Regular Review

Diagnosis and treatment of malaria in Britain

Malcolm Molyneux, Ray Fox

In the tropics malaria is a major killer, especially of young children in areas of intense transmission of *Plasmodium falciparum*: there may be a million or more such deaths in Africa every year.[1] In parts of the world with no transmission of malaria (fig 1) returning travellers and visitors, infected elsewhere, continue to develop the illness. Twelve patients died of malaria in Britain in 1991; 10 died in 1992.

Of the four species of plasmodium that commonly cause human infections, one—*P falciparum*—is responsible for nearly all malaria deaths. The others—*P vivax*, *P ovale*, and *P malariae*—cause febrile illnesses that are troublesome but rarely fatal. The increased incidence of "imported" malaria in Britain since the 1970s has been due largely to a steady increase in the incidence of *P falciparum* infections (fig 2).

Several factors have combined to increase the problem of imported malaria in Britain and other industrial nations: increased travel (more malaria infections); increasing resistance of *P falciparum*,[2] and recently of *P vivax*,[3] to chemoprophylactic drugs (more infections progressing to disease); inadequate or neglected travel advice (more infections and disease); and delayed diagnosis and treatment (progression of falciparum malaria to life threatening disease).

Making the diagnosis

TRAVEL HISTORY

Clinical presentations of malaria are varied and non-specific: taking a travel history should therefore be a routine part of all medical interviews. There are several main points to remember.

A brief visit to an endemic area is sufficient for exposure to infection—even touchdown at an airport without change of planes ("runway malaria"[4]) might be enough.

Malarial illness may be delayed until several weeks or months after exposure (rarely, up to a year for *P falciparum* and several years for the others).

Frequent travel to endemic areas does not convey useful immunity against malaria (box).

In countries where it is endemic malaria is not transmitted uniformly. An immigrant from such a country may not have acquired immunity and may be susceptible to severe malaria.

Even in people with acquired immunity, that immunity is partial and wanes with time. Immigrants resident for some years in Britain who then visit their home country are at risk of severe malaria. (They accounted for 36% of the cases of falciparum malaria and 56% of other malarias reported in Britain in 1991.)

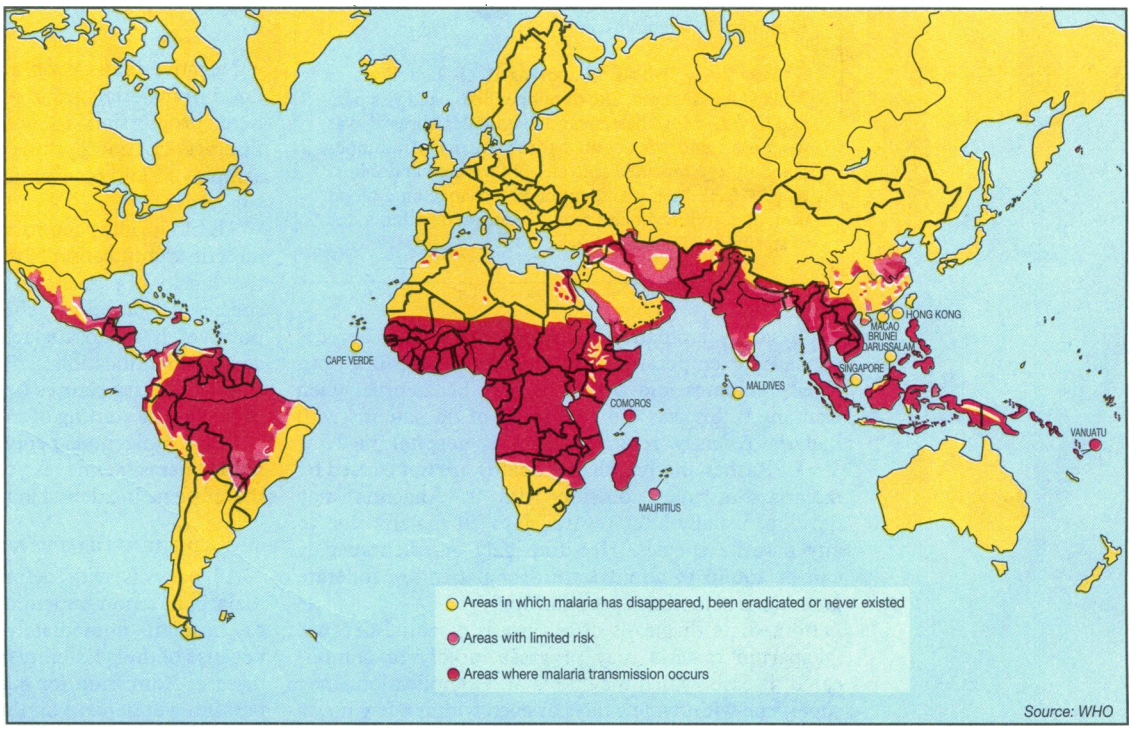

FIG 1—*Status of malaria, 1990. Source: Weekly Epidemiological Review 1992;66:160*

Liverpool School of Tropical Medicine, Liverpool L3 5QA
M E Molyneux, *senior lecturer*

Regional Infectious Diseases Unit, Fazakerley Hospital, Liverpool L9 7AL
R Fox, *senior registrar*

Correspondence to:
Dr Molyneux.

