Liver enzymes, including aminotransferases and alkaline phosphatase, are some of the most commonly ordered blood tests in a physician’s practice. These enzymes have been valuable in screening for liver disease, as well as in diagnosing and monitoring patients with acute and chronic hepatobiliary disorders. Patients with predominantly aminotransferase elevations are thought to have acute or chronic hepatitis from a variety of causes. In patients with predominantly alkaline phosphatase elevations, imaging evaluation is undertaken upfront to exclude large bile duct disorders and infiltrative/mass lesions. A liver biopsy may be reserved for patients for whom these less invasive investigations are unfruitful.

Cholestasis develops either from a defect in bile synthesis, impairment in bile secretion, or obstruction to bile flow, and is characterized by an elevated serum alkaline phosphatase and gamma-glutamyltransferase disproportionate to elevation of aminotransferase enzymes. Key elements to the diagnostic workup include visualization of the biliary tree by cholangiography and evaluation of liver histology. The hope is that recent advances in understanding the genetic factors and immune mechanisms involved in the pathogenesis of cholestasis will lead to newer therapeutic interventions in the treatment of these diseases.

Drug-induced liver injury (DILI), also known as hepatotoxicity, refers to liver injury caused by drugs or other chemical agents, and represents a special type of adverse drug reaction. It has been estimated that more than 600 drugs and chemicals have been associated with significant liver injury. Many previous reviews have focused on DILI pathogenesis or have outlined the clinical features of liver injury linked to different drugs. This article briefly touches on several areas that are potentially vexing for both the novice and cognoscenti, with the goal of guiding the consultant through one of the most challenging areas of hepatology.

Changes in the liver biochemical profile are normal in pregnancy. However, up to 3% to 5% of all pregnancies are complicated by liver dysfunction. It
is important that liver disease during pregnancy is recognized because
early diagnosis may improve maternal and fetal outcomes, with resultant
decreased morbidity and mortality. Liver diseases that occur in pregnancy
can be divided into 3 different groups: liver diseases that are unique to
pregnancy, liver diseases that are not unique to pregnancy but can be re-
vealed or exacerbated by pregnancy, and liver diseases that are unrelated
to but occur coincidentally during pregnancy.

Evaluation of Liver Lesions
Alan Bonder and Nezam Afdhal

The differential diagnosis of a liver mass is large and requires understand-
ing of the clinical and imaging features of liver lesions. A detailed history,
physical examination, hepatic biochemical tests, and imaging studies
are all essential in making the diagnosis. Decisions regarding specific im-
ageing modalities for diagnoses, the use of liver biopsy, therapeutic options,
and appropriate follow-up are all determined by the presentation of the
lesion and associated patient characteristics.

Ascites
Fredric D. Gordon

Ascites is the pathologic accumulation of fluid in the peritoneum. It is the
most common complication of cirrhosis, with a prevalence of approxi-
mately 10%. Over a 10-year period, 50% of patients with previously com-
penated cirrhosis are expected to develop ascites. As a marker of hepatic
decompensation, ascites is associated with a poor prognosis, with only a
56% survival 3 years after onset. In addition, morbidity is increased
because of the risk of additional complications, such as spontaneous
bacterial peritonitis and hepatorenal syndrome. Understanding the patho-
physiology of ascites is essential for its proper management.

Hepatic Encephalopathy
Vandana Khungar and Fred Poordad

Hepatic encephalopathy (HE) represents a continuum of transient and re-
versible neurologic and psychiatric dysfunction. It is a reversible state of
impaired cognitive function or altered consciousness in patients with liver
disease or portosystemic shunting. Over the last several years, high-quality
studies have been conducted on various pharmacologic therapies for HE;
as more data emerge, it is hoped that HE will become a more easily treated
complication of decompensated liver disease. In the interim, it is important
that physicians continue to screen for minimal HE and treat patients early in
addition to continuing to provide current treatments of overt HE.

Shortness of Breath in the Patient with Chronic Liver Disease
Paul Y. Kwo

Shortness of breath is a common complaint in those with chronic liver dis-
ease. The differential diagnosis for this complaint includes primary pulmo-
ary disorders, systemic disorders that affect the liver and lungs, and
extrahepatic manifestations of portal hypertension. Orthotopic liver trans-
plant, when appropriate, is the most effective therapy for many patients
with dyspnea and chronic liver disease, although therapies to treat the underlying complications of cirrhosis may provide relief. Shortness of breath in patients with cirrhosis often portends a poor prognosis, and these patients should be evaluated for orthotopic liver transplant because this therapy is most likely to provide long-lasting benefit.

