Alcoholic hepatitis: Clinical manifestations and diagnosis

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INTRODUCTION

Excessive alcohol consumption is associated with a range of hepatic manifestations, including alcoholic fatty liver disease (with or without steatohepatitis), alcoholic hepatitis, and cirrhosis. The burden of alcoholic liver disease continues to grow [1,2]. While asymptomatic steatohepatitis due to alcohol could be referred to as "alcoholic hepatitis" (also called "alcohol-associated" or "alcohol-induced hepatitis"), the term is typically used to describe the acute onset of symptomatic hepatitis. The amount of alcohol intake that puts an individual at risk for alcoholic hepatitis is not known, but the majority of patients have a history of heavy alcohol use (more than 100 g per day) for two or more decades (figure 1) [3-5]. Clinicians should not overlook the long-term need to encourage treatment for alcohol use disorder (AUD) once the acute episode of alcoholic hepatitis has resolved [6]. However, even among liver specialists, referrals for behavioral therapy or prescriptions to treat AUD are disappointingly low [7], despite the fact that AUD therapy is associated with reduced incidence of alcohol-associated liver disease [8] and lower rates of relapse in patients undergoing liver transplantation for alcoholic liver disease [9]. The stigma of alcohol-related liver disease also contributes to reluctance for patients to seek treatment [10]. Alcoholic hepatitis has a high mortality that has not improved over time [11,12]. In fact, the incidence of alcoholic hepatitis and referrals for liver transplantation in patients with alcoholic hepatitis has soared during the coronavirus disease 2019 (COVID-19) pandemic [13-16]. (See "Risky drinking and alcohol use disorder: Epidemiology, clinical features, adverse consequences, screening, and assessment".)

This topic will review the clinical manifestations and diagnosis of alcoholic hepatitis. The management of alcoholic hepatitis, the pathogenesis of alcoholic liver disease, and the approach to patients with alcoholic fatty liver disease or alcoholic cirrhosis are discussed separately. (See "Management and prognosis of alcoholic hepatitis" and "Pathogenesis of alcohol-associated liver disease" and "Clinical manifestations and diagnosis of alcohol-associated fatty liver disease and cirrhosis" and "Management of alcohol-associated steatosis and alcohol-associated cirrhosis".)

The discussion that follows is generally consistent with society guidelines [17]. (See 'Society guideline links' below.)

HISTORY

Patients with alcoholic hepatitis are often between 40 and 50 years of age, with most patients presenting before the age of 60 years [18]. Patients with alcoholic hepatitis typically have a history of daily heavy alcohol use (>100 g per day) for more than 20 years (figure 1) and in some cases, patients will have recently increased their alcohol intake in response to stressful life events [19]. Patients often stop drinking as they become ill, so it is common for patients to have ceased alcohol intake several weeks prior to presentation [3,4,20,21]. Drinking patterns may vary, however, and heavy drinking can be intermittent (ie, weekends only) or surreptitious, such that family members, friends, or coworkers may not recognize a pattern of problem drinking. In addition, alcoholic hepatitis can develop in patients with much shorter histories of heavy alcohol use [22]. With the rising prevalence of obesity and metabolic syndrome, co-existent alcoholic and nonalcoholic steatohepatitis is increasingly common and together often increase the severity of alcoholic liver disease.

Obtaining an accurate history of alcohol use from a patient with suspected alcoholic hepatitis may be difficult. Questioning the patient's family in private, after receiving permission from the patient to discuss his or her care with family members, may help elicit important information about the patient's alcohol use. It is also absolutely essential that health care providers take a careful alcohol history, supplemented by use of either the CAGE or AUDIT questionnaires to establish the likelihood of problem alcohol drinking or abuse (table 1 and table 2). (See "Screening for unhealthy use of alcohol and other drugs in primary care", section on 'Unhealthy alcohol use'.)

CLINICAL MANIFESTATIONS

The characteristic clinical features of alcoholic hepatitis are jaundice, anorexia, fever, and tender hepatomegaly [23]. Laboratory testing reveals moderately elevated transaminases (typically less than 300 int. unit/mL), with an aspartate aminotransferase (AST) to alanine aminotransferase (ALT) ratio of two or greater. Patients may also present with right upper-quadrant/epigastric pain, hepatic encephalopathy, and signs of malnutrition.