BMJ 1993;306:1175-80

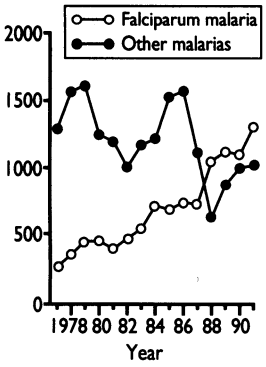

FIG 2—*Number of cases of malaria diagnosed in Britain, 1977-91, and reported to Malaria Reference Laboratory, London School of Hygiene and Tropical Medicine*

Absence of a history of travel greatly reduces the likelihood of malaria but does not exclude it. Occasional small outbreaks of "airport malaria" have occurred near international airports, transmitted in suitably warm weather by "commuter mosquitoes."[5] Malaria should be considered in the differential diagnosis of a fever after blood transfusion, organ transplantation, or needlestick injury and in a neonate or infant whose mother travelled in pregnancy.

Frequent travel and malaria

A British businessman who had visited several sub-Saharan African countries every year for 26 years returned from one visit with fever and chills. He had not taken chemoprophylaxis, believing that by now he was immune to malaria. He delayed reporting his fever for three days, developed cerebral malaria with renal failure, and required three weeks in intensive care.

CLINICAL FEATURES OF UNCOMPLICATED DISEASE

Malaria cannot be diagnosed with confidence on the basis of clinical features alone; nor can uncomplicated falciparum malaria be distinguished from illness due to any of the other three species of plasmodium causing human disease.

The usual symptoms are non-specific: fever, malaise, headache, myalgia, sweating. Influenza is the commonest misdiagnosis in patients with malaria. The classic periodicity of malarial fever cannot be recognised with the first episode, and, especially in falciparum malaria, may not develop at all.[6] Fever may precipitate a febrile convulsion in a young child. Other symptoms—especially diarrhoea, vomiting, anorexia, cough, and abdominal pain—commonly accompany or precede fever and may suggest another diagnosis (box).

Fever and malaria

Case 1—An Indian woman aged 58 developed a dry cough and feverishness one week after arrival in Britain. Two general practitioners on successive days diagnosed an upper respiratory tract infection. She was admitted to hospital a week later with multiorgan failure complicating falciparum malaria, and died after two weeks in intensive care.

Case 2—A British woman aged 49 had lived in Malawi for 27 years. She developed left iliac fossa pain and fever, with diarrhoea. Diverticular disease was diagnosed and shown on barium enema. Antibiotics failed to stop repeated episodes of fever and abdominal pain. *P falciparum* was identified by chance on a blood film, and both fever and pain disappeared within a day of starting antimalarial drugs.

Physical examination is also not diagnostic. Fever is usual, and temperature commonly exceeds 40°C; but fever fluctuates and a patient may be afebrile when examined: this was the case in 23 of 86 patients with malaria recently reported from a hospital in New York.[7] Rashes and lymphadenopathy are not caused by malaria but may coincide with it. Anaemia may develop, usually after several days, in malaria due to any parasite species. Hepatomegaly or splenomegaly can be found in about a third of patients. Moderate jaundice is sometimes present (box).

Immediate diagnosis of malaria is essential because falciparum malaria may progress rapidly to complicated disease, which may be fatal. Complications may supervene within a few days or even within a few hours of the first symptom.

Jaundice and malaria

A Nigerian student who had been resident in the United Kingdom for 10 years visited his family in Nigeria. Ten days after returning to Britain he developed malaise, anorexia, and fever, with jaundice. Hepatitis was diagnosed. Blood films revealed a 5% *P falciparum* parasitaemia. Liver enzymes were marginally raised. He recovered fully after antimalarial treatment.

BLOOD FILMS

Malaria can be diagnosed with confidence only by microscopy of stained blood films. Blood must be taken, examined, and reported on immediately: the same day (the next day may be too late). The timing of taking the blood sample in relation to a peak of fever is less important.

When malaria is diagnosed from blood films a low but dangerous parasitaemia may be missed if only thin blood films are inspected. Thick blood films are much more sensitive (box).

Blood films and malaria

Thick blood films—A British laboratory technician developed fever during a week's leave from his hospital post in East Africa. By the same evening he was prostrated and delirious. Thin blood films were negative for malaria, but a thick film revealed occasional *P falciparum* rings. Treatment was started immediately. He made a full recovery.

