

19 MALARIA AND OTHER TROPICAL DISEASES

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MALARIA

Malaria is endemic in almost all parts of the tropical world as far north as southern Turkey, as far south as north-eastern South Africa, as far west as Mexico and as far east as Vanuatu in the western Pacific (see Figure 19.2). The females of certain species of mosquito (genus *Anopheles*), which nearly always bite between dusk and dawn, transmit malaria (Figure 19.1). Four different species of malarial parasites commonly infect humans: life-threatening *Plasmodium falciparum* and the three so-called benign malarias, *P. vivax*, *P. ovale* and *P. malariae*. *P. falciparum* malaria kills 1 to 2 million people each year and is particularly dangerous to those who have not acquired immunity to it by growing up in a malarious part of the world. About 2,000 cases of imported malaria are reported in the UK each year, but over the last few years the proportion of dangerous *P. falciparum* cases has increased to over 60%. Each year, a few people die of imported malaria in the UK and an unknown number die abroad. Most of these deaths could have been prevented by better education of the travellers, use of approved methods of prevention and prompt medical attention when a person falls ill.

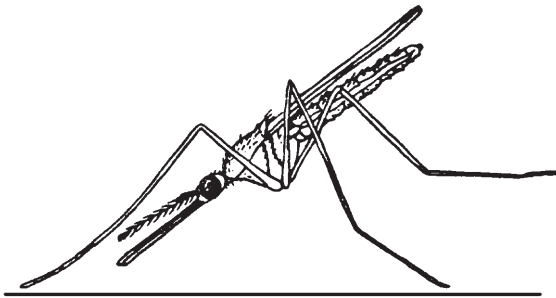


Figure 19.1 *Anopheles* mosquito

Prevention**TABLE 19.1 PRINCIPLES OF PERSONAL PROTECTION AGAINST MALARIA**

1. **Awareness of risk:** vulnerable individuals, such as pregnant women, infants or immunocompromised people, should avoid entering a malarious area
2. **Anti-mosquito measures:** kill, exclude, repel and avoid mosquitoes
 - Sensible clothing (long sleeves, long trousers) between dusk and dawn
 - Diethyltoluamide (DEET) – containing insect repellent applied to exposed skin
 - Insecticide (pyrethroid) – impregnated mosquito bed net or screened accommodation sprayed with insecticide each evening
 - Vaporising insecticide in the sleeping quarters (electrical, mosquito coil, knock-down insecticide)
3. **Chemoprophylaxis:** mefloquine (Lariam) or other drugs, depending on the particular geographical area
4. **Standby treatment:** Fansidar, mefloquine, quinine, Malarone
5. **In case of feverish illness within a few months of return: see a doctor and mention malaria specifically!**

Assessing the risk

Within malarious countries, the areas of malaria transmission may be patchy, depending on environmental factors such as temperature, altitude and vegetation as well as the season. Thus there is no malaria transmission in some African capital cities that are at a comparatively high altitude, such as Addis Ababa and Nairobi, and in other areas malaria transmission occurs only during a brief rainy season. If possible, reliable local advice should be obtained about the status of malaria transmission in the area where, and at the time when, the expedition is to take place. Even within a transmission area, the risk of being bitten by an infected mosquito can vary from less than once per year to more than once per night. The chances of catching malaria during a 2-week visit, while taking no protection at all, has been estimated at about 0.2% in Kenya and 1% in West Africa.

