria is now well documented[3]. It occurs in persons working or living near airports, recipients of flights from Africa in particular.

Chloroquine and indeed multidrug resistant malaria is one of the most worrying developments of recent years, especially as it has now established a firm foot-hold in Africa South of the Sahara, in several countries where *P.falciparum* transmission is hyperendemic, and basic health services relatively poorly developed.[4]

The chemotherapy and management of malaria have recently been reviewed.[5,6,7] The approach is a two-pronged one - chemotherapeutic and supportive - both are equally important, and common errors should be avoided.

a. COMMON ERRORS IN THE MANAGEMENT OF SEVERE P. FALCIPARUM MALARIA.

1) Failure to take a travel history
2) Assumption that chemoprophylaxis is completely protective
3) Failure to consider 'induced' malaria - i.e. blood transfusion and contaminated needles
4) Misjudgment of severity
5) Poor standard of laboratory diagnosis
6) Missed hypoglycaemia
7) Errors of fluid and electrolyte balance
8) Inadequate nursing care
9) Failure to control convulsions
10) Failure to recognise and treat severe anaemia
11) Use of potentially dangerous ancilliary therapies, e.g. corticosteroids, heparin
12) Delay in starting haemo or peritoneal dialysis

b. THE MANAGEMENT OF THE SEVERE MANIFESTATIONS OF FALCIPARUM MALARIA IS GIVEN IN TABLE 1.

Table I. Severe complications of falciparum malaria and their management (After WHO 1989 - in press)

Complication	Management*
1. Coma (cerebral malaria)	Maintain airway, nurse on side, exclude other treatable causes of coma(e.g., bacterial meningitis). Avoid harmful adjuvant treatments such as corticosteroids, heparin and adrenaline.
2. Hyperpyrexia	Tepid sponging, fanning, dipyrone injection.
3. Convulsions	Maintain airway, diazepam or paraldehyde injection (Prevent with phenobarbital intramusculary - 3.5 mg/kg one single dose on admission)
4. Severe anaemia (packed cell volume less than 20%)	Transfuse fresh whole blood or packed cells
5. Acute pulmonary oedema	Prop up at 45°, give oxygen, venesect 250 ml of blood into donor bag, give diuretic, stop intravenous fluids.
6. Acute renal failure	Exclude dehydration: strict fluid balance, peritoneal dialysis (haemodialysis if available).
7. Spontaneous bleeding and coagulopathy	Transfuse fresh whole blood, vitamin K injection.
8. Metabolic acidosis	Exclude or treat hypoglycaemia, hypovolaemia and Gram-negative septicaemia. Give oxygen.
9. Hypoglycaemia	Give 50% dextrose injection followed by 5% to 10% dextrose infusion.
10. Gram-negative septicaemia ("Algid malaria")	Give parenteral antimicrobials, correct haemodynamic disturbances.
11. Aspiration pneumonia	Give parenteral antimicrobials, change position, physiotherapy, give oxygen.
12. Hyperparasitaemia (> 20%)	Exchange transfuse 4 or more units of fresh whole blood

It is assumed that quinine or chloroquine infusion will have been started in all cases.

c. ERRORS OF ANTIMALARIAL CHEMOTHERAPY

1) Delay in starting treatment
2) Incorrect dosage
3) Inadequate dosage
4) Inappropriate route of administration e.g. "bolus" injection intravenously
5) Failure to control the rate of intravenous infusions
6) Failure to switch patients from parenteral to oral therapy as soon as they can swallow

d. THE CHEMOTHERAPY OF P. FALCIPARUM MALARIA[8]

Quinine is the treatment of choice:-

(i) In areas of the world where chloroquine resistance is established or suspected
(ii) In cases of doubt as to the origin of the malaria or the existence of resistance
(iii) Where malaria has been acquired despite chloroquine prophylaxis.

The drug is given *orally* in uncomplicated cases or by slow intravenous infusion in severe malaria.

Chloroquine is an effective treatment if the parasite is fully sensitive to the drug. Unfortunately, in many of the malarious countries this is no longer the case. However, if the cinchonal alkaloids - quinine or quinidine - are not available, chloroquine can be life-saving since it will reduce parasitaemia if resistance is at the RI or RII level.

Antimalarial chemotherapy is summarised in Table II.

NOTES

1. For *P.vivax* and *P.ovale* infections add primaquine, 15 mg daily for 14-21 days
2. Sulpha-antifolate resistance is widespread, therefore check current pattern of drug resistance.
3. Tetracycline should not be given to children under 8 years or pregnant women.
4. Quinidine can be substituted for quinine. ECG changes (prolongation of the QT interval) and hypotension will occur, so these effects should be monitored.
5. A loading dose should not be used if quinine has been given in the previous 12 hours.

As soon as the patient can swallow tablets quinine 600 mg (salt) 8 hourly for 7 days should be substituted or preferably an oral dose of 1000 mg (salt) of mefloquine is given either as a single dose or in two divided doses 500 mg each dose at an interval of 6 hours. The latter regimen may reduce the possibility of vomiting.