Pruritus in Chronic Cholestatic Liver Disease

Chalermrat Bunchorntavakul and K. Rajender Reddy

Pruritus is a troublesome complication in patients with cholestatic liver disease. Several links to its pathogenesis have been proposed, including the role of bile acids, endogenous opioid and serotonin, and lysophosphatidic acid. The management of pruritus in cholestasis is challenging. Medical treatment of the underlying cholestatic condition may provide benefit. Extracorporeal albumin dialysis can be pursued for those who have a poor quality of life and failed the various therapeutic interventions, while awaiting liver transplantation. Experimental interventions, and the management of pruritus in certain conditions such as intrahepatic cholestasis of pregnancy and benign recurrent intrahepatic cholestasis, are also briefly reviewed.

Chronic Hepatitis B Infection

Alexander Kuo and Robert Gish

The management of chronic hepatitis B virus (HBV) infection requires understanding the natural history of the disease as well as the risks, benefits, and limitations of the therapeutic options. This article covers the principles governing when to start antiviral therapy, discusses recent advances using hepatitis B surface antigen quantification to better define various phases of infection, describes the use of HBV core, precore, and viral genotyping as well as host IL28B genotyping to predict response to interferon therapy, and reports on the management of HBV in 3 special populations (pregnancy, postliver transplantation, and in the setting of chemotherapy or immunosuppression).

Alcoholic Hepatitis: A Clinician’s Guide

Gina Choi and Bruce Allen Runyon

Alcoholic hepatitis is a frequent reason for admission and a common consultation request for hepatologists and gastroenterologists. Although it seems to occur acutely, it is usually subacute and often superimposed on underlying alcoholic cirrhosis. Typically patients have a background of drinking on a daily basis, but, in response to a life crisis, patients have started drinking massively.

Granulomatous Liver Disease

Steven L. Flamm

Hepatic granulomata are not infrequently encountered in liver biopsy and often are associated with systemic disease. The clinical presentation varies with the particular systemic process. From a biochemical standpoint, the most common abnormalities are elevated serum alkaline phosphatase and γ-glutamyltransferase. The observation of granulomata in a liver biopsy specimen warrants workup to identify a possible cause.
Clues may be obtained in the medical history, on physical examination, or with specialized blood testing or radiologic studies. Treatment involves therapy of the underlying cause of the disease associated with the development of the granulomatous hepatitis.

**Nonalcoholic Fatty Liver Disease**

Angelo H. Paredes, Dawn M. Torres, and Stephen A. Harrison

As the hepatic manifestation of the metabolic syndrome, nonalcoholic fatty liver disease (NAFLD) has become the most common cause of asymptomatic liver enzyme elevations in Western nations. Although it is easy to diagnose NAFLD, a liver biopsy is currently required to diagnose nonalcoholic steatohepatitis (NASH). Patients with NASH are those at greatest risk of progression to cirrhosis and, thus, treatment efforts are targeted to these individuals. Although currently there are no FDA-approved treatments for NASH, a multidisciplinary approach that addresses comorbid conditions and promotes modest weight loss comprises the backbone of therapy.

**Surgical Clearance for the Patient with Chronic Liver Disease**

Andrew J. Muir

Patients with chronic liver disease face greater risk of perioperative morbidity and mortality, with the greatest risk among patients with cirrhosis. Both the Child-Pugh score and the Model for End-Stage Liver Disease have been evaluated as predictors of postoperative mortality. Other comorbidities, age, and American Society of Anesthesiologists physical status classification are also important predictors of these outcomes. In patients with liver disease, elective surgeries should be delayed to allow complete evaluation of the severity of liver disease, including the role of transplantation in the event of hepatic decompensation postoperatively.

**Is the Patient a Candidate for Liver Transplantation?**

Alyson N. Fox and Robert S. Brown Jr

Identifying whether someone is a good candidate for liver transplantation is a complex process that requires a team approach. There are several medical and psychosocial considerations involved, each of which is thoroughly explored during the evaluation process. Both the indications and contraindications to transplantation can change over time, reflecting advances in understanding of, and ability to treat, certain disease processes. Ultimately, the goal of liver transplantation remains to provide a survival benefit to those with acute or chronic liver diseases.

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