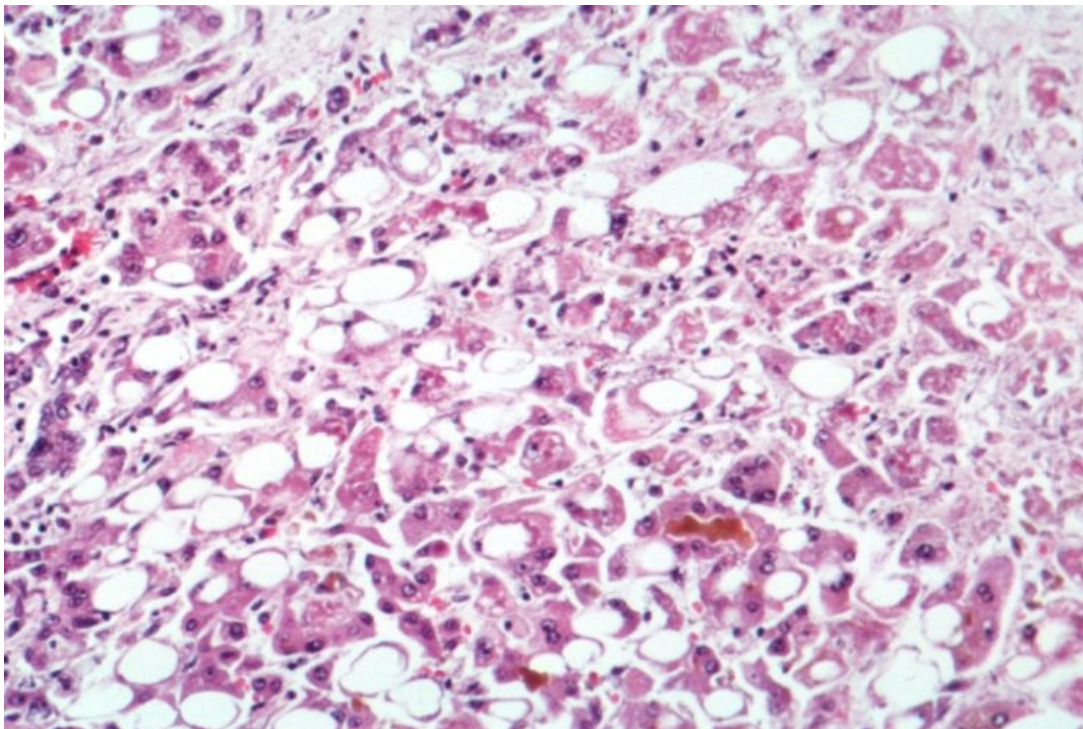


Alcoholic Hepatitis, Alcoholic Cirrhosis & Non-Alcoholic Fatty Liver Disease (NAFLD)

[See online here](#)

Alcoholic hepatitis is a progressive disease characterized by inflammation and damage of the liver caused by long-term excessive intake of ethanol. Non-alcoholic fatty liver disease is also a progressive disease of the liver; it is characterized by the accumulation of fat in the liver without the abuse of alcohol. Both diseases show similar pathological changes resulting in fibrosis or scarring of the liver. The extensive fibrosis of the liver due to continued abuse of alcohol is called alcoholic cirrhosis. These diseases remain asymptomatic at early stages. Common initial symptoms are slight discomfort at the right side of the upper abdomen with fatigue and unexplained weight loss. Lifestyle modification and alcohol abstinence are essential for management along with required therapeutic and surgical interventions.



Definition

Hepatitis is the inflammation of the [liver](#), or more specifically, **inflammation of the liver cells**. There are different types of hepatitis, which may occur due to multiple reasons, ranging from **consumption of contaminated food** to **certain sexual practices** to **alcohol overdose**. Here, however, we will study a particular form of hepatitis, known as alcoholic hepatitis, in depth.

Alcoholic liver disease presents as three forms: (1) fatty liver, (2) alcoholic hepatitis, and (3) cirrhosis.

Alcoholic hepatitis is the inflammation of the liver cells due to excess alcohol consumption over an extended period of time. Between 10% and 20% of individuals with alcoholism develop alcoholic hepatitis. This disease is still curable if detected in the early stages. However, if alcohol consumption is not tapered off, and the disease is not treated properly, it may worsen. Alcoholic hepatitis left untreated can even lead to additional health issues, such as **cirrhosis** or **complete liver failure**. Alcoholic hepatitis is usually accompanied by **fatty liver disease**, which is another disease that may be caused by excess intake of alcohol.