People who are especially vulnerable to malaria should seriously consider whether they need to enter the malarious area at all. These include pregnant women, infants and young children, and those who have had their spleens removed or are otherwise immunosuppressed

Anti-mosquito measures

Since most malaria-transmitting mosquitoes bite in or near human dwellings during

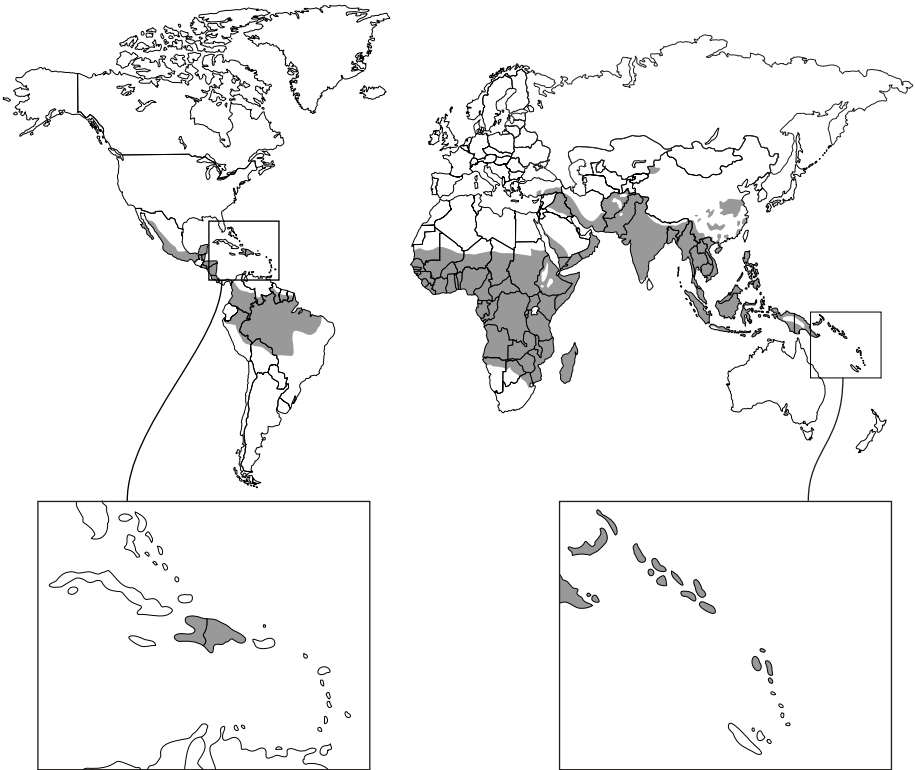


Figure 19.2 *Malaria is endemic in almost all parts of the tropical world as far north as southern Turkey, as far south as north-eastern South Africa, as far west as Mexico and as far east as Vanuatu in the western Pacific*

the hours of darkness, the risk of infection can be reduced by insect-proofing sleeping quarters or by sleeping under a mosquito net. Individual, lightweight, self-supporting mosquito nets are available. Protection against mosquitoes and other biting invertebrates (sandflies, lice, fleas, bed bugs and so on) is greatly enhanced by soaking the net in a pyrethroid insecticide such as permethrin (0.2g per m² of material every 6 months). Screens and curtains can also be impregnated with insecticide. In addition, bedrooms should be sprayed in the evening with a knock-down insecticide to kill any mosquitoes that may have entered the room during the day. Mosquitoes may also be killed or repelled by vaporising synthetic pyrethroids (Bioallethrin 4.2% w/w) on electrical heating devices (such as No Bite and Buzz Off) where electricity is available or over a methylated spirit burner (Travel Accessories UK Ltd, PO Box 10, Lutterworth, Leicester LE17 4FB). Burning cones or coils of mosquito repellent “incense” may also be

effective. To avoid bites by any flying insect, light-coloured long-sleeved shirts and long trousers are preferable to vests and shorts. To avoid malaria-transmitting mosquito bites, this sensible clothing should be worn particularly after dark. Exposed areas of skin should be rubbed or sprayed with repellents containing *NN*-diethyl-*m*-toluamide (DEET). Insecticide-containing soaps and suntan oil are available and clothes can be soaked in repellent solution.

