Alcoholic liver disease is a major cause of morbidity and mortality among people who drink excessive amounts of alcohol. There is a spectrum of liver injury that ranges from steatosis to varying stages of hepatic fibrosis and cirrhosis, with subsequent risk for hepatocellular carcinoma. Steatohepatitis can occur at any stage of disease.

This article describes the pathways and factors that modulate blood alcohol levels and metabolism and describes how the body disposes of alcohol. The various factors that play a role in the distribution of alcohol in the body, influence the absorption of alcohol, and contribute to first-pass metabolism of alcohol are described. Most alcohol is oxidized in the liver, and general principles and overall mechanisms for alcohol oxidation are summarized. The kinetics of alcohol elimination in-vivo and the various genetic and environmental factors that can modify the rate of alcohol metabolism are discussed.

Hepatic fibrosis is a known consequence of long-term use of alcohol and is regarded as a turning point in alcohol-induced liver disease because it can lead to cirrhosis. The mechanisms of injury are not well understood, but recent studies have helped advance the understanding of the earliest events in the process that eventually leads to hepatic injury and, in some cases, fibrosis. It is hoped that increasing understanding of the role played by the immune system in the process will lead to the development of new therapies for these patients.

The necessity of the liver being the organ responsible for metabolism of alcohol exposes it to many untoward toxic side effects. In the first instance of hepatic steatosis, fibrosis may occur indolently over years, slowly converting a greasy, steatotic liver into a cirrhotic liver. In the case of alcoholic hepatitis, brisk sinusoidal fibrosis may lead to more rapid development of cirrhosis, with the liver extensively subdivided by sublobular fibrous septa developing in the midst of extensive ongoing inflammation and hepatocellular destruction. Continued destruction of the parenchyma after cirrhosis
has developed may produce a densely fibrotic organ with little remaining parenchyma.

Diagnosis and Management of Alcoholic Hepatitis 717

Umair Sohail and Sanjaya K. Satapathy

Alcoholic hepatitis is a form of severe, cholestatic liver disease that results from consumption of large amount of alcohol during a sustained period of time in a subset of alcoholics. Symptoms could be mild and nonspecific to more severe. The diagnosis of alcoholic hepatitis can be made with a thorough history, physical examination, and review of laboratory results. Liver biopsy is confirmatory but generally not indicated for the diagnosis. Abstinence is the key form of therapeutic intervention. Despite variable results in clinical trials, corticosteroids and pentoxifylline seem to provide moderate survival benefit. Liver transplantation in acute alcoholic hepatitis is contentious.

Management of Alcohol Abuse 737

Anthony P. Albanese

This article reviews the spectrum of alcohol use disorders. The pharmacologic properties of ethanol and its metabolism, and the historical, physical, and laboratory elements that may help diagnose an alcohol use disorder are examined. The concepts of motivational interviewing and stages of change are mentioned, along with the American Society of Addiction Medicine patient placement criteria, to determine the best level of treatment for alcoholism. Various therapeutic management options are reviewed, including psychological, pharmacologic, and complementary/alternative choices. This article provides a basic understanding of available tools to diagnose and treat this cunning and baffling brain and multi-system disease.

Long-term Management of Alcoholic Liver Disease 763

Garmen A. Woo and Christopher O’Brien

Alcoholic liver disease is a major cause of morbidity and mortality worldwide. Patients with cirrhosis caused by alcohol are at risk for developing complications associated with a failing liver. The long-term management of alcoholic liver disease stresses the following: (1) Abstinence of alcohol (Grade 1A), with referral to an alcoholic rehabilitation program; (2) Adequate nutritional support (Grade 1B), emphasizing multiple feedings and a referral to a nutritionist; (3) Routine screening in alcoholic cirrhosis to prevent complications; (4) Timely referral to a liver transplant program for those with decompensated cirrhosis; (5) Avoid pharmacologic therapies, as these medications have shown no benefit.