Negative films—A British doctor working in an African hospital developed fever and rigors. Thick and thin blood films were negative for malaria parasites. Suggestive symptoms continued the next day, when blood films revealed a 1% *P falciparum* parasitaemia.

Parasitaemia on blood films—A girl aged 12 years accompanied her family to Britain from west Africa, where she had always lived. After a week she developed progressive fever with headache, malaise, and constipation. Blood films revealed *P falciparum* (1% of red cells), but there was no improvement on antimalarial treatment. *Salmonella typhi* was grown from blood and stool cultures.

Negative findings on a blood film reduce the likelihood of malaria, and in particular the danger of imminent progression to complicated disease. Negative findings do not exclude malaria entirely, and more samples should be examined if clinical features remain suggestive.

All blood films reported positive for malaria should include identification of the species of plasmodium and the density of parasitaemia. If there is doubt about the species *P falciparum* should be assumed. "Malaria positive" is an unsatisfactory report. Expert help with species identification can be obtained from one of the tropical disease centres (see Appendix), but this should not delay the starting of treatment.

In the indigenous people of endemic areas asymptomatic parasitaemia is common. Parasitaemia may therefore be incidental in the course of another illness.

SHOULD THE PATIENT BE ADMITTED TO HOSPITAL?

All patients with definite or possible *P falciparum* malaria in a non-endemic country should be admitted to hospital immediately for supervised treatment because of the possibility of progression to complicated disease. Admission for malaria due to other species of parasite will depend on the circumstances and severity of the illness.

Falciparum malaria

Any of several complications (box) may develop during the course of falciparum malaria.[8] In adults it is common for many complications to occur in combination during the same illness.[9] Children seem to differ from adults in that complications other than cerebral malaria and severe anaemia are unusual.[10]

Box 1—Features of severe falciparum malaria[8]

Complications:

- Unrousable coma ("cerebral malaria")
- Renal failure
- Respiratory distress syndrome
- Haemorrhage due to disseminated intravascular coagulation
- Severe normochromic anaemia
- Shock state
- Haemoglobinuria
- Hypoglycaemia
- Convulsion

Other indications for management as "severe" malaria:

- Impaired consciousness but rousable
- Prostration (extreme weakness)
- Parasitaemia > 2%
- Jaundice
- Hyperpyrexia
- Continued vomiting

Treatment has three components: elimination of the parasite by antiparasitic drugs; supportive measures; and recognition and management of complications. The antiparasitic drug must be chosen according to the species of parasite, and the route of its administration must be appropriate to the condition of the patient.

UNCOMPLICATED FALCIPARUM MALARIA

In view of widespread resistance chloroquine cannot be recommended for any patient with imported falciparum malaria.[11] The treatment for patients with none of the severe features listed in the box should be with one of three possible regimens of oral antimalarial drugs:

(1) Quinine sulphate (adult 600 mg thrice daily, child 10 mg/kg thrice daily) for seven days; during this period, add a single oral dose of pyrimethamine-sulfadoxine (Fansidar): for adults three tablets; for children see product literature; this is contraindicated if the patient has a history of sulphonamide sensitivity. If resistance to Fansidar is known or suspected, use doxycycline 200 mg once, then 100 mg daily for six days[12] (not for a child under 8 years or for a pregnant woman).

(2) Mefloquine 20 mg of base/kg (maximum 1500 mg) divided into two doses six hours apart. This is contraindicated in pregnancy, in people taking β blocking drugs, and if there is a history of neuropsychiatric disease, including epilepsy.

(3) Halofantrine (adult 500 mg, child 8 mg/kg) every six hours for three doses; repeat after one week).

Monitoring treatment

Observations during treatment have three objectives: to assess the efficacy of treatment, to recognise complications of malaria as promptly as possible, and to identify drug toxicity. Blood films should be examined daily until erythrocytes containing asexual parasites no longer appear. A rise in parasitaemia in the first 24 hours is common and does not imply treatment failure. Asexual parasitaemia should decrease thereafter and disappear by day 5. Gametocytaemia may persist for days or weeks and does not imply treatment failure or require treatment.

Temporary tinnitus and reduced clarity of hearing are common with therapeutic doses of quinine and do not indicate a need to change the drug, although it is reasonable to reduce the frequency of quinine doses from 8 hourly to 12 hourly in a patient with uncomplicated malaria who develops these symptoms.

SEVERE OR COMPLICATED FALCIPARUM MALARIA

Falciparum malaria should be regarded as severe if the patient is unable to take oral medication, if parasitaemia is over 2%, or if any of the complications listed in Box 1 is present or develops during the course of treatment. (For research purposes a more precise definition of severity should be used[8] so that results can be compared between different centres.)