Signs and symptoms — Common signs and symptoms of alcoholic hepatitis include [24,25]:

- Jaundice that developed within three months prior to presentation.
- Anorexia.
- Fever. A fever should only be ascribed to alcoholic hepatitis once other sources are excluded, including spontaneous bacterial peritonitis, pneumonia, and urinary tract infections. (See "Management and prognosis of alcoholic hepatitis", section on 'Treatment considerations for all patients'.)
- Right upper-quadrant/epigastric abdominal pain, which may be severe enough to mimic an acute abdomen.
- Abdominal distension due to ascites.
- Proximal muscle weakness due to muscle wasting.

Patients with severe alcoholic hepatitis and/or underlying cirrhosis may exhibit signs of hepatic encephalopathy (table 3).

Physical examination — On physical examination, patients typically have hepatomegaly, which often reflects the combined effects of fatty liver and swelling of hepatocytes due to cell injury-associated protein retention [26]. The liver may be tender, but the presence of more diffuse abdominal pain is unusual and suggests other diagnoses, such as spontaneous bacterial peritonitis. A bruit heard over the liver is also a feature of severe alcoholic hepatitis and has been reported to occur in >50 percent of patients [27].

Patients often have ascites, which may be due to underlying cirrhosis with portal hypertension or transient portal venous obstruction from hepatic swelling. Paracentesis should be performed, under ultrasonic guidance if necessary, in all patients with confirmed ascites present on ultrasonography. The presence of stigmata of chronic liver disease (eg, spider angiomata, palmar erythema, gynecomastia) suggests advanced disease with underlying cirrhosis. (See "Cirrhosis in adults: Etiologies, clinical manifestations, and diagnosis", section on 'Physical examination'.)

In patients who are malnourished (common in those with severe alcoholic hepatitis), the physical examination may reveal proximal muscle wasting and decreased grip strength [28]. Malnutrition is an independent risk factor for both mortality and infectious complications [29], and infections are more common in patients with alcoholic hepatitis than those with only alcoholic cirrhosis [30].

Laboratory tests — Patients with alcoholic hepatitis typically have:

- Moderate elevations of the AST and ALT (typically less than 300 int. unit/L, rarely higher than 500 int. unit/L)
- An AST:ALT ratio ≥2
- An elevated serum bilirubin
- An elevated gamma-glutamyl transferase (GGT)
- A leukocytosis with a predominance of neutrophils
- An elevated international normalized ratio (INR)

In addition, patients may have low serum albumin and prealbumin levels due to malnutrition and decreased synthesis in the setting of hepatic dysfunction. (See "Evaluating nutritional status in adults with cirrhosis", section on 'Laboratory studies'.)

Liver test abnormalities — The serum AST and ALT are typically less than 300 int. unit/L and are rarely higher than 500 int. unit/L, except in patients with alcoholic foamy degeneration (a histologic variant of alcoholic hepatitis) [31,32]. Higher transaminase concentrations should raise the suspicion of concurrent liver injury due to viral or ischemic hepatitis or acetaminophen use (which can be toxic even at therapeutic doses in patients who abuse alcohol) [33]. The most common pattern of liver biochemical test abnormalities is a disproportionate elevation of serum AST compared with ALT. This ratio is usually two or greater in alcoholic hepatitis, a value that is rarely seen in other forms of liver disease [34-36].

The lower elevation of the serum ALT relative to the AST has been ascribed to hepatic deficiency of pyridoxal 5'-phosphate in individuals with alcohol use disorder, which is a cofactor for the enzymatic activity of ALT [37]. According to this hypothesis, the altered ratio reflects a failure to appropriately increase the ALT, rather than a disproportionate elevation in AST.

Patients with alcoholic hepatitis typically have elevated serum bilirubin and GGT levels. In addition, the serum albumin and prealbumin may be low in patients who are malnourished or who have impaired synthetic function. In a therapeutic trial that included 174 patients with severe alcoholic hepatitis, mean bilirubin levels were 14 to 15 mg/dL (238 to 260 micromol/L), mean GGT levels were 223 to 309 int. unit/L, and mean albumin levels were 2.4 to 2.5 g/dL (24 to

25 g/L) [38]. Similarly, in a second trial, the median bilirubin level was 13 mg/dL (222 micromol/L) and the median albumin level was 2.4 g/dL (24 g/L) [39].

Coagulation abnormalities — Patients with moderate to severe alcoholic hepatitis typically have an elevated INR due to impaired production of coagulation factors by the inflamed liver. In a trial with 121 patients with severe alcoholic hepatitis, the median INR at baseline was 2.1 (range 1.3 to 6.4) [39].