Anti-malarial chemoprophylaxis

At one time comparatively harmless drugs, such as chloroquine (Nivaquine), pyrimethamine (Daraprim) and proguanil (Paludrine), gave a high degree of protection against malaria parasites. However, the rapid emergence of resistant strains of *P. falciparum* has made chemoprophylaxis much more difficult. In particular, chloroquine-resistant strains of *P. falciparum* now predominate in most parts of the tropics except in Mexico and Central America, north-west of the Panama Canal, Haiti, parts of West Africa and the Middle East. The failure of travellers to take their antimalarial tablets regularly, and in particular to continue taking them for 4 weeks after leaving the malarious area, also reduces the effectiveness of chemoprophylaxis. During bouts of vomiting and diarrhoea (traveller's diarrhoea), these drugs may not be adequately absorbed. In choosing chemoprophylaxis, the risk of contracting malaria should be balanced against the risk of side-effects from the drug. This is illustrated by the case of mefloquine (Lariam) which has recently excited a heated debate. Although mefloquine is probably twice as effective as the chloroquine plus proguanil combination in preventing malaria in Africa, the incidence and severity of side-effects, especially in young women, is greater with mefloquine.

Chemoprophylactic drugs and combinations

Mefloquine (Lariam)

This drug is effective against most multiresistant *P. falciparum* strains. It has some unpleasant side-effects: nausea, stomachache and diarrhoea in 10–15% of people who take it; insomnia and nightmares; giddiness and ataxia (unsteadiness and incoordination) in some; and, much more serious, a rare “acute brain syndrome” consisting of psychological changes and in very rare cases generalised convulsions (epileptic attacks). For these reasons it is recommended for use only in areas with a high risk of resistant malaria (such as Africa, the Amazon region and south-east Asia). The dose is one tablet (of 250mg) a week.

Proguanil (Paludrine) and chloroquine (Nivaquine)

The combination of proguanil – two tablets (each of 100mg) every day – and chloroquine – two tablets (each of 150mg base) once a week – was the standard recommended and most widely used prophylactic regime in areas where *P. falciparum* is

chloroquine resistant. Unfortunately, its efficacy has now declined, so that it is no longer recommended for Africa, the Amazon region or south-east Asia and Oceania. It is safe in pregnancy and (in a lower dose) in children. The only side-effects are rare mouth ulcers, mild indigestion and hair loss. Since this combination is no longer effective, it should be pointed out to travellers that despite taking antimalarials they may still develop malaria. However, if they are on antimalarials they are unlikely to become seriously ill with malaria, but *they must seek medical treatment if they get a fever, especially during the first few months after returning from the malarious area.*

There is no evidence that chloroquine, taken in the doses recommended for prophylaxis against malaria, ever causes damage to the eyes in people who take the drug continuously for 5–6 years. Checks after chloroquine prophylaxis are therefore unnecessary, unless the individual has taken the drug for a very long time (more than 6 years continuously) and the total cumulative dose approaches 100g.

Atovaquone–proguanil (Malarone)

This safe, effective but expensive drug needs to be continued for only 7 days after leaving the malarious area. The dose is one tablet each day for adults.

Doxycycline (Vibramycin)

This tetracycline antibiotic has proved useful for prophylaxis in areas where mefloquine resistance is prevalent, such as the Thai–Cambodian border region. It gives some protection against other traveller's diseases such as typhus, leptospirosis and some types of traveller's diarrhoea. One 100mg tablet a day should be taken. Side-effects include photosensitive rashes, skin irritation, diarrhoea, and oral/oesophageal or vaginal thrush. It should not be used by pregnant women and young children.

Maloprim, Deltaprim

This is a combination of dapsone 100mg and pyrimethamine 12.5mg which, unlike mefloquine and chloroquine, is safe for sufferers from epilepsy. Its manufacture may soon be stopped. When used, one tablet a week (for example every Sunday), no more, no less, should be taken.

Choice of prophylactic drug/combination in different geographical areas

- Middle East, West Asia, Indian subcontinent, parts of South America (except Amazon region of Brazil), China: use proguanil plus chloroquine.
- Mexico, Central America, Haiti, Dominican Republic, parts of South America (except Amazon region of Brazil): use chloroquine.
- Africa, Amazon region of Brazil, south-east Asia (except Thai–Cambodian border region): use mefloquine, doxycycline or Malarone.
- West Pacific, New Guinea: use mefloquine or doxycycline.
- Thai–Cambodian border region: use doxycycline or Malarone.