Severe or complicated disease may develop rapidly in anyone with uncomplicated falciparum malaria, even if the density of parasitaemia is low; the likelihood of progression to severe disease is, however, greatest in patients with heavy parasitaemia. In the presence of any one complication, other complications are likely to develop, especially in adults.

A patient with severe malaria should be managed in a high dependency unit or intensive therapy unit.

SUPPORTIVE MEASURES

Fluid balance, anticonvulsants, antipyretics

The patient may be underhydrated as a result of fever, sweating, vomiting, diarrhoea, and reduced fluid intake. Fluid deficit increases the risk of acute renal failure and should be urgently but carefully corrected. Excessive fluid input increases the serious risk of pulmonary oedema.[13] Fluid balance must therefore be carefully controlled by frequent clinical examination aided by measurement of urine output and by monitoring of the central venous pressure or pulmonary artery wedge pressure.

In adults with cerebral malaria a single injection of phenobarbitone reduces the likelihood of subsequent seizures.[14] If a convulsion does occur an anticonvulsant drug should be given and predisposing factors such as hyperpyrexia, hypoglycaemia, or hyponatraemia should be sought and corrected.

Moderate fever is not harmful, but a core temperature above 39°C should be treated with tepid sponging and fanning and an antipyretic drug such as oral or rectal paracetamol. This is particularly important in young children, in whom high fever may trigger convulsions.

Specific antimalarial chemotherapy

Quinine is the drug of choice and must be given initially by slow intravenous infusion. Schedules of quinine therapy (see box 2[8]) are designed to achieve therapeutic blood levels quickly but safely: the purpose of a loading dose is not to provide a higher blood concentration of quinine but to achieve the desired concentration more quickly.[15] Quinine should never be given by bolus injection. If quinine is not immediately available, quinidine is an equally effective alternative.[16] Oral quinine should replace parenteral therapy as soon as the patient is able to drink. Additional doxycycline or pyrimethamine-sulfadoxine should be given as for uncomplicated falciparum malaria. Quinine may be given by deep intramuscular injection if circumstances preclude intravenous infusion[18]: use the same dosage schedule, but we recommend dividing the loading dose into two equal portions given four hours apart.

Complications in severe falciparum malaria

CEREBRAL MALARIA

Cerebral malaria is characterised by altered consciousness, ranging from drowsiness and confusion

Box 2—Intravenous therapy for severe falciparum malaria

Quinine dihydrochloride: 7 mg/kg* (loading dose)** intravenously by infusion pump over 30 minutes, followed immediately by 10 mg/kg* diluted in 10 ml/kg isotonic fluid by intravenous infusion over 4 hours, repeated at intervals of 8 hours after start of first infusion (that is, 4 hours on quinine, 4 hours off) until patient can swallow[17]; then oral quinine 10 mg/kg* thrice daily to complete 7 days' treatment.

Or:

Quinine dihydrochloride: 20 mg/kg* (loading dose)** intravenously over 4 hours; then at 8 hour intervals after start of therapy, 10 mg/kg* infused over 4 hours (that is, 4 hours on quinine, 4 hours off) until patient can swallow; then oral quinine as above.

Or:

Quinidine gluconate: 10 mg/kg* (loading dose)** intravenously by infusion over 1-2 hours, followed by 0·02 mg/kg/min* by infusion pump for 72 hours or until the patient can swallow; then quinine tablets to complete 7 days' treatment.

Or:

Quinidine gluconate: 15 mg/kg* (loading dose)** intravenously over 4 hours, then after an interval of 4 hours, 7·5 mg/kg* over 4 hours, repeating 8 hourly until able to swallow; then oral quinine as above.

*Doses are of salt. All doses for patients weighing >70 kg should be calculated as for a body weight of 70 kg.
**Omit loading dose and start maintenance doses if patient received quinine, quinidine, or mefloquine in the preceding 24 hours.

to profound unrousable coma. Focal or generalised convulsions are common. Abnormal neurological signs may be present,[8] including opisthotonos, extensor posturing of decorticate or decerebrate pattern, sustained posturing of limbs, conjugate deviation of the eyes, nystagmus, dysconjugate eye movements, bruxism, extensor plantar reflexes, and generalised flaccidity. Corneal, pupillary, and oculovestibular reflexes are usually intact. Retinal haemorrhages are common, and retinal arteriolar occlusions are sometimes seen. Papilloedema may be found but is unusual. Abnormal patterns of breathing are common, including irregular periods of apnoea and hyperventilation. The patient with cerebral malaria needs intensive nursing and supportive care, with attention to posture and airway.