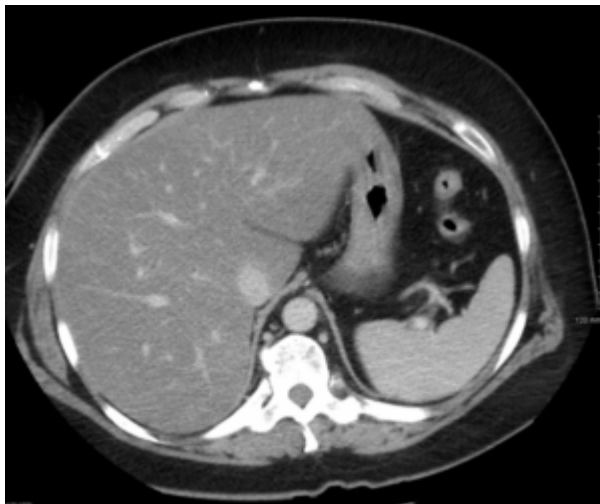


Image: "Liver steatosis (fatty liver disease) as seen on CT" by James Heilman, MD. - Own work, License: [CC BY-SA 3.0](https://creativecommons.org/licenses/by-sa/3.0/)

Fatty liver disease occurs when there is an **abnormal accumulation of fat** in the liver cells. Although it is often studied in relation to alcohol consumption, it actually occurs in two forms: **alcoholic fatty liver disease** and **non-alcoholic fatty liver disease (NAFLD)**. **Non-alcoholic steatohepatitis (NASH)** is a type of NAFLD. Fatty liver is seen in > 90% of daily/binge drinkers.

While the cause of alcoholic fatty liver disease is clear, non-alcoholic fatty liver disease occurs due to many reasons other than alcohol consumption. These reasons include problems such as **diabetes**, **high blood pressure**, and **a high level of blood lipids** (e.g., in those with obesity). This type of fatty liver disease also eventually results in cirrhosis if not treated properly.

Cirrhosis, which is the end result of both alcoholic hepatitis and non-alcoholic fatty liver disease, is a condition where the **liver fails to function properly** due to long-term damage. This damage is usually caused by either alcohol or the risk factors for non-alcoholic fatty liver disease. This condition can lead to many complications and even more serious diseases, such as **liver cancer**.

Risk Factors

- **Alcohol:** The major and most obvious risk factors for alcoholic hepatitis are the quantity of alcohol one consumes and the duration of intake. Though the exact amount which puts someone at risk is not known, it is roughly calculated

to be about **seven glasses of alcohol every single day for a period of at least 20 years.**

- **Gender:** Apart from alcohol consumption, gender is also a risk factor because the way alcohol is processed in the body also plays an important role. This is why **women tend to be at a greater risk** of developing alcoholic hepatitis than men. The threshold for developing alcoholic liver disease in men is >14 drinks per week, whereas it is >7 drinks per week in women.
- **Obesity:** High levels of alcohol, accompanied by excess body weight, make someone more vulnerable not only to **alcoholic hepatitis** but also to **fatty liver disease**, which may progress to **cirrhosis** in the long run. **High cholesterol levels** also put patients at greater risk of developing **non-alcoholic fatty liver disease**.
- **Genetic factor:** Many studies indicate that there is a genetic component for alcohol-induced liver diseases.
- **Environmental factors:** Although it is hard to separate the genetic factors from the environmental ones, factors such as **race and ethnicity** also play a part. For example, African-Americans and Hispanics seem to be at greater risk for alcoholic hepatitis.
- **Existing diseases:** Pre-existing diseases, such as chronic infection with hepatitis C virus, metabolic syndrome, **type 2 diabetes**, **hypothyroidism**, or **underactive pituitary gland**, can increase the risk of developing NAFLD.



Image: "Macroscopic image of micronodular (liver) cirrhosis caused by alcohol consumption" by Amadalvarez - Own work, License: [CC BY-SA 4.0](https://creativecommons.org/licenses/by-sa/4.0/)

Pathophysiology

Alcoholic cirrhosis

The damaged hepatocytes undergo abnormal repair, which leads to **fibrosis**. Fibrosis is the scarring and hardening of the liver and its cells. Extensive fibrosis disrupts the structure of the liver, **causing the liver to shrink**.

