Imported Infections

Unexplained Fever

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People returning from abroad frequently consult their general practitioners because of a febrile illness developing after arriving home. The cause of the fever may be immediately obvious when it is due to common conditions such as streptococcal tonsillitis or infectious mononucleosis. Sometimes, however, the doctor may be unable to make an immediate diagnosis and must consider the possibility that the patient is suffering from a communicable disease acquired abroad.

The nature of the infection will depend on the areas of the world that the patient has visited. A traveller returning from Northern Europe or North America is unlikely to be suffering from an infection not normally prevalent in the United Kingdom, though the occasional outbreak of smallpox in northern countries must always be considered. Holidaymakers visiting Southern European countries may contract enteric fever, which may present with unexplained fever. Visits to North Africa or the Middle East take the traveller into malarious areas—which are widespread throughout Africa, Arabia, India, and the whole of the Indo-China peninsula. Malaria also occurs in Central and South America and in some areas of northern Australasia. Other causes of fever in patients returning from tropical countries include the typhus fevers, brucellosis, trypanosomiasis, filariasis, schistosomiasis, amoebiasis, kala azar, viral hepatitis, yellow fever, dengue, smallpox, and rare virus infections such as Lassa fever.

Diagnosis

A detailed history must be taken which includes the following questions:

- (1) Where have you been, and where did you stop on the way?
- (2) Which prophylactic immunizations did you have before travelling and what precautions were taken against contracting communicable disease—example, did you drink untreated water or take antimalarial prophylaxis?
- (3) Did you knowingly come into contact with any infectious diseases?
- (4) Have other members of your party been ill?

Physical examination must then be performed with particular attention to the presence of skin lesions, splenomegaly, or cerebral symptoms.

Preliminary investigations should include a white blood count and also examination of blood films for malaria if the patient has visited a malarious area. Urine culture and a chest x-ray film may also be helpful.

At this stage the practitioner may be left with three possible courses of action:

- (1) He may have made a confident diagnosis of a disease such as urinary tract infection which he can treat at home.

- (2) He may refer the patient to hospital, preferably to a communicable or tropical diseases unit, for further investigation.

- (3) He may be unable to exclude the possibility of smallpox and must therefore seek the opinion of the appropriate community physician.

Antibiotics or antimalarial drugs should not be prescribed empirically as these may obscure or delay the diagnosis. In this context it is important to remember that co-trimoxazole can suppress both typhoid fever and malaria. Similarly, ampicillin may delay the diagnosis of enteric fever.

Protozoal Infections

MALARIA

Malaria is regularly imported into the United Kingdom by holidaymakers, businessmen, and immigrants. Malignant tertian malaria caused by *Plasmodium falciparum* is responsible for several deaths each year in northern countries as a result of missed or delayed diagnosis. The onset of malaria is frequently similar to that of influenza and the unsuspecting practitioner may treat the infection as such. The commonest presenting features of malaria are rigors, fever, and headache. All patients who have recently visited malarious areas of the world and who seek medical advice because of these symptoms must have thick and thin blood films examined for malaria parasites. A single negative film does not exclude malaria and it may be necessary in some instances to examine several before the diagnosis is confirmed.

Associated cerebral symptoms suggest the possibility of falciparum malaria, which is a medical emergency, and in these circumstances the patient should be referred immediately to hospital. Most patients developing falciparum malaria in the United Kingdom do so within two to three weeks of arrival, whereas the first attack of benign tertian malaria may be delayed for several months and may be further prolonged in patients who have taken antimalarial prophylaxis.

Benign tertian malaria can usually be treated successfully by a standard course of chloroquine starting with four tablets (each containing 150 mg of chloroquine base), followed by two tablets six hours later and two tablets a day for a further 48 hours. Malignant tertian malaria also normally responds to chloroquine, which should be given by injection to seriously ill patients—but parasites resistant to this agent are being increasingly recognized in the Far East and in South America. Most patients with falciparum malaria in the United Kingdom have travelled from Africa, where chloroquine resistance has not proved to be a problem so far. If there is any possibility of chloroquine resistance the patient must be treated with quinine.

HEPATIC AMOEBIASIS

Hepatic amoebiasis may present with unexplained fever and may be difficult to diagnose. There is usually pain in the right hypochondrium and the liver may be enlarged and tender, but

the symptoms may be non-specific and physical signs minimal. A chest x-ray film may show elevation of the right hemidiaphragm, and a radioactive scan of the liver may be helpful in confirming and localizing an abscess. Cysts of *Entamoeba histolytica* are found in the stools of only a minority of patients but the serum fluorescent antibody test may support the diagnosis of hepatic amoebiasis. There is frequently an increase in the white blood count. Liver abscess formation can be confirmed by aspiration using the scan for localization, with amoebae being found in the aspirated pus.