Hematologic abnormalities — Hematologic abnormalities are common in moderate to severe alcoholic hepatitis. Moderate leukocytosis (<20,000/microL) is a frequent finding [20,38,40]. In a study of 174 patients with alcoholic hepatitis, the mean white blood cell count was 11,000/microL [38]. The majority of the white blood cells are neutrophils, which are also commonly seen in liver biopsies from patients with alcoholic hepatitis, suggesting these cells may play an important pathogenetic role in the hepatic injury. (See "Pathogenesis of alcohol-associated liver disease".)

Rarely, extremely high white blood cell counts (a leukemoid reaction) are seen and are associated with very high mortality rates. In a review of 10 cases of patients with alcoholic hepatitis and a leukemoid reaction, the white blood cell counts ranged from 57,000/microL to 129,000/microL, and only one patient survived [41].

Macrocytosis suggests longstanding disease and may reflect poor nutritional status, cobalamin or folate deficiency, toxicity of alcohol, and/or increased lipid deposition on red cell membranes. Similarly, thrombocytopenia can result from primary bone marrow hypoplasia (which can be due to alcohol and is usually brief) and/or splenic sequestration due to portal hypertension and an enlarged spleen ("hypersplenism"). (See "Hematologic complications of alcohol use".)

Other laboratory test abnormalities — Patients with severe alcoholic hepatitis may develop hepatorenal syndrome and thus may have an elevated creatinine. Acute phase reactants, such as serum ceruloplasmin, ferritin, and alpha 1-antitrypsin may be elevated in patients with severe alcoholic hepatitis [42-44]. (See "Hepatorenal syndrome", section on 'Clinical presentation' and "Acute phase reactants".)

Imaging tests — Abdominal imaging (ultrasound, computed tomographic scan, magnetic resonance imaging) in patients with alcoholic hepatitis may suggest fatty change in the liver, evidence of underlying cirrhosis, or ascites. Transabdominal ultrasound may also reveal parallel tubular structures in the liver, thought to represent the dilated hepatic artery adjacent to a portal vein radical [45]. Doppler flow studies of the hepatic artery may reveal an elevated peak systolic velocity or an increase in vessel diameter [46]. Transient elastography may be useful in determining the likelihood of cirrhosis, although elevated liver stiffness in this setting may also

reflect edema and inflammation [47]. A reduction in liver stiffness may indicate abstinence or withdrawal from alcohol [48]. Assessment of stiffness by transient elastography during the first two months after alcohol cessation can assist in determining the risk of advanced chronic liver disease [49]. (See "Noninvasive assessment of hepatic fibrosis: Ultrasound-based elastography".)

Microbiome abnormalities — Studies have identified changes in the microbiome associated with alcoholic hepatitis, with a specific microbiome signature that can distinguish alcohol consumption from alcoholic hepatitis [50] and identify advanced fibrosis [51]. Additionally, fungal dysbiosis with lower fungal diversity, higher *Candida* representation, and a systemic immune response has been described [52]. *Candida albicans* can release a peptide toxin, or Candidalysin, that is cytoxic to hepatocytes and may worsen alcoholic hepatitis [53]. Similarly, *Enterococcus faecalis*, which is also increased in patients with alcoholic hepatitis, can secrete a toxin that correlates with severity of disease [54].

DIAGNOSIS

Diagnostic approach — Clinical and laboratory features are often adequate for establishing the diagnosis of alcoholic hepatitis in a patient with a long history of heavy alcohol use (typically >100 g per day for more than 20 years) (figure 1), provided the patient does not have risk factors for other causes of acute hepatitis and testing for other common causes of hepatitis is negative. In such patients, we will make a clinical diagnosis of alcoholic hepatitis if the patient presents with jaundice, moderately elevated aminotransferases (typically <300 U/L and rarely higher than 500 U/L), an AST:ALT ratio ≥2, an elevated serum bilirubin (>5 mg/dL or 86 micromol/L), and an elevated international normalized ratio (INR) [3,4,20,21,31]. The presence of a fever or leukocytosis supports the diagnosis.