Non-alcoholic fatty liver disease

NAFLD results when the uptake of lipids by the liver overwhelms the mechanisms for triglyceride disposal, leading to the accumulation of fat within hepatocytes. This increased delivery of fatty acids to the liver causes the liver to swell up and malfunction.

Insulin resistance is created, which leads to alcoholic hepatitis. NAFLD is also said to be the leading cause of **cryptogenic cirrhosis**, with varying degrees of fibrosis.

Clinical Features of Alcohol-Related Liver Diseases

Alcoholic Fatty Liver Disease

- Can be asymptomatic
- Hepatomegaly
- Right upper quadrant discomfort
- Nausea

Alcoholic Hepatitis

- It can be asymptomatic
- Lack of appetite
- Weight loss, also as a result of a change in appetite
- Yellow color in skin and eyes, **jaundice or icterus**
- Fever
- Fatigue or a general sense of weakness and lack of energy
- Nausea and vomiting
- Pain in the abdomen, accompanied by tenderness (especially pain in the upper right abdomen)
- Swollen abdomen due to accumulation of excess fluid
- Mental confusion or problems with thinking clearly

Alcoholic Cirrhosis

In addition to the above features, some additional ones include:

- **Edema** (building up of fluid in the legs causing swelling)
- Redness in palms
- Easy bruising, abnormal bleeding at even the slightest of cuts
- In men, smaller **testicles**.

Non-Alcoholic Fatty Liver Disease

In addition to all of the symptoms of alcoholic hepatitis, a few other features are unique to NAFLD:

- Itching
- Red spider-like blood vessels throughout the skin
- Swelling of legs

Investigations and Diagnosis of Alcohol-Related Liver Diseases

Clinical manifestations and **laboratory features** are enough to identify alcoholic hepatitis in a patient with a long-term habit of heavy alcohol drinking. Heavy alcohol use is defined as **drinking more than 100 g of alcohol per day for more than 20 years**. It is the likely cause of acute hepatitis, provided other common causes of acute hepatitis are absent.

History

Thorough research must be done to understand the patient's drinking habits – how often the patient drinks, whether they can function without it, and other such questions to **gauge the body's dependency on alcohol**.

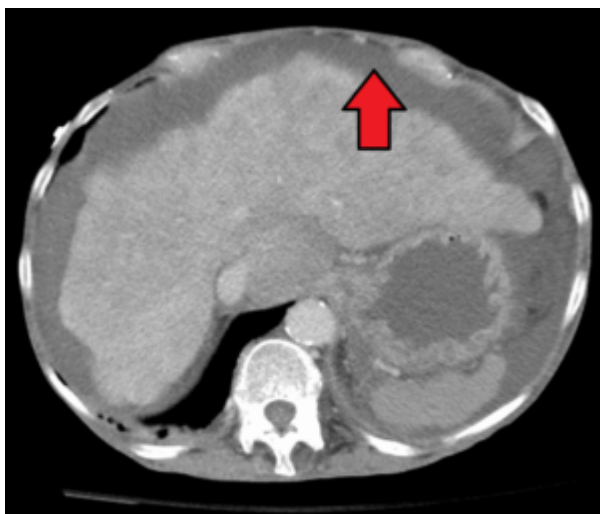
A patient with alcoholic hepatitis is **typically 40 to 50 years of age**, with a history of daily heavy alcohol drinking (more than 100 g per day for more than 20 years), which might occur in response to stressful situations.

Physical examination

Physical examination may reveal symptoms such as **tender hepatomegaly, jaundice, and fever**. In patients with advanced disease, signs of **portal hypertension** and **ascites** may be present; a bruit might be heard over the liver.

Ascites may result from either **portal hypertension**, or **obstruction of portal venous flow** caused by swelling of hepatic cells.

The presence of **stigmata of chronic liver disease**, such as **ascites, palmar erythema, spider angiomas, gynecomastia**, and others, suggest underlying liver cirrhosis.