- Turkey, Egypt, Mauritius (rural, seasonal only): use chloroquine or proguanil.

(Malarone is an alternative to mefloquine or doxycycline in all areas, for those who can afford it!)

During pregnancy it is vital for the expectant mother to take antimalarials or, preferably, to avoid entering a malarious area. The hazards of getting malaria, particularly *P. falciparum* malaria, during pregnancy are great. The remote hazard of adverse effects on the baby of the antimalarial drugs is far outweighed by the advantages. Chloroquine plus proguanil as outlined above should be used. Maloprim and other pyrimethamine-containing drugs, mefloquine, doxycycline and Malarone, should be avoided during pregnancy.

It is wise to start weekly mefloquine 3 weeks before leaving for the malarious area in case side-effects develop and you have to switch to another drug. All antimalarial drugs except Malarone must be continued for 4 weeks after return.

Remember that no antimalarial drug is perfect. Much depends on whether it is taken regularly. If you are ill at all after your return you should consult your doctor and *mention the possibility of malaria*. If there is *any doubt* you should be referred to an infectious disease unit for exclusion of malaria. If you have been taking an antimalarial it may be difficult to find the parasites and yet you may be quite ill.

Standby treatment for malaria in high-risk areas

If you are going to a remote malarious area you would be wise to take a supply of quinine, 600mg to be taken 8 hourly for 7 days if you get a fever. Mefloquine, two tablets (each of 250mg) repeated after 8 hours (1,000mg total for an adult, 20mg/kg for children), is an alternative unless that is the drug you have been taking for prophylaxis. Fansidar and Malarone *are* also useful standby treatments. A new combination drug, artemether plus lumefantrine (Riamet or Co-artemether) will also be suitable for standby treatment.

Prevention of the “benign” malarias (*P. vivax*, *ovale* and *malariae*)

Weekly chloroquine or mefloquine will usually prevent *P. vivax*, *ovale* and *malariae* malarias. However, *P. vivax* and *P. ovale* can establish themselves in the liver despite chloroquine prophylaxis and may re-emerge to cause relapsing infections months or years later. Primaquine, 15mg a day for 2 weeks, will usually eradicate the liver cycle and should be given to travellers who have spent more than a few months in areas where these species are endemic. In parts of Indonesia, particularly Irian Jaya, and in Papua New Guinea, Thailand, the Philippines and the Solomon Islands, *P. vivax* malaria may not be eradicated by the usual 2-week course of primaquine. In these cases a 4-week course of primaquine should be given after the person returns home.

In New Guinea and adjacent areas of Indonesia (for example, Lombok), *P. vivax* malaria has become resistant to chloroquine. A double dose of chloroquine or the standard dose of mefloquine followed by a 4-week course of primaquine can be used to treat such resistant infections. Advice on malarial prophylaxis can be obtained from the following tropical medicine units.

Malaria Reference Laboratory

Tel. +44 20 7636 3924
Tel (24 hr): +44 9065 508908
Website: www.lshtm.ac.uk/centres/malaria

Hospital for Tropical Diseases

Tel. +44 20 7387 9300/4411
Healthline: +44 9061 337733
Fax: +44 20 7388 7645
Website: www.thehtd.org

London School of Tropical Medicine

Tel. +44 20 7636 8636
Website: www.lshtm.ac.uk

Liverpool School of Tropical Medicine

Tel. +44 151 708 9393
Fax: +44 151 708 8733
Website: www.liv.ac.uk/lstm/lstm.html

Oxford University Centre for Tropical Medicine

Tel. +44 1865 220968
Fax: +44 1865 220984

OTHER TROPICAL DISEASES

Bilharzia (schistosomiasis)