In order to rule out other common causes of acute hepatitis, patients should be tested for the following:

- Anti-hepatitis A IgM
- Hepatitis B surface antigen, anti-hepatitis B core IgM
- Anti-hepatitis C virus (HCV) antibodies, hepatitis C ribonucleic acid
- In patients with the hepatitis B virus, check anti-hepatitis delta virus (HDV) antibodies, and HDV polymerase chain reaction if antibodies are present
- Drug screen including serum acetaminophen levels
- Biliary obstruction or Budd-Chiari syndrome using transabdominal ultrasound with Doppler

In a patient with chronic liver disease (eg, alcoholic cirrhosis or HCV), diagnosing alcoholic hepatitis may be difficult because the signs, symptoms, and laboratory test findings may be similar. In such patients, the diagnosis is made based on the strength of the clinical findings as well as the likelihood of an alternative diagnosis (eg, decompensated cirrhosis). While some advocate liver biopsy in all cases of suspected alcoholic hepatitis, this rarely changes the clinical diagnosis unless there are atypical clinical features [55] (see 'Signs and symptoms' above). Despite this difficulty, there is increasing interest in clinical trials for the disease, which has generated more rigorous, standardized criteria for establishing a diagnosis of alcoholic hepatitis, which should allow more consistent inclusion and characterization of patients in therapeutic trials [56,57]. These include: onset of jaundice within prior eight weeks; ongoing consumption of >40 (female) or 60 (male) g alcohol per day for six months or more, with less than 60 days of abstinence before the onset of jaundice; aspartate aminotransferase >50, aspartate aminotransferase/alanine aminotransferase >1.5-fold, and both values <400 U/L; serum bilirubin (total) >3 mg/dL; and liver biopsy confirmation in patients with confounding factors. In addition, stratification should be based on severity as assessed by: Maddrey discriminant function >32, assuming a control prothrombin time of 12 seconds; and model for end stage liver disease (MELD) >20. In addition, the authors have defined common data elements and end points to be assessed in an effort to further standardize clinical trial design for experimental therapies [56]. (See 'Chronic liver disease' below.)

In a study of patients with chronically elevated liver biochemical tests, the sensitivity and specificity of clinical findings for diagnosing alcoholic liver disease were 91 and 97 percent, respectively, when liver biopsy was used as the gold standard [58]. However, the sensitivity and specificity of clinical findings for diagnosing the subset of patients with alcoholic hepatitis are unclear. There are no laboratory or radiologic tests currently being used that are specific for alcoholic hepatitis.

Patients with risk factors for other causes of acute hepatitis (eg, hypotensive episodes, pregnancy, possible acetaminophen overdose, or other drug toxicity) or with a clinical picture that is only partially consistent with alcoholic hepatitis require a more extensive evaluation. In some cases, if the serologic and radiologic evaluations do not provide a diagnosis, a liver biopsy may be required. In addition, some groups recommend a liver biopsy in patients with severe alcoholic hepatitis for whom treatment is being contemplated to confirm the diagnosis [17]. However, it is our practice to obtain a biopsy only when there is doubt about the diagnosis and other co-factors or concurrent causes of liver disease are suspected, or if enrollment in a clinical trial requires an entry biopsy to confirm the diagnosis. Liver biopsies in patients with alcoholic hepatitis are typically performed transvenously because patients often have coagulopathies.

(See 'Differential diagnosis' below and "Approach to the patient with abnormal liver biochemical and function tests" and "Transjugular liver biopsy".)

Pathologic criteria for alcoholic hepatitis — Approximately 10 to 35 percent of patients who abuse alcohol will have changes in liver histology suggestive of alcoholic hepatitis [59]. While many patients with suspected alcoholic hepatitis will not require a liver biopsy, pathologic findings may help with the diagnosis if there is uncertainty [60]. However, the histologic findings are not specific for alcoholic hepatitis and may also be seen in patients with nonalcoholic steatohepatitis. As noted below, a standardized scoring system has been developed in order to stratify severity more accurately based on pathologic appearance [61].

Histologic findings in liver biopsies from patients with alcoholic hepatitis include (picture 1 and picture 2) [62,63]:

- Steatosis: Typically micro- or macrovesicular steatosis, but in some cases alcoholic foamy degeneration is seen
- Hepatocellular ballooning with cytoplasmic rarefaction
- Infiltration by neutrophils or lymphocytes
- Mallory-Denk bodies
- Fibrosis with a perivenular, perisinusoidal, and pericellular distribution
- Cholestasis
- Bile duct proliferation

In early stages, the inflammatory changes affect the perivenular regions (zone 3). However, as the disease progresses, the histologic changes may extend to the portal tracts. The findings may vary among patients with regard to their extent and severity.

The presence of neutrophils is a hallmark of alcoholic hepatitis and is unusual in chronic viral hepatitis. Their role in pathogenesis is discussed separately. (See "Pathogenesis of alcohol-associated liver disease".)

