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Norman L. Sussman and Michael R. Lucey

Introduction: Alcohol and Alcoholism 1
Saira Aijaz Khaderi

This article discusses alcohol use throughout history. The discovery and cultivation of wine and beer and distillation of spirits are explored. The article spans prehistory, Egypt, Ancient Greece, Ancient Rome, Europe, and the Americas; and the religions Judaism, Christianity, and Islam. Also explored are the history and distillation of rum, gin, and champagne. Effects of alcohol use on society are discussed.

Histopathology of Alcohol-Related Liver Diseases 11
Nitzan C. Roth and Jia Qin

Excessive alcohol consumption can lead to a spectrum of liver histopathology, including steatosis, steatohepatitis, foamy degeneration, fatty liver with cholestasis, and cirrhosis. Although variability in sampling and pathologist interpretation are of some concern, liver biopsy remains the gold standard for distinguishing between steatohepatitis and noninflammatory histologic patterns of injury that can also cause the clinical syndrome of alcohol-related hepatitis. Liver biopsy is not routinely recommended to ascertain a diagnosis of alcohol-related liver disease in patients with an uncertain alcohol history, because the histologic features of alcohol-related liver diseases can be found in other diseases, including nonalcoholic steatohepatitis and drug-induced liver injury.

Alcohol and the Law 25
Maya Balakrishnan and Stephen Chris Pappas

In the intersection of alcohol ingestion with the law, medical ethics, and public safety, physicians are often unsure about how to proceed. Physicians’ primary focus should be on patient education with an ethical and legal duty to warn the patient of the adverse effects of alcohol. Warning third parties of potential harm related to alcohol-related impairment may involve a breach of patient confidentiality; therefore it should only be undertaken after careful analysis suggests that the risk for significant harm exceeds the burden that results to the patient from warning others. The law remains vague in this area.

Epidemiology of Alcohol Consumption and Societal Burden of Alcoholism and Alcoholic Liver Disease 39
Page D. Axley, Crit Taylor Richardson, and Ashwani K. Singal

Alcohol abuse is a major determinant of public health outcomes. Worldwide data from 2016 indicate that alcohol is the seventh leading risk factor
in terms of disability-adjusted life years, an increase of more than 25% from 1990 to 2016. Understanding the epidemiology of alcoholic liver disease, including the regional variations in consumption and public policy, is an area of active research. In countries where the per capita consumption of alcohol decreases, there appears to be an associated decrease in disease burden. Given alcohol’s health burden, an increased focus on alcohol control policies is needed.

Adolescent Alcoholic Liver Disease 51
Sharonda Alston Taylor and Tamir Miloh

Alcohol use is common during adolescence. Adolescent alcohol use is a global problem. The risk of alcohol dependence increases based on genetic and psychosocial factors. If a provider is concerned about use of alcohol, screening is recommended. From a public health perspective, alcohol abuse should be addressed.

Alcohol Use Disorders in Alcoholic Liver Disease 55
Jessica L. Mellinger and Gerald Scott Winder

Alcohol use disorder (AUD) is common in alcoholic liver disease (ALD) and intrinsic to its pathophysiology. Optimal treatment requires a multidisciplinary team approach and a working alliance between patients and providers. Diagnosing AUD involves a combination of thorough history taking, physical examination, screening questionnaires, and alcohol biomarkers. Alcohol biomarkers have advantages and limitations of use of which clinicians should be aware. AUD treatment is effective, multifaceted, and can be tailored to each individual. Available treatment modalities are myriad: motivational enhancement therapy, cognitive behavior therapy, 12-step facilitation, group therapies, intensive outpatient programs, inpatient and residential treatment, and relapse prevention medications.

Pathogenesis of Alcoholic Liver Disease: An Update 71
Themistoklis Kourkoumpetis and Gagan Sood

Apart from the classic knowledge that ethanol mediates its hepatotoxicity through its metabolism to acetaldehyde, a well-known hepatotoxic molecule, recent research has elucidated several key mechanisms that potentiate ethanol’s damage to the liver parenchyma, such as generation of free radicals, activation of Kupffer cells, and alterations to the human bacterial and fungal microbiome. Genetic studies have suggested the role of PNPLA3 and TM6SF2 gene mutations in the progression of alcoholic liver disease.