This fluke infection occurs in Africa, the Middle East, eastern South America, China and south-east Asia (Figure 19.3). Infection is acquired through contact with fresh water from lakes and sluggish rivers, usually by bathing or washing with water taken from these sources. Infected humans contaminate the lake by defecating or urinating into it and infect, in turn, the intermediate snail hosts. Snails release tiny cercariae into the water which burrow through the skin of bathers. The earliest symptom of possible infection is “swimmer’s itch”, experienced soon after contact with infected

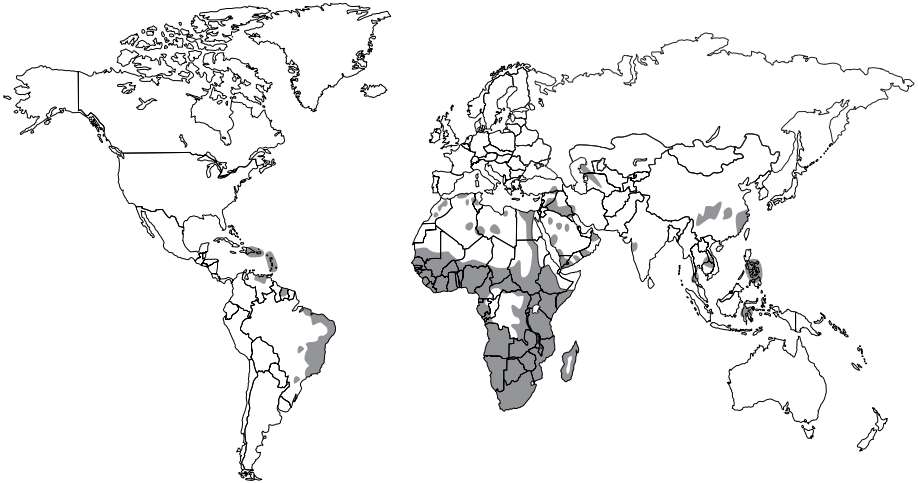


Figure 19.3 *Bilharzia (schistosomiasis)*

water. Some people develop an acute feverish illness associated with an urticarial rash and blood eosinophilia a few weeks after infection. Later symptoms include passage of cloudy or frankly bloodstained urine or dysentery and, rarely, ascending paralysis and loss of sensation in the lower limbs.

Travellers usually get worried about bilharzia when they get back from their trip and remember bathing in forbidden lakes or hear that another member of the party has been diagnosed as having schistosomiasis. Diagnosis is confirmed by finding ova in stool, urine or rectal biopsies, or by a blood test. Treatment is fairly simple with one to two doses of praziquantel (Biltricide).

Prevent bilharzia by not bathing in sluggish fresh water sources in endemic areas. Local advice may be misleading. Lake Malawi, officially declared free of bilharzia, has been the source of many imported cases of bilharzia in the UK over the last few years.

Dengue fever (“break bone” fever)

Mosquitoes such as *Aedes aegypti* and *A. albopictus* transmit dengue viruses from human to human in almost every part of the tropics, notably in south-east Asia and the Caribbean, and increasingly in urban areas (Figure 19.4). In most foreign travellers, dengue causes an acute fever associated with headache, backache and pains in the muscles and joints (“break bone” fever). The most obvious reddish blotchy rash often appears after a temporary lull in the fever. Petechial haemorrhages may be found in the skin and conjunctivae. The blood count usually shows leucopenia with relative lymphocytosis and thrombocytopenia. The diagnosis can be confirmed by testing two blood samples, one taken immediately and the other 2 weeks after the acute illness.