Mallory-Denk bodies (previously called Mallory bodies or Mallory's hyaline) are eosinophilic accumulations of intracellular protein aggregates within the cytoplasm of hepatocytes (picture 2). They represent condensations of intracellular "intermediate filaments" or cytokeratins, which are normal components of the hepatocyte cytoskeleton [64]. The mechanisms underlying Mallory-Denk body formation in alcoholic hepatitis are unclear. Furthermore, they are not specific for alcoholic hepatitis and can be seen in nonalcoholic steatohepatitis [65], Indian childhood cirrhosis (thought in part to be due to high copper intake), starvation, after jejunoileal bypass surgery for obesity, or after the use of certain drugs

(such as amiodarone or perhexiline). (See "Epidemiology, clinical features, and diagnosis of nonalcoholic fatty liver disease in adults".)

Mallory-Denk bodies do not appear to have a pathogenic role in the hepatic injury. However, their presence is an important marker of alcohol-induced injury. In a large, multicenter Veterans Administration study, for example, Mallory-Denk bodies were detected in 76 percent of those with alcoholic hepatitis and 95 percent of those who also had cirrhosis [66].

Assessing disease severity — Several models have been proposed to determine the severity of a patient's alcoholic hepatitis. The models are discussed in detail elsewhere. (See "Management and prognosis of alcoholic hepatitis", section on 'Determining disease severity'.)

DIFFERENTIAL DIAGNOSIS

There are numerous causes of acute hepatitis, including viral infection, drug reactions, and ischemia. The primary features that differentiate alcoholic hepatitis from other causes of acute hepatitis include a history of heavy alcohol use and an AST:ALT ratio of ≥2. An AST:ALT ratio of ≥2 is rarely seen in other forms of liver disease [34-36]. Decompensated cirrhosis should also be considered in patients with underlying chronic liver disease (including alcoholic cirrhosis). (See 'Chronic liver disease' below.)

Acute hepatitis — The differential diagnosis of patients presenting with acute hepatitis is broad and includes other liver diseases such as:

- Acetaminophen toxicity
- Drug-induced liver injury/idiosyncratic drug reactions (including herbal supplements and illicit drugs)
- Nonalcoholic steatohepatitis
- Acute viral hepatitis (hepatitis A, hepatitis B, hepatitis C, hepatitis D, hepatitis E, herpes simplex virus, Epstein-Barr virus, cytomegalovirus)
- Ischemic hepatitis
- Budd-Chiari syndrome
- HELLP (hemolysis, elevated liver enzymes, low platelets) syndrome
- Acute fatty liver of pregnancy
- Wilson disease
- Autoimmune hepatitis
- Alpha-1 antitrypsin deficiency
- Toxin-induced hepatitis (eg, mushroom poisoning, carbon tetrachloride)

Elevated aminotransferases may also be seen in patients with diseases such as:

- Muscle diseases
- Thyroid disease
- Celiac disease
- Adrenal insufficiency
- Anorexia nervosa

Differentiating among these entities requires a through history to identify risk factors and physical examination to look for signs that may point to a specific cause (eg, Kayser-Fleisher rings in a patient with Wilson disease). The history and physical examination are then followed by laboratory testing. Causes of acute hepatitis other than alcoholic hepatitis are often associated with higher transaminase levels than typically seen with alcoholic hepatitis (eg, viral hepatitis, ischemic hepatitis, drug toxicity or idiosyncratic drug reactions,) and typically have an aspartate aminotransferase to alanine aminotransferase ratio of <2 (and often <1).

Liver biopsy may be required if the cause for a patient's elevated aminotransferases cannot be determined noninvasively. A histologic scoring system has been developed that may make biopsy more useful in more accurately assessing prognosis [61]. (See "Histologic scoring systems for chronic liver disease", section on 'Alcoholic liver disease and alcoholic hepatitis'.) The approach to the evaluation of a patient with abnormal liver tests is discussed in detail elsewhere (see "Approach to the patient with abnormal liver biochemical and function tests" and "Acute liver failure in adults: Etiology, clinical manifestations, and diagnosis").

Chronic liver disease — Patients who abuse alcohol may have chronic liver disease due to either alcohol (alcoholic steatosis, hepatitis, or cirrhosis) and/or to nonalcohol-related causes (eg, hepatitis C, nonalcoholic fatty liver disease [NAFLD], metabolic diseases) [67,68]. Making a diagnosis in such patients may be complicated because the signs, symptoms, and laboratory test findings may be similar. Viral hepatitis can be excluded with appropriate serum tests, but distinguishing alcoholic liver disease from NAFLD may be more difficult [69], especially as the prevalence of NASH is rising. Some experts have argued that the similarities between alcoholic liver disease and NAFLD are so great that they should be considered as different features of the same disease, using the term "metabolic-associated liver disease" instead [70]. Distinguishing alcoholic from nonalcoholic liver disease can be aided by the use of a validated model formula that incorporates mean corpuscular volume, body mass index, sex, and the AST to ALT ratio [71]. (See "Clinical manifestations and diagnosis of alcohol-associated fatty liver disease and cirrhosis", section on 'Differentiating alcohol-associated from nonalcoholic liver disease'.)

