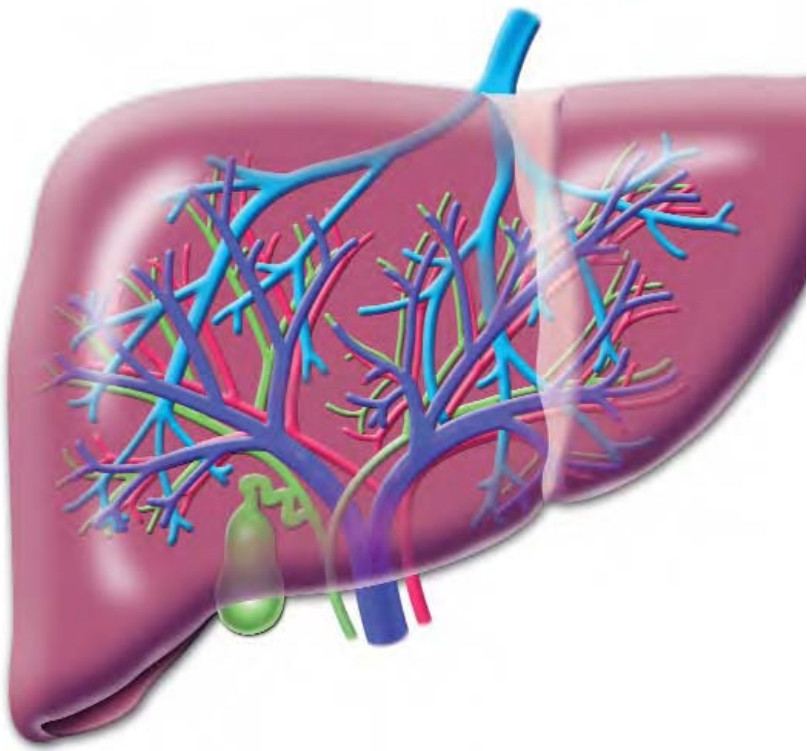
Fast Facts

Fast Facts:
Liver Disorders

Thomas Mahl and John O'Grady



HEALTH PRESS

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Fast Facts: Liver Disorders

Thomas Mahl MD
University at Buffalo School of Medicine
Buffalo, New York, USA

John O'Grady MD
Institute of Liver Studies
King's College School of Medicine
London, UK

Declaration of Independence
This book is as balanced and as practical as we can make it. Ideas for improvement are always welcome: feedback@fastfacts.com

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Thomas Mahl, John O'Grady

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Glossary of abbreviations

AFP: alpha fetoprotein

AIH: autoimmune hepatitis

ALD: alcoholic liver disease

ALT: alanine aminotransferase

AMA: antimitochondrial antibodies

AST: aspartate aminotransferase

ATD: α_1 antitrypsin deficiency

BMI: body mass index

CT: computed tomography

DILD: drug-induced liver disease

EVL: endoscopic variceal ligation

ES: endoscopic sclerotherapy

GGT: gamma-glutamyltransferase

HBeAg/Ab: hepatitis B 'e' antigen/antibody

HBsAg/Ab: hepatitis B 'surface' antigen/antibody

HBV: hepatitis B virus

HCC: hepatocellular carcinoma

HCV: hepatitis C virus

HELLP: hemolysis, elevated liver enzymes, low platelet count

***HFE*:** High Fe (gene – mutations result in hemochromatosis)

Ig: immunoglobulin

INR: international normalized ratio

LDLT: living donor liver transplant

LVP: large-volume paracentesis

MELD: model for end-stage liver disease

NAFLD: non-alcoholic fatty liver disease

NASH: non-alcoholic steatohepatitis

5NT: 5'nucleotidase

pANCA: perinuclear antineutrophil cytoplasmic antibody

PCR: polymerase chain reaction

PELD: pediatric end-stage liver disease

***PiZZ*:** protease inhibitor, Z variant, homozygous (a mutation of the α_1 antitrypsin gene)

PBC: primary biliary cirrhosis

PSC: primary sclerosing cholangitis

PT: prothrombin time

PTLD: post-transplant lymphoproliferative disease

SAAG: serum–ascites albumin gradient

SBP: spontaneous bacterial peritonitis

TIPS: transjugular intrahepatic portosystemic shunt

TNF: tumor necrosis factor

UDCA: ursodeoxycholic acid

WBC: white blood cell

Introduction

Our aim in this book is to provide a succinct and useful guide to the clinical management of patients with liver disease. Acute presentations of liver disease are common and most resolve spontaneously. However, establishing an accurate diagnosis and understanding the indicators of severe disease are very important in order to avoid delay in identifying the small cohort in need of referral for specialist treatment.