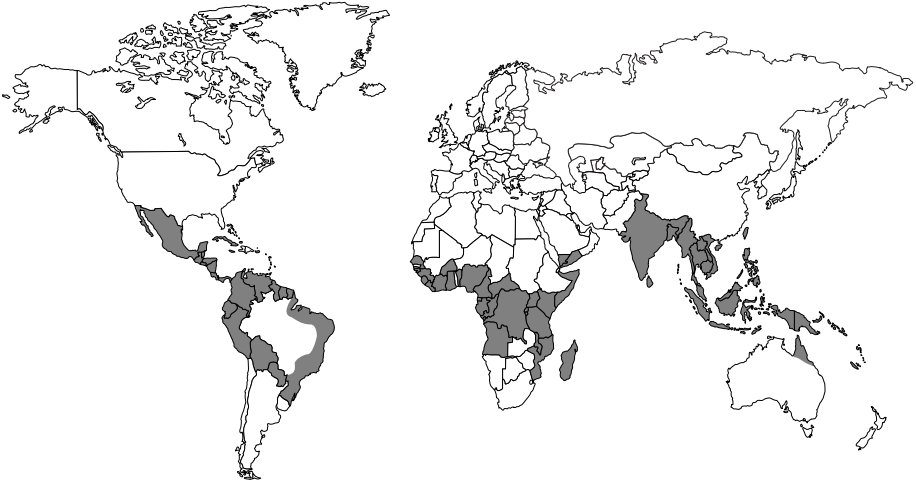


Figure 19.4 *Dengue fever* (“break bone” fever)

Severe, life-threatening forms of dengue (dengue haemorrhagic fever and dengue shock syndrome) occur almost exclusively in children who have been brought up in endemic areas and are suffering their second dengue infection.

Treatment of dengue fever is symptomatic (bed rest, control of fever and paracetamol).

Prevention is by wearing sensible clothing (see above) during the daytime biting period and applying DEET-containing repellents to exposed skin surfaces.

Rabies

Rabies or hydrophobia (literally fear of water) is a virus disease of mammals that is usually transmitted to humans by a dog bite. Although dogs are the most important source of human rabies worldwide, some countries have other vector species, such as cats, wolves, foxes, jackals, skunks, mongooses, racoons, vampire bats (Caribbean and Latin America only), flying foxes and insectivorous bats. Rabies occurs in almost every country (see Figure 2.5, page 15); the fortunate exceptions include Antarctica, Scandinavian countries (except Greenland and Svalbard), Malaysia, New Guinea, New Zealand, Japan, the UK and some smaller islands. It is especially common in parts of Latin America, the Indian subcontinent, Vietnam, Thailand and the Philippines. The disease probably causes at least 60,000 human deaths each year.

The rabies virus can enter the body in a number of ways. Virus in an animal’s saliva can penetrate skin that has been broken by a bite or graze, and can invade unbroken mucous membranes, such as those covering the eye and lining the mouth and nose. Very rarely, the virus has been inhaled, for example, from the atmosphere

of caves infested with insectivorous bats. Transmission of rabies from human to human must be excessively rare, but at least eight patients are known to have developed rabies after receiving infected corneal grafts. After the virus has entered the body, one of two things may happen. The virus may be killed by antiseptics or immune mechanisms before it does any harm, or it may spread along the nerves to reach the brain where it multiplies and causes inflammation (encephalitis), which is almost invariably fatal. The incubation period (the interval between the bite and the first symptoms of encephalitis) is usually about 2 months but can vary from 4 days to many years. The earliest symptom is itching or tingling at the site of the healed bite. Later the patient may develop headache, fever, confusion, hallucinations and hydrophobia. Attempts to drink water induce spasm of the muscles of breathing and swallowing associated with an indescribable terror. Death supervenes after a few days of these terrible symptoms. In a form of rabies that is less often recognised there is spreading paralysis without excitement or hydrophobia. There have been only six known survivors from rabies encephalitis: they were treated with intensive care.

Prevention

Details of pre-exposure immunisation are given in Chapter 2 (see Table 2.1, page 10).

Stroking stray dogs and apparently tame wild animals, keeping carnivores as pets and other unnecessary contact with mammals should be avoided in areas where rabies is endemic. Irrespective of the risk of rabies, mammal (including human) bites and scratches and licks on mucous membranes or broken skin should be cleaned immediately.