[Image](#): "Cirrhosis with ascites (marked)" by James Heilman, MD - Own work, License: [CC BY-SA 4.0](#)

Blood tests

1. Liver tests abnormalities:

a. **Gamma-glutamyl transaminase (GGT):**

- Lone elevation (with/without alanine transaminase [ALT] and aspartate aminotransferase [AST]) is a possible sign of occult alcohol abuse.

b. **AST:ALT ratio (liver transaminase):**

- ALT is more specific for the liver than the AST because AST is also found in cardiac and **skeletal muscle, the kidneys, and the lungs**
- Both AST and ALT are usually moderately elevated (< 500 IU/mL and < 400 IU/mL), with or without elevated GGT, in alcoholism.
- AST:ALT ratio ≥ 2 is associated with alcohol abuse (alcoholic hepatitis).

c. **Elevated serum bilirubin (> 5 mg/dL)**

d. **Other liver marker abnormalities:** Hypoalbuminemia, coagulopathy, and modest elevations of alkaline phosphatase.

e. **Mean corpuscular volume (MCV):**

- A larger size of **red blood cells** (due to **nutritional deficiencies**) that resembles **macrocytic anemia** (MCV > 100 fL)

Laboratory investigations to rule out other causes of acute hepatitis should be done, such as:

- Anti-hepatitis A IgM
- Hepatitis B surface antigen, anti-hepatitis B core IgM
- Anti-hepatitis C virus (HCV) antibodies, hepatitis C RNA

Imaging tests

- Tests such as **trans-abdominal U/S, MRI, and CT scans** are carried out to obtain images of the liver, which provide valuable input in understanding the state of liver functioning.
- The imaging tests may reveal **parallel tubular structures in the liver** (venous collaterals). Portal vein flow reversal, ascites, and intra-abdominal venous collaterals on ultrasound indicate serious/irreversible liver injury.

Liver biopsy

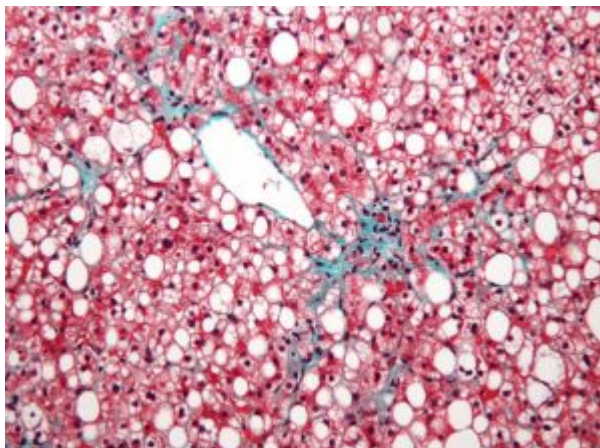


Image: "Micrograph of non-alcoholic fatty liver disease (NAFLD)"
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Whether liver biopsy is necessary **depends on the severity** of the disease. A biopsy of the liver is useful in diagnosing the full extent of the liver damage, which helps in understanding the severity of both the **fibrosis** and the **level of inflammation**.

Furthermore, it helps in evaluating other possible liver diseases, such as the **fatty liver disease** that may accompany alcoholic hepatitis. Liver biopsies are vital not only for alcoholic hepatitis; they are also used in non-alcoholic fatty liver disease to **confirm the accumulation of fat in the liver**.

Differential Diagnosis of Alcoholic Hepatitis

Alcoholic hepatitis should be differentiated from other causes of acute hepatitis. The striking features that identify alcoholic hepatitis are:

- [Heavy alcohol drinking](#)
- AST:ALT ratio ≥ 2 , which is rarely observed in other causes of acute liver disease.

Acute hepatitis

The differential diagnosis of acute hepatitis is wide and includes the following:

- [Acetaminophen toxicity](#)
- [Drug-induced liver injury](#)/idiosyncratic drug reactions (including herbal supplements and illicit drugs)
- Non-alcoholic 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's disease](#)
- Autoimmune hepatitis
- [Alpha-1 antitrypsin deficiency](#)
- Toxin-induced hepatitis (e.g., mushroom poisoning, carbon tetrachloride).