Hypoglycaemia may complicate malaria and may cause altered consciousness and neurological signs very similar to those of cerebral malaria; hypoglycaemia may also result from quinine induced hyperinsulinaemia.[19] Repeated measurements of blood glucose at the bedside are therefore mandatory, every four hours or so, and immediately in the event of a convulsion or deepening coma. Hypoglycaemia (whole blood glucose <2·2 mmol/l) should be treated promptly with an intravenous bolus of 50% dextrose and regular glucose supplementation.

During the management of a patient with cerebral malaria it is helpful to make regular assessments of the depth of coma, using a scale such as the Glasgow coma score[20] or an appropriate modification for children.[10] A deterioration in coma score should then prompt a search for any correctable cause, in particular hypoxia, hypoglycaemia, hyperpyrexia, convulsion, electrolyte disturbance, or severe anaemia.

The possible role of raised intracranial pressure in the pathogenesis of cerebral malaria remains unestablished. In both adults and children, cerebrospinal fluid opening pressures are commonly, but not invariably, high[21,22]; pressures are not on average higher in fatal than non-fatal cases.[21,23] Treatment with dexamethasone has failed to improve the overall outcome of cerebral malaria in adults and children,[9,24] but the benefit of other measures (for example, mannitol) in patients—especially children—with identified or suspected intracranial hypertension remains to be studied.

In cerebral malaria, coma may persist for several days despite early clearance of parasitaemia. Children tend to regain consciousness more quickly than adults. In those who survive, neurological recovery is usually complete, but about 5% of adults and 10% of children have residual neurological sequelae.[9,10,25]

ACUTE RENAL FAILURE

Oliguric renal failure in falciparum malaria is usually due to acute tubular necrosis.[26] Patients at increased risk of this complication are those with hyperparasitaemia, hypovolaemia, shock, or intravascular haemolysis. Every effort should be made to maintain renal function with intravenous fluids, diuretics, and low dose dopamine. In view of the risk of fluid overload, these measures must be carefully controlled by monitoring the central venous and pulmonary artery wedge pressures. Dialysis is commonly required, the indications being the same as for acute renal failure from any cause.

In the presence of renal failure the dosage of quinine or quinidine should be reduced by half after 48 hours. If possible, blood levels of the drugs should be monitored so that the drug concentration can be maintained in the therapeutic range (quinine 10-15 mg/l, quinidine 4-6 mg/l).

SHOCK

An uncommon complication of falciparum malaria is a state of shock ("algid malaria"). The clinical picture resembles bacteraemia and endotoxaemia, and Gram negative organisms have been cultured from the blood of some patients. Antibiotic cover should be given while results of bacterial cultures are awaited.

SEVERE ANAEMIA

Anaemia, due to destruction of red cells and marrow dysplasia, is a usual consequence of severe malaria. Anaemia may develop rapidly, especially in patients with hyperparasitaemia, intravascular haemolysis, or haemorrhage associated with disseminated intravascular coagulation. Blood transfusion may be life saving, but in view of the risk of precipitating pulmonary oedema, transfusion must be administered with care and the need for it assessed in the individual patient. Blood transfusion can be avoided in many patients with a haemoglobin concentration greater than 6 g/dl.[8]

COAGULOPATHY

Thrombocytopenia is almost invariable in falciparum malaria and does not of itself indicate the presence of severe disease. Clinically important disseminated intravascular coagulation develops in a

Should a lumbar puncture be done in a patient with suspected cerebral malaria?

Lumbar puncture is done to exclude other or coincident causes of encephalopathy, in particular meningitis. In patients with localising neurological signs, lumbar puncture may be deferred until urgent computed tomography has excluded an intracranial mass. If in doubt, or if there is papilloedema, omit lumbar puncture and treat possible bacterial infection with an appropriate antibiotic.

Box 3—Common errors contributing to deaths from malaria in Britain

Error	*Correction*
Failure to prevent:	
Public ignorance of risks	Publicity in media, travel agencies, surgeries
Complex or inconsistent advice (national guidelines needed)	Make advice simple and uniform
Drug resistance of parasite	Emphasise other preventive measures in addition to drugs
Failure to diagnose:	
Patient ignores symptoms	Publicity; pretravel advice to include warning about post travel fever
Misplaced trust in prophylaxis	Recognise that no preventive measure guarantees protection
No travel history	Improve teaching in medical schools; place posters in waiting rooms and clinics
Incomplete travel history	Routinely take travel history in all medical interviews
Unusual route of infection ignored	Remember blood transfusion, needlestick, and transplacental routes
Atypical presentation	Consider malaria in differential diagnosis of hepatitis, influenza, upper respiratory tract infection, gastroenteritis, meningitis or encephalitis, heat stroke, psychosis, eclampsia, acute renal failure
Blood films delayed	Immediate diagnosis is essential
Only thin films taken	Thick films are more sensitive
Single blood film	Further samples may be needed
Failure in management:	
Delayed start of treatment	Falciparum malaria is a medical emergency
Delayed admission to hospital	Immediate hospital admission is required for falciparum malaria
Complications not recognised	Anticipate complications and monitor the patient's condition frequently
Wrong drug, dose, or route	See cases of fever in box, and ref 32.