First, scrub with soap and water under a running tap if possible, or else immerse in water, for at least 5 minutes. The best virucidal agents are 40–70% alcohol (gin and whisky contain more than 40% alcohol) and povidone–iodine. Mammal bites are frequently contaminated by a variety of micro-organisms other than rabies virus, so a doctor or the expedition nurse should be consulted. Immediate thorough cleaning of the wound is of the utmost importance in preventing infection.

Second, rabies should be considered if it is known to occur in the area. The decision whether or not to give post-exposure vaccination and rabies immune serum is made by a doctor. Ideally, it is based on examination of the biting animal, but usually this is not possible. The species of animal, its behaviour, the circumstances of the bite and, in the case of a domestic animal, when it was last vaccinated are useful pieces of information. The decision must be made as soon as possible by a doctor working in the area where the bite occurs. On no account should it be delayed until patients return to their own country. *If in doubt, vaccinate.* Modern vaccines such as HDCV, PVRV, PCEC and PDEV are potent and safe. They require fewer injections than the older type of nervous tissue vaccine which was given on at least 21 consecutive days under the skin of the abdomen. The old Semple vaccine deserved its reputation for

being dangerous; the tissue culture vaccines are safe. Timely cleaning of the bite wound combined with vaccination and use of immune serum has proved very effective in preventing rabies. If a suspected rabid animal later bites someone who has received pre-exposure immunisation, immunity must be boosted with two injections of vaccine on days 0 and 7.

If the bitten person has not previously been immunised, a full course of post-exposure vaccination is required. The conventional course, using modern vaccines (detailed above), involves intramuscular injections of one whole vial (0.5ml or 1ml of reconstituted vaccine) intramuscularly on days 0, 3, 7, 14 and 30. These individuals should also receive a dose of rabies immune globulin. Half is infiltrated around the bite wound and the rest given intramuscularly into the front of the thigh. The dose of equine rabies immune globulin is 40 units/kg body weight; the dose of human rabies immune globulin is 20 units/kg body weight.

If rapid induction of active immunity is required and there is a shortage of vaccine, modern vaccines can be used effectively and economically by employing an alternative *multiple* site intradermal regime. On day 0, one ampoule of vaccine is divided between eight different sites (both deltoids, both thighs, both sides of the umbilicus and above both shoulder blades at the back). At each site 0.1ml (in the case of 1ml ampoules of vaccine) or 0.05ml (in the case of 0.5ml ampoules of vaccine) is injected intradermally (so that it raises a small *peau d'orange* papule). On day 7, four intradermal injections are given (both deltoids and both thighs) and single intradermal injections are given on days 30 and 90.

It is essential to take rabies seriously and minimise the risk of infection by avoiding potentially rabid animals. If bitten by a suspected rabid animal and no suitable vaccine is available, the individual should be repatriated without delay so as to start post-exposure prophylaxis as soon as possible.

For dog bite/rabies queries contact:

Public Health Laboratory Health Centre
Virus Reference Laboratory
Tel. +44 20 8200 4400 ext. 3204

River blindness (onchocerciasis)

In parts of east, west, central and southern Africa, Mexico and Central America and north-eastern South America (Figure 19.5), pernicious little black flies (for example, *Simulium damnosum*) transmit this infection from human to human in the vicinity of fast-flowing rivers and streams. The adult filarial worms live in subcutaneous nodules, especially around the waist. They produce enormous numbers of microfilariae which cause irritation and changes in the pigmentation and texture of the skin and damage the eyes, eventually causing river blindness. Foreign travellers have contracted onchocerciasis after only brief stops in the transmission zone.