CHEMOPROPHYLAXIS

Several basic points must be emphasized -

1. It must never be assumed that chemoprophylaxis, even when taken regularly, will always protect against malaria - protection is relative. Thus, every non-immune person residing temporarily or for longer periods in a malarious area must be warned that, if he feels ill, malaria must still be excluded as a possible diagnosis. This is particularly relevant because of the spread of resistance to many antimalarial drugs and the absence of accurate and comprehensive maps of the distribution of resistance to the antimaliarials in current use. Evidence of resistance based on 'clinical' experience often without concomitant and competent microscopic diagnosis of malaria has aggravated an already complex situation.

2. Accept with the greatest scepticism that any potentially malarious area is free from risk. Anecdotes that in West Africa, for example, cities are malaria free are quite inaccurate.

3. Malaria can be acquired at relatively short stops on a journey, for example, while refuelling the aeroplane.

4. It is important to have adequate blood levels of antimalarials by the time a person is at risk. This can be achieved by taking a dose the day before departure. Despite this, it is considered wise to begin antimalarials 1 week before travelling in order to get used to the habit and to detect rare cases of idiosyncrasy.

5. Antimalarial chemoprophylaxis must be continued for 4 weeks after returning from an endemic area and the need to continue must be stressed.

6. It is important to remember that *P.falciparum* can recrudesce for 1 year and *P.vivax* up to 5 years. Any fever occurring during this period should be suspected to be malaria until the contrary is proved, irrespective of whether the person has been on chemoprophylaxis or not.

7. Special risk groups, such as pregnant women, infants, over 70 year old, immunodeficient patients or those on other long-term medication, should seek up-to-date advice on the appropriate prophylaxis from specialized centres in their respective countries.

The regiments for chemoprophylaxis currently recommended in Britain are given in Table III.

Table II. Antimalarial drugs for the treatment of malaria in adults

Uncomplicated infections (able to swallow tablets)
Chloroquine-sensitive areas (and areas of *Plasmodium vivax, Plasmodium ovale*[1] and *Plasmodium malariae*)
Chloroquine base, 600 mg immediately, followed by chloroquine base, 300 mg 8 hours later and daily on days 2, 3 and 4

Chloroquine resistant areas
(1) Quinine 600 mg (salt) 8 hourly for 7 days plus single dose of Fansidar 3 tablets, i.e. (Sulfadoxine 1500 mg + pyrimethamine 75 mg)[2]
OR
(2) Quinine, 600 mg (salt) 8 hourly for 7 days plus tetracycline[3], 250 mg 6 hourly for 7 days
OR
(3) Mefloquine, 1000 mg (salt) single dose

Complicated infections
Chloroquine-sensitive areas
Chloroquine 5 mg base/kg i.v. infusion given over 4-6 hours, every 12 hours (total dose 25mg/kg)

Chloroquine-resistant areas
Quinine dihydrochloride[4] 20 mg salt/kg loading dose[5] i.v. infusion given over 4 hours, followed by 10 mg/kg i.v. infusion given over 4 hours every 8 hours (intramuscular injection into the lateral thigh can be used if intravenous infusion is impossible).

Table III. Chemoprophylaxis regimens for short-term (< 4 weeks) travellers

Countries where Plasmodium falciparum is sensitive to chloroquine
(North Africa[1], the Middle East[1], and Central America)
Chloroquine, 300 mg base (2 tablets) once weekly
OR
Proguanil hydrochloride, 200 mg daily

Countries where Plasmodium falciparum is resistant to chloroquine
(all countries except those above and the 'hard-core' countries below)
Chloroquine, 300 mg base (2 tablets) once weekly (for *P.vivax* infections) plus proguanil hydrochloride, 200 mg daily

'Hard-core' Plasmodium falciparum multidrug resistant countries
(Thailand, Laos, Kampuchean border areas, South Vietnam, Papua New Guinea, rural areas of the Philippines)
Pyrimethamine plus dapsone (Maloprim), one tablet weekly plus chloroquine, 300 mg base (2 tablets) weekly
OR
Mefloquine (if available), 250 mg once weekly

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NOTE

1 Malaria transmission in North Africa and the Middle East is low, focal, seasonal and predominantly due to *P.vivax*. Chemoprophylaxis is not essential providing prompt treatment is sought in the event of an illness occurring 10 days after exposure.

Long-term travellers and non-immune residents of malarious areas should follow the same regimen as 'short-term' travellers unless advised otherwise by the competent authorities in the countries concerned.

SELF TREATMENT

Under certain conditions self-treatment is not only permissible, but justified. It is mandatory, however, that this practice should not be abused. Standby antimalarial agents for 'self-treatment' are pyrimethamine plus sulfadoxine (Fansidar), or in very special circumstances mefloquine (if available). Treatment for malaria should not be considered until at least 10 days have elapsed after entering an endemic area (the incubation period of *P.falciparum* malaria is usually 10-12 days).

PERSONAL PROTECTION

Personal protection has become as important as taking antimalarial drugs. Some basic measures for reduction of exposure to mosquito bites are:

Use of mosquito nets
Screening of houses
Use of repellants
Spraying of rooms before retiring to bed
Use of mosquito coils
Adequate clothing (e.g. long sleeves and trousers in the evenings)

SUMMARY

A review of the modern management and chemotherapy of malaria, the most important parasitic disease in the world.

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