minority of cases. In the patient with severe malaria the prothrombin time and activated partial thromboplastin time should be measured; if these are prolonged, the presence of disseminated intravascular coagulation may be confirmed by measuring plasma concentrations of fibrinogen and fibrin split products. A bleeding diathesis due to disseminated intravascular coagulation requires treatment with fresh whole blood, fresh frozen plasma, or platelet infusions. Disseminated intravascular coagulation may be caused by coincidental Gram negative sepsis, which should be covered by appropriate antibiotics.

PULMONARY OEDEMA AND RESPIRATORY DISTRESS SYNDROME

Tachypnoea and bilateral pulmonary interstitial shadowing seen on *x* ray films may be due to fluid overload causing pulmonary oedema. A similar clinical and radiological picture may develop in the absence of fluid excess (fig 3); this is a form of adult respiratory distress syndrome and carries a grave prognosis.[27] This syndrome and fluid overload are difficult to distinguish clinically, and they may coexist. Treatment must be guided by frequent measurements of the pulmonary artery wedge pressure, and diuretics and oxygen should be given as necessary. Endotracheal intubation and assisted ventilation may be life saving in patients with falciparum malaria complicated by adult respiratory distress syndrome.

HYPERPARASITAEMIA

Patients with heavy parasitaemia are at increased risk of developing all the dangerous manifestations of falciparum malaria. Exchange transfusion has been advocated and frequently reported[28]; this measure accelerates the clearance of circulating parasites (but not of mature parasites sequestered in tissues) and is sometimes followed by dramatic clinical improvement. Exchange transfusion also allows replacement of red blood cells and clotting factors without volume overload. There has, however, been no controlled trial of exchange transfusion: the benefits of the procedure are unproved and the indications undefined.[29]

Management of non-falciparum malaria

Two features distinguish malaria due to *P vivax*, *P malariae*, or *P ovale* from malaria due to *P falciparum*: organ complications are rare in the non-falciparum malarias, and resistance to chloroquine is unusual. Recently, however, an increasing prevalence of chloroquine resistant *P vivax* malaria has been reported in New Guinea.[3]

Supportive measures include attention to fever, pain, and fluid requirements. An antiparasitic drug should be given by mouth if possible, the treatment of choice being chloroquine: 600 mg (child 10 mg/kg) on the first and second days, 300 mg (child 5 mg/kg) on the third day. (Chloroquine is dispensed as the phosphate or sulphate; the dose refers to chloroquine base. A syrup is available for young children.)

If the patient is unable to take medication by mouth (unusual in non-falciparum malaria), chloroquine may be given by slow intravenous infusion (10 mg of base/kg given by constant rate infusion in isotonic fluid over eight hours). Oral therapy should then be resumed if possible; in a patient still unable to drink, a further 15 mg chloroquine base/kg can be given by constant slow infusion over 24 hours.

Parasitaemia should begin to decrease within 24-36 hours and be eliminated within three to five days. Failure to clear parasitaemia suggests chloroquine resistance; oral quinine (10 mg/kg twice daily for five days) may be given.

P vivax and *P ovale* have hepatic parasites (hypnozoites) that are not eliminated by chloroquine. If not eradicated hypnozoites may cause relapses of malaria in subsequent months or years. Chloroquine treatment should therefore be followed by primaquine (adult dose 15 mg daily, child 0·25 mg/kg daily) for 15 days, or 21 days for *P vivax* infections acquired in south east Asia, where resistance to primaquine is common. Primaquine may cause severe haemolysis in patients deficient in glucose-6-phosphate dehydrogenase (G6PD), erythrocyte levels of which must be checked before primaquine is prescribed. Patients deficient in G6PD may instead be treated with chloroquine 300 mg weekly for six months, or cautiously with primaquine 15 mg weekly for four months.

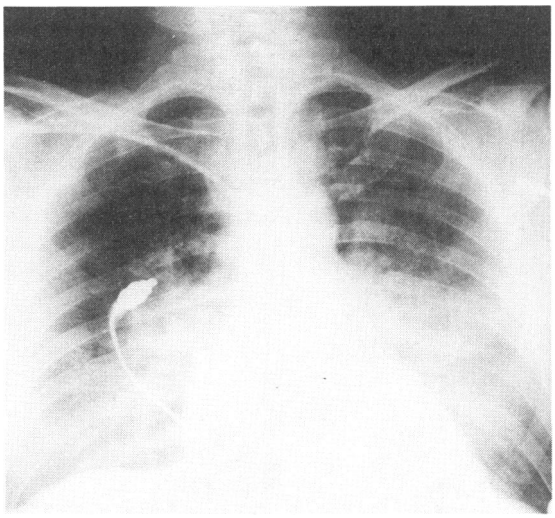

FIG 3—*Falciparum malaria and adult respiratory distress syndrome in a British man*