Infections in Alcoholic Liver Disease 783

Angela C. Kim, Marcia E. Epstein, Pranisha Gautam-Goyal, and Thien-Ly Doan

Alcoholic individuals are at increased risk of infection in general, in part because of immune defects. In addition, associated situations, such as depressed mental status, increase risk to specific syndromes such as
lung abscess related to depressed consciousness and aspiration. Social factors related to hygiene and living situations are also linked to specific microorganisms, such as *Mycobacteria tuberculosis*, *Bartonella quintana*, *Vibrio vulnificus*, and *Capnocytophaga canimorus*.

**Nutrition in Alcoholic Liver Disease**

Ashwani K. Singal and Michael R. Charlton

The liver plays an important role in the metabolism, synthesis, storage, and absorption of nutrients. Patients with cirrhosis are prone to nutritional deficiencies and malnutrition, with a higher prevalence among patients with decompensated disease. Mechanisms of nutritional deficiencies in patients with liver disease are not completely understood and probably multifactorial. Malnutrition among patients with cirrhosis or alcoholic liver disease correlates with poor quality of life, increased risk of infections, frequent hospitalizations, complications, mortality, poor graft and patient survival after liver transplantation, and economic burden. Physicians, including gastroenterologists and hepatologists, should be conversant with assessment and management of malnutrition and nutritional supplementation.

**Alcohol’s Effect on Other Chronic Liver Diseases**

Maximilian Lee and Kris V. Kowdley

In addition to directly causing liver disease, alcohol consumption is a common comorbid condition with other chronic liver diseases and may exacerbate liver injury, particularly in nonalcoholic fatty liver disease, chronic viral hepatitis, hereditary hemochromatosis, and autoimmune liver diseases. This synergism can result in increased hepatic inflammation and accelerated rates of fibrosis, with more rapid and earlier development of cirrhosis, and also increase the risk for liver cancer and death from liver disease.

**Liver Cancer and Alcohol**

Priya Grewal and Vijay Anand Viswanathen

Annually, hepatocellular carcinoma is diagnosed in approximately a half-million people worldwide. Based on the association of alcohol with cancer, a International Agency for Research on Cancer working group recently deemed alcoholic beverages “carcinogenic to humans,” causally related to occurrence of malignant tumors of the oral cavity, pharynx, larynx, esophagus, liver, colorectum, and female breast. Alcohol metabolism in the liver leads to reactive oxygen species production, induction of activity of cytochrome P450s, and reduction of antioxidants. This review analyzes the epidemiology and pathogenesis of alcohol in hepatocellular cancer.

**Evaluation and Selection of the Patient with Alcoholic Liver Disease for Liver Transplant**

Jennifer Leong and Gene Y. Im

Alcoholic liver cirrhosis is the second most common indication for liver transplantation in the United States. Studies have shown that these patients do as well as those transplanted for nonalcoholic liver disease.
Recently, transplantation of patients with alcoholic liver disease has come under closer scrutiny following an article in the *New England Journal of Medicine* demonstrating comparable outcomes and survival in patients transplanted for acute alcoholic hepatitis. This article reviews the literature and data on the evaluation and selection of patients with alcoholic cirrhosis for liver transplant, and discusses the most recent indication (once a contraindication), acute alcoholic hepatitis.

**Complications in Patients with Alcohol-Associated Liver Disease Who Undergo Liver Transplantation**

Paul J. Gaglio Jr and Paul J. Gaglio Sr

Cirrhosis caused by alcohol-associated liver disease is a common indication for liver transplantation worldwide. Patients with alcohol-associated liver disease who undergo liver transplantation face multiple challenging comorbid medical issues that enhance the potential for perioperative and postoperative complications. Awareness of these issues and appropriate therapeutic intervention may minimize the negative effect of these complications on posttransplantation survival. This article reviews important posttransplantation problems in patients transplanted for alcohol-associated liver disease.

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