Acute Alcoholic Hepatitis 81
Gene Y. Im

Alcoholic hepatitis is a unique type of alcohol-associated liver disease characterized by acute liver inflammation caused by prolonged heavy alcohol use. Treatment is mostly supportive. The short-term prognosis of acute alcoholic hepatitis depends on liver recovery, and ranges widely from rapid improvement to grim multiorgan failure despite treatment.
Refinement of scoring systems have enhanced prognostication to guide clinical decision making in alcoholic hepatitis. Recent advances in the treatment of alcoholic hepatitis have solidified corticosteroids as the cornerstone of treatment to enhance short-term survival, but not intermediate or long-term survival.

**Nutrition in Alcoholic Liver Disease: An Update**

Brett Styskel, Yamini Natarajan, and Fasiha Kanwal

Malnutrition is a change in body composition owing to disordered nutrition associated with a decrease in function and poor clinical outcomes. Malnutrition can result from overnutrition, undernutrition and inflammatory activity. Patients with alcoholic liver disease are at increased risk for malnutrition. In this article, we discuss the different methods used to assess malnutrition, prevalence of malnutrition, potential mechanisms underlying malnutrition, and its treatments in patients with alcoholic liver disease.

**Alcohol-Associated Cirrhosis**

Michael R. Lucey

Alcohol-associated cirrhosis (AC) contributes up to 50% of the overall cirrhosis burden in the United States. AC is typically a comorbid condition in association with alcohol-use disorder. AC is often coexistent with other conditions. Several noninvasive methods are available to assist in recognizing the presence of AC. The natural history of AC is governed by the patients continued drinking or abstinence. All treatment starts with abstinence. After decompensation, the progression to acute-on-chronic liver failure heralds death. When patients who have deteriorated are declined liver transplant, palliative care should be considered.

**Liver Transplantation for Alcoholic Liver Disease: An Update**

Elizabeth L. Godfrey, Rise Stribling, and Abbas Rana

Alcoholic liver disease is a serious and increasing contributor to the global liver disease burden. Extensive selection criteria, including a minimum abstinence period, has previously been used to secure good outcomes but new research questions the effectiveness of abstinence periods and has recommended changes in integrated alcohol use treatment to effectively prevent relapse. Patients have unique health concerns, including posttransplantation risks of malignancy and metabolic complications, but overall very good long-term outcomes. Severe alcoholic hepatitis has been increasingly treated with early transplantation without a set sobriety period, with overall favorable outcomes, even with respect to recidivism.

**Chronic Neurologic Effects of Alcohol**

Nadia Hammoud and Joohi Jimenez-Shahed

Chronic alcohol use induces silent changes in the structure and function of the central and peripheral nervous systems that eventually result in irreversible, debilitating repercussions. Once identified, nutritional
supplementation and cessation measures are critical in preventing further neurologic damage. The proposed mechanisms of neuronal injury in chronic alcohol abuse include direct toxic effects of alcohol and indirect effects, including those resulting from hepatic dysfunction, nutritional deficiencies, and neuroinflammation. Clinical manifestations include cerebellar ataxia, peripheral neuropathy and Wernicke-Korsakoff encephalopathy. Continued exploration of the pathophysiologic mechanisms may lead to the discovery of early interventions that can prevent permanent neurologic injury.

Will Studies in Nonalcoholic Steatohepatitis Help Manage Alcoholic Steatohepatitis?

Vinay Sundaram and Timothy R. Morgan

Hepatic steatosis and steatohepatitis have several etiologies; the most common are alcoholic steatohepatitis (ASH) and obesity/metabolic syndrome–induced steatohepatitis, also known as nonalcoholic steatohepatitis (NASH). Although the etiology of these 2 conditions is different, they share pathways to disease progression and severity. They also have differences in physiologic pathways, and shared and divergent mechanisms can be therapeutic targets. There is no approved pharmacologic therapy for NASH, but several molecules are under study. Focus remains on modulation of insulin resistance, oxidative stress, the inflammatory cascade, hepatic fibrosis, and cell death. This review provides an overview of pathophysiologic similarities and differences between ASH and NASH.