Malaria in pregnancy

In endemic areas pregnant women (especially primigravidas) are more susceptible to malaria and develop higher parasitaemias than non-pregnant women. In non-immune travellers, pregnancy increases the risk of severe malaria. Even in uncomplicated malaria, fever puts the fetus at risk of abortion or premature delivery. Pregnant women are at particular risk of hypoglycaemia associated with malaria and also of quinine induced hypoglycaemia.[19] Quinine is the drug of choice for severe, or potentially severe, malaria in pregnancy: the benefits of the antimalarial effect of the drug outweigh the relatively minor risk of a stimulant effect on uterine muscle.[30] Management should include measures to reduce excessive fever and to identify and correct hypoglycaemia. In pregnant patients with vivax or ovale malaria, treatment with primaquine should be postponed until the pregnancy is over; give chloroquine weekly during the remaining weeks of pregnancy.

Congenital malaria

Malaria contracted in utero may cause a puzzling illness in an infant; it is most likely in the first three months of life. Fever, anaemia, hepatosplenomegaly, and jaundice are usual features[31]; agents of the TORCHS syndrome may be suspected (toxoplasma, rubella, cytomegalovirus, herpes simplex, and syphilis). The evaluation of infants with this presentation should routinely include the mother's travel history and the scrutiny of thick and thin blood films. Treatment is appropriate to the parasite species, but primaquine to clear hypnozoites of *P vivax* or *P ovale* is unnecessary since the infection is acquired through the transmission of the blood stage of the parasite, from which hypnozoites do not develop.

Conclusion

Malaria will continue to be seen in Britain: no prophylactic measures can guarantee total protection for travellers. Deaths can be prevented if the infection is suspected readily, diagnosed promptly, and treated urgently.

Appendix: Centres in Britain where advice on malaria may be obtained

Liverpool School of Tropical Medicine, Pembroke Place, Liverpool L3 5QA (tel 051 924 6852);
Hospital for Tropical Diseases, 4 St Pancras Way, London NW1 0PE (tel 071 387 4411);
Centre for Tropical Medicine, John Radcliffe Hospital, Headington, Oxford OX3 9DU (tel 0865 741166);
Lister Unit, Northwick Park Hospital, Harrow, Middlesex (tel 081 869 2831/2);
Department of Communicable and Tropical Diseases, East Birmingham Hospital, Birmingham B9 5ST (tel 021 772 4311);
Communicable Diseases (Scotland) Unit, Ruchill Hospital, Glasgow G20 9NB (tel 041 946 7120).

The following centres offer advice on blood films sent by post:
Diagnostic Laboratory, Liverpool School of Tropical Medicine, Liverpool L3 5AQ (tel 051 708 9393);
Malaria Reference Laboratory, London School of Hygiene and Tropical Medicine (tel 071 636 8636).

Postal and communication time must not be allowed to delay the start of treatment in a patient with suspected malaria.