In a patient with chronic liver disease without cirrhosis or who has compensated cirrhosis, we will make a diagnosis of alcoholic hepatitis if the clinical history is consistent with alcoholic hepatitis (eg, recent onset of jaundice, AST and ALT both <500 int. units/L with an AST:ALT ratio ≥2). We will pursue liver biopsy if there is doubt with regard to the correct diagnosis, if there is concern that the patient may have concurrent liver disease (eg, drug induced or NAFLD), or if the findings will influence management or enrollment in a clinical trial of novel therapies. (See "Management and prognosis of alcoholic hepatitis", section on 'Severe alcoholic hepatitis'.)

In a patient with Child B or C cirrhosis, differentiating alcoholic hepatitis from decompensated cirrhosis is particularly difficult because many of the manifestations are the same (jaundice, ascites, hepatorenal syndrome, hepatic encephalopathy), and alcohol use is a risk factor for hepatic decompensation. However, it is important to recognize, that bouts of acute alcoholic hepatitis may occur in a patient who already has cirrhosis, which confers a higher risk of liver failure compared with those who have alcoholic hepatitis or cirrhosis alone [72,73]. In such cases, patients are at high risk for hepatic decompensation (eg, spontaneous bacterial peritonitis, gastrointestinal bleeding) and must be monitored especially closely. Disease-specific therapy (eg, corticosteroids) and more general measures for treating liver failure may be required concurrently. (See 'Differential diagnosis' above and "Management and prognosis of alcoholic hepatitis", section on 'Severe alcoholic hepatitis' and "Cirrhosis in adults: Overview of complications, general management, and prognosis", section on 'Major complications'.)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Alcoholic liver disease".)

SUMMARY AND RECOMMENDATIONS

- **History** – Patients with alcoholic hepatitis typically have a history of heavy alcohol use (>100 g per day) for more than 20 years, but heavy drinking may be surreptitious or intermittent, without episodes of obvious intoxication (figure 1). (See 'History' above.)

- **Clinical manifestations** – The characteristic clinical features of alcoholic hepatitis are jaundice, anorexia, fever, and tender hepatomegaly. Laboratory testing reveals moderately elevated transaminases (typically less than 300 U/L), with an aspartate aminotransferase (AST) to alanine aminotransferase (ALT) ratio of two or greater. Patients may also present

with right upper quadrant/epigastric pain, hepatic encephalopathy, and signs of malnutrition. (See 'Clinical manifestations' above.)

- **Diagnosis** – Clinical and laboratory features are often adequate for establishing the diagnosis of alcoholic hepatitis in a patient with a long history of heavy alcohol use, provided the patient does not have risk factors for other causes of acute hepatitis and testing for other common causes of hepatitis is negative. If the diagnosis is not certain, then liver biopsy can establish alcohol as the likely etiology with greater certainty. (See 'Diagnosis' above.)

- **Differential diagnosis** – There are numerous causes of acute hepatitis, including viral infection, drug reactions, and ischemia. The primary features that differentiate alcoholic hepatitis from other causes of acute hepatitis include a history of heavy alcohol use and an AST:ALT ratio of ≥2. Decompensated cirrhosis can occur concurrently with acute alcoholic hepatitis and confers a higher risk of liver failure compared with those who have alcoholic hepatitis or cirrhosis alone. (See 'Differential diagnosis' above.)