Alcoholic liver disease presents in many forms, and there is an emerging epidemic of similar disease in non-alcohol consumers, particularly related to obesity. Recognition of chronic hepatitis B and C is improving, with more patients receiving antiviral therapy. This is a particularly dynamic area with new therapies emerging quite regularly. The review of these topics is pitched at understanding the most important issues within these chronic liver diseases.

Increasing numbers of patients are undergoing liver function tests and ultrasonic evaluation of the liver, resulting in the identification of abnormalities that need to be put into perspective. We have given this clinical scenario considerable attention, as we believe that in this situation quick access to a common-sense approach to investigation or a simple explanation will be of benefit.

At the other end of the spectrum, many non-specialists and primary care physicians are encountering patients who have been recipients of liver transplants. We deal with some of the commoner associated clinical problems that may need attention in the community.

We hope that you will find this book helpful.

1 Investigating liver disease

Liver disorders are encountered frequently in general practice. Recent data suggest that 5.5 million Americans have chronic liver disease. At least 1% of asymptomatic patients will have elevated liver test results, although the incidence of abnormal results varies considerably with the population studied. The goals of the physician's investigation are to understand the origin of the liver injury, to correct its cause and to prevent permanent organ dysfunction (i.e. cirrhosis). An organized approach to investigating liver abnormalities allows the physician to reach conclusions promptly, and avoids excessive cost or risk to the patient.

Acute liver injuries

Acute liver injuries are defined by hepatologists as those that resolve within 6 months. Patients with acute liver disease typically have no previous history of liver injury. They may complain of fatigue, anorexia, malaise and discomfort in the right upper quadrant of the abdomen. Jaundice may be seen and tender hepatomegaly elicited. Acute liver injuries (e.g. viral hepatitis, exposure to a toxin or medication) typically resolve once the offending agent is removed or the viral infection resolves, and usually there are no sequelae. Occasionally, however, liver injury is so severe that the patient does not have enough hepatocytes remaining to allow for homeostasis – a condition called fulminant hepatic failure or acute liver failure (see page 20).

Chronic liver injuries

The primary care provider more often encounters chronic, rather than acute, liver disease. Patients typically present with few symptoms, and diagnosis is on the basis of abnormal blood results on routine examination. They may complain of fatigue and malaise. The examiner may find stigmata of chronic liver disease, such as gynecomastia, spider nevi, telangiectasia and palmar erythema. The liver is usually enlarged and may be firm; a tender liver is uncommon. If advanced liver disease

has developed (e.g. cirrhosis), signs of portal hypertension, such as caput medusae or ascites, may be present.

History

As with all medical conditions, it is vital to obtain a thorough and accurate history. With respect to liver disease, it is necessary to determine if there is any history of jaundice. Risk factors for viral hepatitis include prior transfusion, multiple sexual partners, tattoo application and needle sharing. Alcohol, of course, is a common hepatic toxin, and physicians must be adept at determining a patient's alcohol consumption. Unfortunately, this is significantly more difficult to accomplish in practice than in theory. Alcoholism is a disease of denial, and many patients will not admit to, or even realize, how much alcohol they consume.

Medications may also cause liver disease, so it is important to determine which medications a patient is taking, and particularly those temporally related to the development of the liver disorder. Some over-the-counter medications and herbal remedies have also been reported to cause liver abnormalities. Although most hepatic toxins are no longer common in the workplace, an occupational history may reveal relevant exposures.

A family history of liver disease is equally important. In our experience the liver disease that most commonly clusters in a family is alcoholic liver disease (ALD), but other diseases such as Wilson's disease and hemochromatosis (see Chapter 6, Metabolic liver diseases) should be considered.

Liver tests

Liver enzymes. The liver typically responds to injury by releasing enzymes from hepatocytes and/or biliary epithelium. Elevated levels of enzymes of hepatocellular origin, such as aspartate aminotransferase (AST) and alanine aminotransferase (ALT), suggest injury to hepatocytes. Elevations in alkaline phosphatase suggest injury to structures of the biliary tree.