1 World malaria situation in 1990. *WHO Weekly Epidemiological Record* 1992;67:161-8.
2 Lewis SJ, Davidson RN, Ross EJ, Hall AP. Severity of imported falciparum malaria: effect of taking antimalarial prophylaxis. *BMJ* 1992;305:741-3.
3 Murphy GS, Basri H, Purnomo, Anderson EM, Bangs MJ, Mount DL, *et al*, Vivax malaria resistant to treatment and prophylaxis with chloroquine. *Lancet* 1993;341:96-100.
4 Conlon CP, Berendt AR, Dawson K, Peto TEA. Runway malaria. *Lancet* 1990;335:472-3.
5 Curtis CF, White GB. *Plasmodium falciparum* transmission in England: entomological and epidemiological data relative to cases in 1983. *J Trop Med Hyg* 1984;87:101-14.
6 Gilles HM, Warrell DA. *Bruce-Chwatt's essential malariology*. 3rd ed. London: Heinemann, 1993.
7 Winters RA, Murray HW. Malaria—the mime revisited: fifteen more years of experience at a New York City teaching hospital. *Am J Med* 1992;93:243-6.
8 Warrell DA, Molyneux ME, Beales PF. Severe and complicated malaria. *Trans R Soc Trop Med Hyg* 1990 (suppl 2):1-65.
9 Warrell DA, Looareesuwan S, Warrell MJ, Kasemsarn P, Intaraprasert R, Bunnag D, *et al*. Dexamethasone proves deleterious in cerebral malaria: a double-blind trial in 100 comatose patients. *N Engl J Med* 1982;306:313-9.
10 Molyneux ME, Taylor TE, Wirima JJ, Borgstein J. Clinical features and prognostic indicators in paediatric cerebral malaria: a study of 131 comatose Malawian children. *Q J Med* 1989;71:441-59.
11 Bjorkman A, Phillips-Howard PA. The epidemiology of drug-resistant malaria. *Trans R Soc Trop Med Hyg* 1990;84:177-80.
12 Meek SR, Doberstyn EB, Gauzere BA, Thanapanich C, Nordlander E, Phuphaisan S. Treatment of falciparum malaria with quinine and tetracycline or combined mefloquine/sulfadoxine/pyrimethamine on the Thai-Kampuchean border. *Am J Trop Med Hyg* 1986;35:246-50.
13 Bergin JJ. Malaria and the lung. *Military Medicine* 1967;132:522-6.
14 White NJ, Looareesewan S, Phillips RE, Chanthavanich P, Warrell DA. Single dose phenobarbitone prevents convulsions in cerebral malaria. *Lancet* 1988;ii:64-6.
15 White NJ, Looareesuwan S, Warrell DA, Warrell MJ, Chanthavanich P, Bunnag D, *et al*. Quinine loading dose in cerebral malaria. *Am J Trop Med Hyg* 1983;32:1-5.
16 Phillips RE, Warrell DA, White NJ, Looareesuwan S, Karbwang J. Intravenous quinidine for the treatment of severe falciparum malaria. Clinical and pharmacokinetic studies. *N Engl J Med* 1985;312:1273-8.
17 Davis TME, Supanaranond W, Pukrittayakamee S, Karbwang J, Molunto P, Mekthon S, *et al*. A safe and effective consecutive-infusion regimen for rapid quinine loading in severe malaria. *J Infect Dis* 1990;161:1305-8.
18 Wattanagoon Y, Phillips RE, Warrell DA, Silamut K, Looareesuwan S, Nagachinta B, *et al*. Intramuscular loading dose of quinine for falciparum malaria. Pharmacokinetics and toxicity. *BMJ* 1986;293:11-3.
19 White NJ, Warrell DA, Chanthavanich P, Looareesuwan S, Warrell MJ, Krishna S, *et al*. Severe hypoglycaemia and hyperinsulinaemia in falciparum malaria. *N Engl J Med* 1983;309:61-6.
20 Teasdale G, Jennett B. Assessment of coma and impaired consciousness. A practical scale. *Lancet* 1974;ii:81-4.
21 White NJ. Pathophysiology. In: Strickland GT, ed. *Clinics in tropical medicine and communicable diseases*. Vol 1. *Malaria*. London: Saunders, 1986:55-90.
22 Newton CRJC, Kirkham FJ, Winstanley PA, Pasvol G, Peshu N, Warrell DA, *et al*. Intracranial pressure in African children with cerebral malaria. *Lancet* 1991;337:573-6.
23 Kwiatkowski D, Molyneux ME, Taylor TE, Klein N, Curtis N, Smit M. Cerebral malaria. *Lancet* 1991;337:1281-2.
24 Hoffman SL, Rustama D, Punjabi NH, Surampaet B, Sanjaya B, Dimpudus AJ, *et al*. High-dose dexamethasone in quinine-treated patients with cerebral malaria: a double-blind placebo-controlled trial. *J Infect Dis* 1988;158:325-31.
25 Brewster DR, Kwiatkowski D, White NJ. Neurological sequelae of cerebral malaria in children. *Lancet* 1990;336:1039-43.
26 Tran Thi My Trang, Nguyen Hoan Phu, Ha Vinh, Tran Tinh Hien, Bui Minh Cuong, Tran Thi Hong Chau, *et al*. Acute renal failure in patients with severe falciparum malaria. *Clin Infect Dis* 1992;15:874-80.
27 Warrell DA. Pathophysiology of severe falciparum malaria in man. *Parasitology* 1987,94:S53-76.
28 Miller KD, Greenberg AE, Campbell CC. Treatment of severe malaria in the United States with a continuous infusion of quinidine gluconate and exchange transfusion. *N Engl J Med* 1989;321:65-70.
29 Chiodini P, Hall AP. Controlled trial of exchange transfusion in falciparum malaria. *Lancet* 1990;335:554.
30 Looareesuwan S, Phillips RE, White NJ, Kietinun S, Karbwang J, Rachow C, *et al*. Quinine and severe falciparum malaria in late pregnancy. *Lancet* 1985;ii:4-8.
31 Hulbert TV. Congenital malaria in the United States: report of a case review. *Clin Infect Dis* 1992;14:922-6.
32 Gilles HM. Management of severe and complicated malaria: a practical handbook. Geneva: World Health Organisation, 1991.

(Accepted 16 February 1993)