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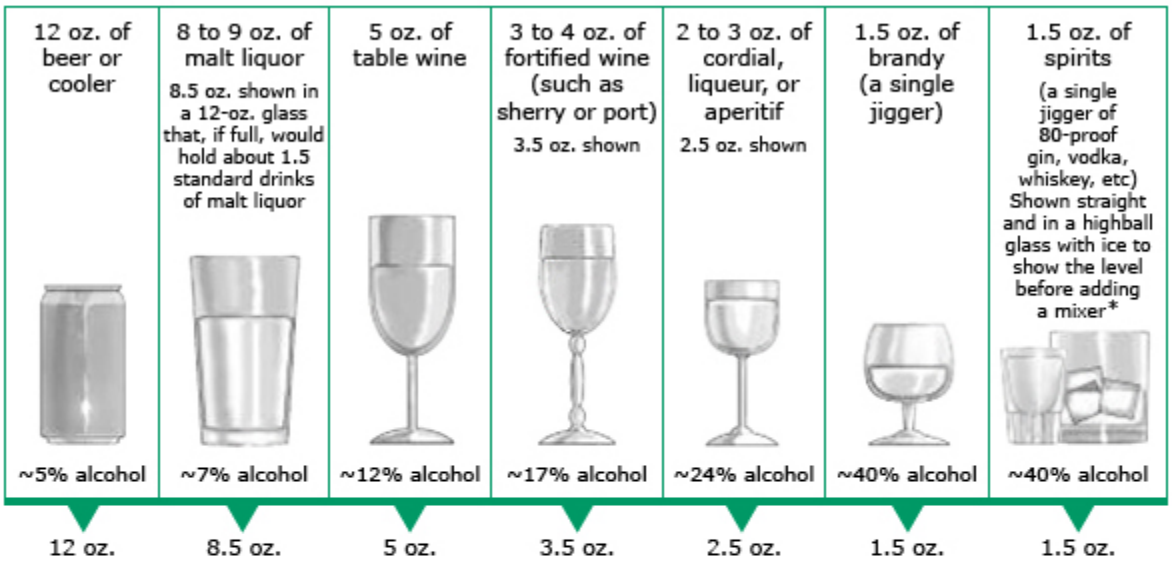
Topic 86934 Version 24.0

GRAPHICS

What is a standard drink?

A standard drink in the United States is any drink that contains about 14 grams of pure alcohol (about 0.6 fluid ounces or 1.2 tablespoons). Below are US standard drink equivalents. These are approximate, since different brands and types of beverages vary in their actual alcohol content.



Many people don't know what counts as a standard drink and so they don't realize how many standard drinks are in the containers in which these drinks are often sold. Some examples:

- For **beer**, the approximate number of standard drinks in:
  - 12 oz. = 1
  - 16 oz. = 1.3
  - 22 oz. = 2
  - 40 oz. = 3.3
- For **malt liquor**, the approximate number of standard drinks in:
  - 12 oz. = 1.5
  - 16 oz. = 2
  - 22 oz. = 2.5
  - 40 oz. = 4.5
- For **table wine**, the approximate number of standard drinks in:
  - a standard 750-mL (25-oz.) bottle = 5
- For **80-proof spirits**, or "hard liquor," the approximate number of standard drinks in:
  - a mixed drink = 1 or more*
  - a pint (16 oz.) = 11
  - a fifth (25 oz.) = 17
  - 1.75 L (59 oz.) = 39

US: United States; oz.: ounces.

* It can be difficult to estimate the number of standard drinks in a single mixed drink made with hard liquor. Depending on factors such as the type of spirits and the recipe, a mixed drink can contain from 1 to 3 or more standard drinks.

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Graphic 56818 Version 5.0

CAGE questionnaire

Have you ever felt you should **C**ut down on your drinking?
Have people **A**nnoyed you by criticizing your drinking?
Have you ever felt bad or **G**uilty about your drinking?
Have you ever had a drink first thing in the morning to steady your nerves or to get rid of a hangover (**E**ye opener)?

Scoring: Item responses on the CAGE are scored 0 or 1, with a higher score an indication of alcohol problems. A total score of 2 or greater is considered clinically significant.

Ewing, JA. Detecting Alcoholism: The CAGE Questionnaire. JAMA 1984; 252:1905-1907.

Graphic 54106 Version 1.0

AUDIT

How often did you have a drink containing alcohol in the past year?
Consider a drink to be a can or bottle of beer, a glass of wine, a wine cooler, or one cocktail or a shot of hard liquor.
Response:
Never: 0 points
Monthly or less: 1 point
2 to 4 times per month: 2 points
2 to 3 times per week: 3 points
4 or more times per week: 4 points
How many drinks did you have on a typical day when you were drinking in the past year?
Response:
0-2 drinks: 0 points
3 to 4 drinks: 1 point
5 to 6 drinks: 2 points
7 to 9 drinks: 3 points
10 or more drinks: 4 points
How often did you have 6 or more drinks on one occasion in the past year?
Response:
Never: 0 points
Less than monthly: 1 point
Monthly: 2 points
Weekly: 3 points
Daily or almost daily: 4 points

A cutoff of 4 points or more identified 86 percent of patients with heavy drinking and/or active alcohol abuse or dependence with a specificity of 72 percent (false positive rate 18 percent).