AST is a mitochondrial enzyme found in the liver and other tissues, such as skeletal and myocardial muscle. ALT is a cytoplasmic enzyme

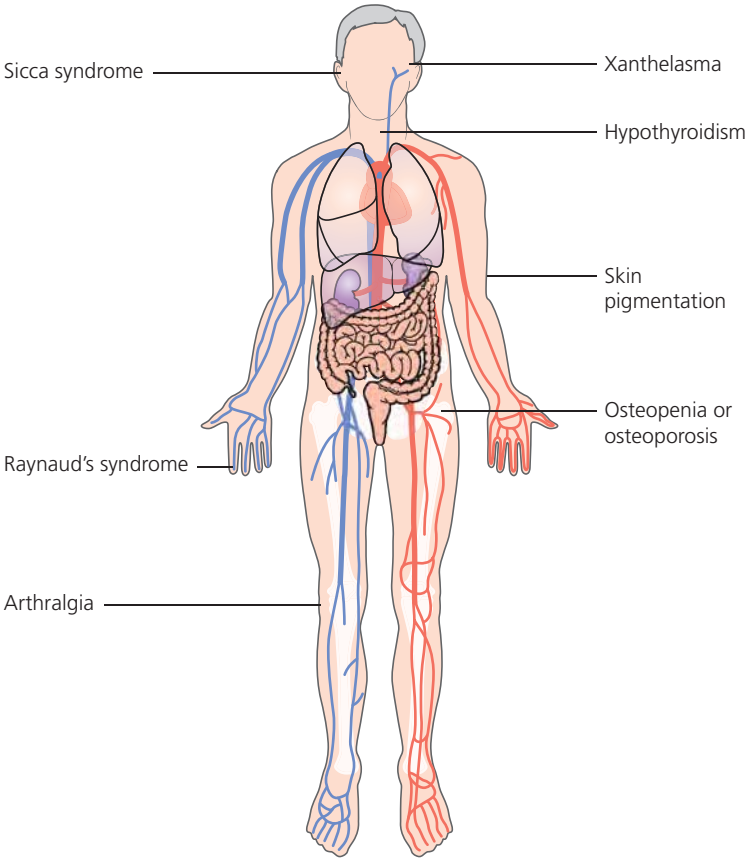

Figure 5.2 Extrahepatic associations in primary biliary cirrhosis.

exhibit signs of portal hypertension, with ascites and esophageal or gastric varices. Encephalopathy is less common than in other causes of end-stage chronic liver disease.

There is no curative medical therapy for PBC. There is some evidence to support treatment with ursodeoxycholic acid (UDCA), as this improves the biochemical profile and possibly the histological appearance. There is, however, limited evidence that UDCA prolongs survival or delays the need for liver transplantation. A number of other immunosuppressive and antifibrotic therapies have failed to demonstrate sufficient benefit to gain widespread use.

Liver transplantation is still the only effective treatment for advanced PBC. The indications for transplantation are:

- serum bilirubin above 100–150 µmol/L (6–10 mg/dL)
- evidence of liver failure or severe portal hypertension at lower serum bilirubin levels
- severe intractable pruritus or lethargy
- severe osteoporosis
- complicating hepatocellular carcinoma.

The results of liver transplantation for PBC are excellent. There is evidence that PBC recurs in the transplanted liver, but this phenomenon appears to be of little clinical relevance in the first 10–15 years after transplantation.

Primary sclerosing cholangitis

PSC can affect all elements of the biliary system. Cholangiography classically shows diffuse stricturing and beading involving both the intrahepatic and extrahepatic bile ducts. In some cases, the extrahepatic bile ducts are spared, and confidence in making the diagnosis on radiological criteria is reduced. Liver histology may show the characteristic lesion of concentric fibrosis around the small bile ducts, termed 'onion-skin' fibrosis. The characteristic autoantibody is perinuclear antineutrophil cytoplasmic antibody (pANCA), but other autoantibodies may also be detected. Hypergammaglobulinemia occurs, with a predominant increase in the IgM fraction.

There is a strong association between PSC and inflammatory disease involving the large bowel – mainly ulcerative colitis but also Crohn's disease. About 75% of patients with PSC have inflammatory bowel disease and up to 7.5% of patients with ulcerative colitis have PSC. The diagnosis of PSC may be suggested by the detection of elevated cholestatic enzymes, particularly alkaline phosphatase, on routine screening of patients with inflammatory bowel disease. More advanced disease presents with jaundice and symptoms of biliary obstruction (dark urine, pale stools, itch) or low-grade cholangitis (fevers, sweats, feeling intermittently hot and cold).