Tropical liver disease

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Abstract

The liver is frequently involved in infections that are prevalent in different regions of the tropics, and chronic liver disease, sometimes with multiple aetiological explanations, is an important cause of early morbidity and mortality. This article describes some hepatic and biliary problems that are seen in the tropics, or which may be imported from resource-poor settings. The epidemiology of hepatitis A is changing in some areas and hepatitis E is now recognized in an increasing range of tropical and non-tropical settings. Vaccines have been developed against hepatitis E. Hepatitis B and C continue to cause chronic liver disease, cirrhosis and hepatocellular carcinoma, but these may be eclipsed in epidemiological importance by the sequelae of the emerging epidemic of non-alcoholic fatty liver disease in many parts of the tropics. The pathophysiology of acute and chronic liver disease due to aflatoxins is better understood, as is the relationship of veno-occlusive disease of the liver to pyrrolizidine alkaloids. Self-poisoning with hepatotoxins is common in many countries. The diagnosis and management of cystic hydatid disease of the liver has been rationalized, based on a systematic approach to the classification of imaging findings.

Keywords Aflatoxins; biliary parasites; hepatitis; hepatobiliary tumours; jaundice; tropical liver disease

What's new?

- Further recognition of acute and chronic hepatitis E in non-tropical settings
- Vaccines against hepatitis E
- Recognition of HIV/hepatitis B or C co-infections in tropics
- Improved understanding of pathogenesis of hepatic disease caused by aflatoxins
- Improved understanding of Indian childhood cirrhosis
- Confirmation of aetiology of veno-occlusive disease of the liver in Afghanistan
- Increasing importance of non-alcoholic fatty liver disease as cause of 'cryptogenic cirrhosis' and hepatocellular carcinoma in the tropics

Some hepatic and biliary problems are specifically seen in the tropics, or may be imported from the tropics; these are summarized in Table 1.

Jaundice and/or hepatitis

Several prehepatic, intrahepatic and posthepatic conditions are specific to resource-poor settings. Haemolysis, due to haemoglobinopathies and other inherited blood disorders, is common, sometimes associated with secondary gallstones, and may be provoked by acute infections, particularly pneumococcal disease and malaria. Many infections cause hepatitis, with varying degrees of jaundice and hepatosplenomegaly. Some, such as viral hepatitis, are widespread, whereas others, such as yellow fever, are found only in specific geographical regions (see also *Medicine* 2005; **33**(7): 21–3).

Hepatitis A used to be a universal childhood infection in most of the tropics, inducing life-long immunity, so a jaundiced adult in the tropics was unlikely to have acute hepatitis A unless he or she was an unvaccinated visitor from a resource-rich setting. However, childhood infection is becoming less common in countries in which sanitation is improving, such as Singapore and the Middle East, and in Sri Lanka only 70% of adults have had childhood exposure, so adults are now being seen with acute hepatitis A. Hepatitis E is present throughout the tropics, has caused several recent epidemics in Sub-Saharan Africa, and is endemic in Central America and the Indian subcontinent. Hepatitis E is now the most common cause of acute viral hepatitis in travellers returning to the UK (see Hepatitis E, A and other hepatotropic viruses, pages 594–598 of this issue). Asymptomatic infections with the glandular fever group of viruses (e.g. Epstein–Barr virus, cytomegalovirus) are also common in childhood in the tropics, and are quite common causes of acute hepatitis in young adults returning to the UK after travelling overseas.

The history and geographical setting usually limit the number of likely diagnoses in patients with abnormal liver function tests (LFT) with or without jaundice. For example, in Sri Lanka, the most likely causes of increased LFT with or without jaundice and fever include cholangitis/cholelithiasis, dengue and leptospirosis.