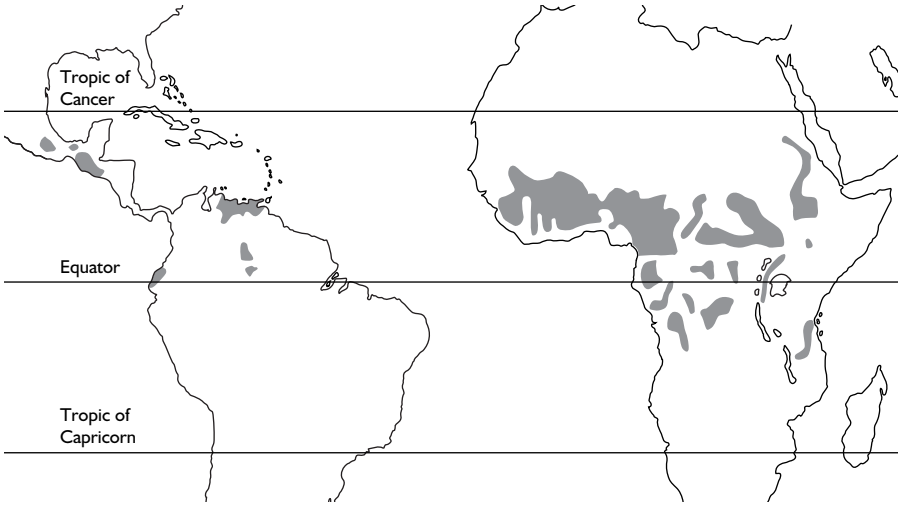


Figure 19.5 *River blindness (onchocerciasis)* (D. Warrell)

Diagnosis is supported by finding blood eosinophilia and is confirmed by microscopical detection of wriggling microfilariae in skin snips taken in affected areas. There is also a blood test of moderate specificity.

Treatment with ivermectin is effective, but may cause a temporary but damaging exacerbation of lesions in the eye and skin and should therefore be supervised in a hospital.

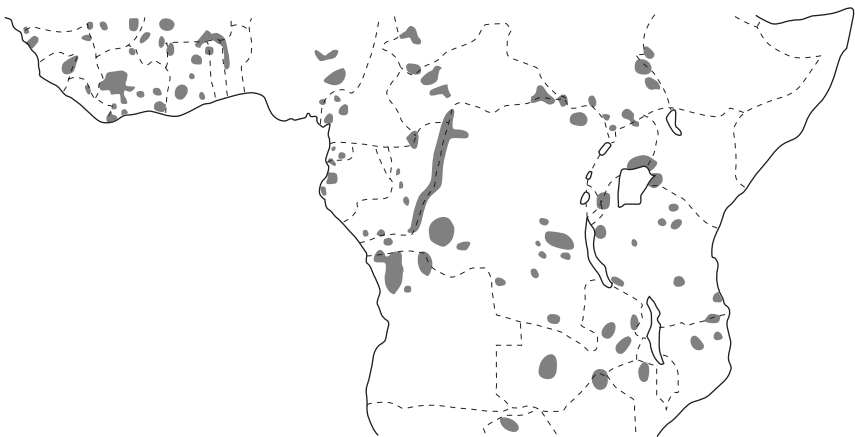


Figure 19.6 *Sleeping sickness (African trypanosomiasis)*

Prevent infection by wearing light-coloured clothing (long sleeves and long trousers) and applying DEET-containing repellents to exposed areas of skin.

Sleeping sickness (African trypanosomiasis)

Tsetse flies (*Glossina*) transmit trypanosomes (*Trypanosoma brucei gambiense*) between humans and *T. b. rhodesiense* between humans and animal reservoir hosts in a number of smallish areas scattered throughout West, Central, East and southern Africa (Figure 19.6). A small ulcer with a scab may appear at the site of the infected tsetse fly bite and, within the next few days, intermittent fever begins associated with headache, loss of appetite and enlargement of lymph glands, especially in the posterior triangle of the neck. Eventually, there is invasion of the central nervous system and patients become apathetic, sleepy and eventually comatose.

The diagnosis is confirmed by finding motile trypanosomes in lymph node aspirates, blood or cerebrospinal fluid. Treatment is difficult, especially after invasion of the central nervous system. Foreign travellers, especially to the game parks of eastern and southern Africa, have been infected and there is currently a massive resurgence of sleeping sickness in central/east Africa.