

Tropical liver disease

Nick Beeching

Anuradha Dassanayake

Abstract

The liver is frequently involved in infections that are prevalent in different regions of the tropics, and chronic liver disease, sometimes of multiple aetiologies, 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 recognised 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 rationalised, based on a systematic approach to the classification of imaging findings.

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

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

A variety of prehepatic, intrahepatic and posthepatic conditions are specific to resource-poor settings. Haemolysis, due to haemoglobinopathies and other inherited blood disorders, is common, sometimes with secondary gallstones, and may be provoked by

Nick Beeching *FRCP FRACP FRCM* is Senior Lecturer and Consultant in Infectious Diseases at the Liverpool School of Tropical Medicine, UK. He trained in Oxford, Liverpool, Adelaide, Birmingham and Auckland and worked in Saudi Arabia for 2 years. His clinical and research interests include gastrointestinal infections, viral hepatitis and hydatid disease. Competing interests: Dr Beeching has received speaker fees and research grants from several companies that manufacture hepatitis vaccines.

Anuradha Dassanayake *MBBS MD* is a Consultant Physician with an interest in Liver disease and a Senior Lecturer at the Faculty of Medicine University of Kelaniya, Ragama, Sri Lanka. He qualified from the University of Colombo, Sri Lanka and trained in Ragama and the Royal Free Hospital, London, UK. His research interests include therapeutics of liver disease. Competing interests: none declared.

What's new?

- Recognition of acute and chronic hepatitis E in non-tropical settings
- Vaccines against hepatitis E
- Improved understanding of pathogenesis of hepatic disease caused by aflatoxins
- 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
- Internationally agreed classification and management schemes for cystic hydatid disease

acute infections, particularly pneumococcal disease and malaria. A large number of 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 un-vaccinated 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, with several recent epidemics in sub-Saharan Africa, and is endemic in Central America and the Indian subcontinent. Hepatitis E routinely affects adults as well as children and pregnant women have high mortality rates. It is now the most common cause of acute viral hepatitis in travellers returning to the UK. It is also increasingly recognized in Western settings as a cause of both acute and chronic liver disease, especially in immunosuppressed individuals, following consumption of undercooked pig products.¹ Effective vaccines have been developed but are not routinely available for travellers.² Asymptomatic infections with the glandular fever group (Epstein–Barr virus, cytomegalovirus, etc.) of viruses 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 of 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, leptospirosis and, in a few areas, malaria. Hepatic dysfunction is a well-recognized complication of dengue, of uncertain pathogenesis. It is more frequent in adults than in children, usually causing raised transaminases.³ Typically the aspartate aminotransferase (AST) level exceeds the alanine aminotransferase (ALT) level, compared to the reverse pattern for viral hepatitis, and bilirubin is normal or minimally raised. Serum transaminase concentrations are occasionally as high as those in viral hepatitis, and fulminant hepatitis is a rare

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

complication. Leptospirosis would be suggested by exposure to water, subconjunctival haemorrhages, raised creatine kinase, mild elevation of transaminases compared to bilirubin, and renal or cardiac involvement. These are initial clues pending availability of specific serology. Jaundice may be a prominent feature of malaria,

which is diagnosed by blood film examination (see also *Medicine* 2010; **38**(1): 41–6).

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.

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.

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).⁴ The worms occasionally migrate further up the biliary tree and can form a nidus for infection and subcapsular hepatic abscesses. Biliary flukes (*Clonorchis/Opisthorchis*) infections in South East Asia cause cholangitis with blood eosinophilia and fluke eggs in faeces. They respond to treatment with praziquantel.⁵

Toxins

Environmental contamination may lead to acute or chronic poisoning; for example, those who work in the polyvinyl chloride industry are at increased risk of cholangiocarcinoma. Illicitly brewed alcohol, sometimes contaminated with methanol, is associated with epidemics of acute and often fatal liver disease every year. Natural contaminants of grain, especially aflatoxins, are important as co-factors in the induction of hepatocellular carcinoma, especially in association with chronic hepatitis B, and are also responsible for outbreaks of severe acute liver disease in parts of Africa and India.⁶ In addition to the hazards of prescribed drugs, especially antibiotics, traditional herbal remedies may be hepato-toxic and are frequently used by patients before seeking allopathic medical advice.⁷ These may be unsuspected reasons for jaundice in immigrants to Western countries unless the history is taken carefully. 'Bush teas' in Africa and the West Indies predispose patients to Budd–Chiari syndrome. Outbreaks of veno-occlusive disease of the liver continue to be reported in Herat Province in Afghanistan, with high mortality.⁸ Known locally as 'camel-belly', this is due to contamination of flour with pyrrolizidine alkaloids from

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