High aminotransferases can also be noticed other diseases such as:

- Muscle diseases
- [Thyroid disease](#)
- [Celiac disease](#)
- Adrenal insufficiency
- [Anorexia nervosa](#)

Treatment of Alcoholic Hepatitis

The management of alcoholic hepatitis includes several measures:

- Abstinence from alcohol
- Treatment of alcoholic withdrawal
- Hemodynamic and nutritional support
- Medical treatment

Abstinence

Patients at the initial stages of liver disease can still **prevent further deterioration** by abstaining from the cause of all the damage. This means abstinence from alcohol in the case of alcoholic hepatitis, and abstinence from obesity-causing products and behaviors in the case of NAFLD. Abstinence will also result in **prevention of cirrhosis**, in both the cases.

Excessive alcohol drinking for a long time places the patient at risk of **withdrawal symptoms**, which also should be treated promptly.

Alcohol abstinence and **general supportive measures** are adequate in the treatment of mild to moderate alcoholic hepatitis. Medical treatment with **glucocorticoids** is not beneficial in the treatment of mild or moderate alcoholic hepatitis.

Hemodynamic and nutritional support

Patients with alcoholic hepatitis should be **hydrated** because poor oral intake associated with the disease may result in **dehydration**.

Overhydration should be avoided in patients with chronic liver disease and signs of cirrhosis because this may increase the volume of the ascites, increase the risk of **hyponatremia**, and predispose the patient to **variceal hemorrhage**.

Nutritional support with **adequate calories**, **proteins**, **vitamins**, and **minerals** is important to improve liver function.

Lifestyle changes, loss of body weight, and dietary modification in NAFLD patients can improve serum aminotransferase levels and reduce hepatic steatosis.

Medical treatment

Medical treatment with glucocorticoids (**prednisolone 40 mg/day for 28 days, followed by gradual tapering of the dose over 2 to 4 weeks**) is indicated in patients with severe alcoholic hepatitis (MELD score > 20) in addition to the general supportive measures.

For **non-alcoholic fatty liver disease**, there are no specific medications, but **anti-inflammatory medicines** like aspirin, ibuprofen, naproxen sodium, or celecoxib, are often prescribed. The drugs currently being studied for the treatment of NAFLD include metformin, pioglitazone, vitamin E, and omega-3 fatty acids. The approach to NAFLD management focuses on the improvement of risk factors for NASH (i.e., obesity, insulin resistance, metabolic syndrome, and dyslipidemia).

Surgical considerations

When the disease becomes chronic, there is a greater risk of **complete liver failure**. In such cases, the only treatment offered is a **liver transplant**. However, surgery, too, is complicated, as the mortality rate in alcoholic patients is high. Nevertheless, surgery is the last resort for end-stage disease despite prevailing complications.

Counseling and therapy

Referral of patients to alcohol counselors/alcohol treatment programs is a routine process

in the management of patients with alcoholic liver disease. **Therapy** helps many patients **break the habit of drinking** or **fight obesity**. **Counseling** helps patients **fight the disease before it gets any worse** and also helps keep the patients and their symptoms **under observation**. There are also many support groups, the most famous being **Alcoholics Anonymous**, which helps patients abstain from alcohol.

Not many counseling methods have been established to help patients deal with NAFLD. **Anti-fibrotic therapy** for non-alcoholic fatty liver disease is still in its initial stages of development.

Prognosis

The presence of ascites, variceal hemorrhage, deep encephalopathy, or hepatorenal syndrome predicts a poor prognosis. Patients with severe alcoholic hepatitis who are critically ill have 30-day mortality rates > 50%. Model for End-Stage Liver Disease (MELD) score ≥ 21 is associated with high mortality in alcoholic hepatitis.

Review Questions

The correct answers can be found below the references.

1. What is the characteristic liver enzymes pattern in alcoholic hepatitis?

- A. AST:ALT ratio ≥ 2
- B. AST:ALT ratio = 2
- C. ALT:AST ratio ≥ 2
- D. ALT:AST ratio = 2

2. What is the definition of heavy alcohol drinking?

- A. More than 100 g per day, for more than 20 years
- B. More than 20 g per day, for more than 30 years
- C. More than 100 g per day, for more than 10 years
- D. More than 200 g per day, for more than 20 years

3. Medical treatment with glucocorticoids is indicated in addition to the general supportive measure in the treatment of what?

- A. Mild alcoholic hepatitis
- B. Moderate alcoholic hepatitis
- C. Non-alcoholic fatty liver disease
- D. Severe alcoholic hepatitis

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Correct answers: 1C, 2A, 3D

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