Data from: Bush, K, Kivlahan, DR, McDonell, MB, et al. The AUDIT Alcohol Consumption Questions: An effective brief screening test for problem drinking. Arch Intern Med 1998; 158:1789.

Graphic 74262 Version 1.0

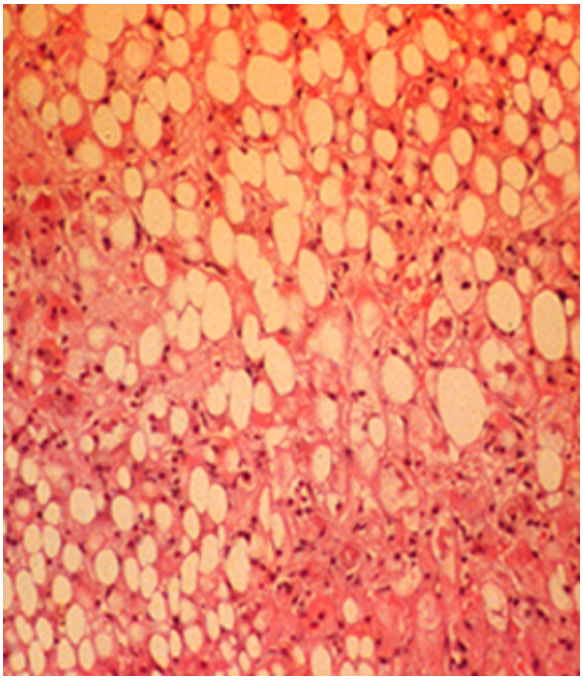
Grading system for hepatic encephalopathy

Grade	Mental status	Asterixis	EEG
I	Euphoria/depression	Yes/no	Usually normal
	Mild confusion		
	Slurred speech		
	Disordered sleep		
II	Lethargy	Yes	Abnormal
	Moderate confusion		
III	Marked confusion	Yes	Abnormal
	Incoherent		
	Sleeping but arousable		
IV	Coma	No	Abnormal

EEG: electroencephalogram.

Graphic 62922 Version 2.0

Alcoholic hepatitis

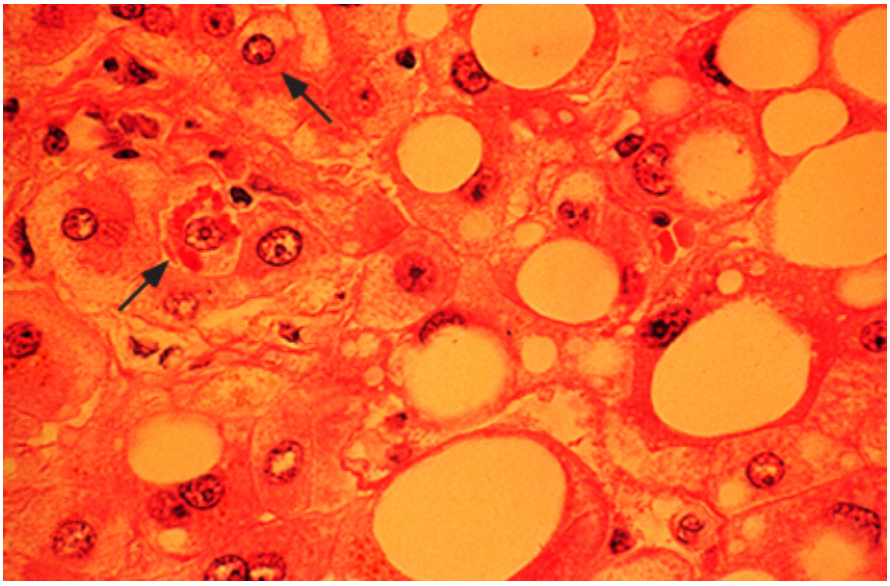


Medium power view of a liver biopsy from a patient with alcoholic hepatitis shows the classic changes of hepatocellular steatosis, neutrophilic infiltration (in contrast to the mononuclear cell infiltration in other forms of chronic hepatitis), and focal hepatocyte necrosis. These changes are indistinguishable from those in nonalcoholic steatohepatitis.

Courtesy of Robert Odze, MD.

Graphic 58504 Version 1.0

Mallory-Denk bodies in alcoholic hepatitis



High power view of a liver biopsy in alcoholic hepatitis shows macrovesicular fat and Mallory-Denk bodies (arrows), which are eosinophilic accumulations of intracellular material. Similar changes can occur in nonalcoholic steatohepatitis.

Courtesy of Robert Odze, MD.

Graphic 75188 Version 3.0

Contributor Disclosures

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