Dengue

Hepatic dysfunction is a well-recognized complication of dengue, more often in adults than in children. Transaminase elevation is observed in almost all patients and the degree of elevation correlates with the severity of the illness. Jaundice and acute liver failure develop in a small proportion of patients. Typically, the aspartate aminotransferase (AST) concentration exceeds that of alanine aminotransferase (ALT), compared to the reverse pattern for viral hepatitis, and serum bilirubin is

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Tropical liver disease by presentation and/or aetiology

Jaundice/hepatitis/hepatosplenomegaly
Inherited haemolytic disorders
Acute viral hepatitis A, B, C, D, E
Biliary flukes
Brucellosis
Dengue
Enteric fever
Hepatobiliary ascariasis
HIV related (e.g. cryptococcosis)
Leptospirosis
Malaria
Rickettsial infection
Secondary syphilis
Sepsis
Tuberculosis
Viral haemorrhagic fevers
Yellow fever
Toxins and drugs
Ackee poisoning
Aflatoxins
Amanita phalloides (death cap mushroom)
Bantu siderosis (iron)
Bush teas
Illicit alcohol (methanol)
Industrial toxins
Indian childhood cirrhosis (copper)
Paraquat
Traditional herbal remedies (pyrrolizidine alkaloids)
Cirrhosis and/or fibrosis
Alcohol
Chronic hepatitis B, D, C
Non-alcoholic fatty liver disease (NAFLD)
Schistosomiasis (fibrosis)
Hepatomegaly
Alveolar hydatid
Amoebic liver abscess
Cholangiocarcinoma
Cystic hydatid
Hepatocellular carcinoma
Liver fluke *Fasciola hepatica*
Pyogenic liver abscess
Massive hepatosplenomegaly
Hyper-reactive malarial splenomegaly
Late stage schistosomiasis
Tropical splenic lymphoma
Visceral leishmaniasis

Table 1

normal or only minimally raised. Serum transaminase concentrations are occasionally as high as those in viral hepatitis and seen late in the illness. This may be a direct viral effect or it may be secondary to aggressive host immune response. Ischaemic hepatitis could contribute to massive elevations of transaminases encountered in circulatory collapse in dengue shock syndrome. One factor that may influence the pattern of disease seen in adults is the greater likelihood of underlying chronic liver disease, potentially compounding the acute infection, such as alcoholic liver disease, non-alcoholic fatty liver disease (NAFLD) and chronic viral hepatitis B or C.[1] In the absence of a specific treatment, most patients with liver involvement due to dengue improve with supportive care but fatalities have been reported.

Leptospirosis

Leptospirosis would be suggested by exposure to water, subconjunctival haemorrhages, raised serum creatine kinase, mild elevation of transaminases relative to bilirubin, and renal or cardiac involvement. These are initial clues pending availability of specific serology.

Tuberculosis

Tuberculosis affects the liver in several ways. Caseating granulomatous hepatitis ranges from mild to severe and can rarely result in hepatic failure, usually in the context of advanced disseminated infection. Obstructive jaundice, although rare, may occur due to lymphadenopathy obstructing the porta hepatis, and therapy of tuberculosis may be complicated by drug-induced hepatitis. Patients with human immunodeficiency virus (HIV) may have invasive non-tuberculous mycobacterial or cryptococcal hepatitis.

Hepatitis D

In tropical communities with high carriage rates of hepatitis B, an outbreak of jaundice with high mortality could suggest an epidemic of 'super-infection' of chronic hepatitis B carriers with hepatitis D (formerly delta hepatitis), known as 'Santa Marta' or 'La Brea fever' in parts of South America.

In most tropical communities experiencing a sudden outbreak of jaundice, the more likely diagnoses are water-borne or food-borne problems including:

- hepatitis E — affects especially young adults; deaths of pregnant women and fetal loss
- leptospirosis — often associated with heavy rains/floods
- food toxins (e.g. aflatoxin) — acute poisoning reported in India and Kenya.

Jaundice may be a prominent feature of malaria, which is diagnosed by blood film examination (see also *Medicine* 2014; **42**(2); 100–106).

Biliary parasites

The roundworm, *Ascaris lumbricoides*, infects billions of people and its major acute morbidity is associated bowel obstruction in children. However, adult worms can occasionally migrate up the biliary tree to cause cholangitis, which can be relieved by endoscopic removal. Hepatopancreatic ascariasis is more common in women and may account for a quarter of cases of pancreatitis in India (Figure 1).[2] The worms occasionally migrate further up the biliary tree and can form a nidus for infection and subcapsular hepatic abscesses. Biliary fluke (*Clonorchis/Opisthorchis*) infections in South East Asia cause cholangitis with blood eosinophilia and can be recognized by the presence of fluke eggs in faeces. They respond to treatment with praziquantel.[3] Chronic fluke infection is associated with cholangiocarcinoma, particularly in male patients.