Hepatic amoebiasis usually responds to a seven-day course of metronidazole (Flagyl) given in a dose of 800 mg three times a day. Amoebiasis of the liver may present many months or even years after leaving the tropics, and it is not necessary for the patient to have had a previous attack of amoebic dysentery.

KALA AZAR

Kala azar (visceral leishmaniasis), which is transmitted by sandflies, is seen very rarely in the United Kingdom. It occurs along the Mediterranean littoral and throughout Africa, South-east Asia, and South America. The incubation period is relatively long, varying from one to two months, but it may extend up to 10 years. The disease starts with fever, which persists for many months and is not accompanied by toxæmia or specific symptoms. Leucopenia and a very high sedimentation rate are characteristic. The spleen enlarges and the liver becomes palpable. Superficial lymphadenopathy usually occurs and skin pigmentation deepens in dark-skinned patients. Diagnosis is made by examination of blood or bone marrow films stained with Leishman's solution, which shows the classical Leishman-Donovan bodies. Kala-azar should be treated by physicians with experience in the management of leishmaniasis.

AFRICAN TRYPANOSOMIASIS

African trypanosomiasis (sleeping sickness) occurs only in Africa, in a belt extending from 12° north to 25° south of the Equator. The incubation period is one to three weeks. *Trypanosoma brucei rhodesiense* infections present acutely with high continued fever and may be associated with hepatitis, pleural effusions, and myocarditis. Diagnosis is made by examination of blood films stained with Leishman's solution.

Trypanosoma brucei gambiense infections develop more insidiously, with low-grade fever, hepatosplenomegaly, and lymphadenopathy. After months or even years the nervous system becomes affected causing headache and personality change. Diagnosis is made by examination of blood films stained with Leishman's solution or by lymph node puncture. The insidious onset of *T. brucei gambiense* trypanosomiasis makes this the more likely of the two forms of African trypanosomiasis to appear in the United Kingdom.

Trypanosomiasis should be treated by physicians with experience of the disease.

Bacterial Infections

ENTERIC FEVER

Enteric fever frequently presents as a pyrexia of undetermined origin. The incubation period is normally 10-14 days. As with

malaria, headaches and fever are prominent early features but repeated rigors are much less common. In children enteric fever may be associated with diarrhoea and vomiting whereas in adults gastrointestinal symptoms tend to occur later in the course of the disease. Abdominal distension is common and the classical "rose spots" may be seen on the periumbilical skin of some white-skinned patients. Mental confusion or dulling, and twitching movements of the lips are characteristic. Relative bradycardia may be noted.

The diagnosis of enteric fever is made by culture of the infecting organism from blood, stool, or urine. The Widal reaction may be helpful from the second week of the illness but previous TAB inoculation may lead to difficulty in its interpretation. Early diagnosis is important in typhoid fever as perforation of the small bowel and gastrointestinal haemorrhage may occur as the disease progresses.

Chloramphenicol is the drug of first choice for the treatment of enteric fever and is given initially in a dose of 3 g per day reducing to 2 g as response occurs. Treatment should be continued for 14 days and the patient observed in hospital for a further two weeks as relapses occur most frequently during this period. Chloramphenicol-resistant *Salmonella typhi* strains are increasing in South-east Asia and Central and South America. Co-trimoxazole has proved effective in these patients and the recent introduction of an intravenous preparation of this compound has added to its value in typhoid fever. Ampicillin is an alternative to chloramphenicol and co-trimoxazole but is less effective in typhoid fever.

TUBERCULOSIS

Though it is relatively unlikely that tuberculosis will be contracted during short visits abroad, this infection is the commonest cause of prolonged unexplained fever in Asian immigrants. The diagnosis may prove difficult in abdominal tuberculosis where there may be no abnormal physical signs. Radiological investigations are usually unhelpful but the sedimentation rate and the serum immunoglobulins are almost invariably raised. Specimens of urine should be sent for tubercle culture and liver biopsy may aid diagnosis. Lymphangiography may be used to outline tuberculous lymph nodes in the abdominal cavity. In some instances it may be necessary to embark on a therapeutic trial of PAS and isoniazid after appropriate specimens have been taken for culture.

BRUCELLOSIS

Holidaymakers and other travellers may contract brucellosis by drinking infected cows' or goats' milk. The incubation period is two to three weeks.

The early diagnosis of brucellosis is important as antibiotic treatment is much more effective in the acute phase of the illness and becomes decreasingly successful as the disease progresses. Brucellosis may be confirmed during the acute illness by isolation of the infecting organism from the blood using selective culture media. Serum agglutination tests may be helpful at this stage but in the chronic disease complement fixation and modified Coombs tests are essential. Brucellosis may occur in the presence of entirely negative serological tests. Acute brucellosis usually responds to 2 g of tetracycline given daily for 21 days. Co-trimoxazole is a satisfactory alternative.