ALCOHOLIC LIVER DISEASE

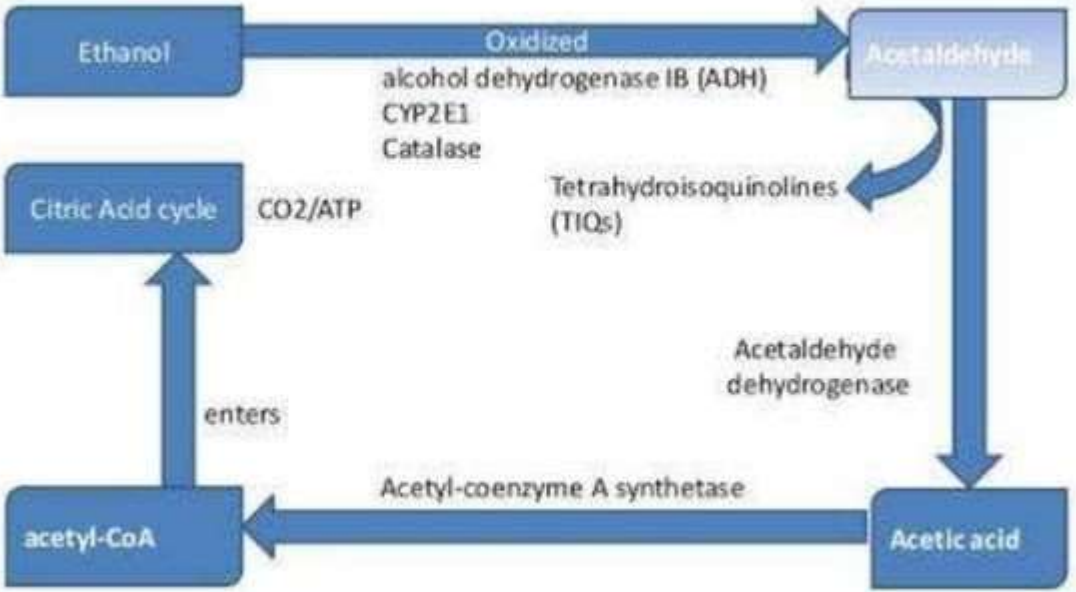
ALD, the term that encompasses the liver manifestations of alcohol overconsumption, including *fatty liver, alcoholic hepatitis, and chronic hepatitis with liver fibrosis or cirrhosis*.

- It may well represent the oldest form of liver injury known to humankind.
- Many people with alcoholic liver disease experience no symptoms in the early stage of the disease.

How much of alcohol cause liver damage

- Consumption of 60–80g per day (about 75–100 ml/day) for 20 years or more in men.
- Consumption of 20g/day (about 25 ml/day) for women significantly increases the risk of liver damage.
- Women have double the risk of getting ALD when compared to men

Metabolism of Alcohol



Note: Disulfiram inhibits Acetaldehyde dehydrogenase

- 80% of alcohol passes through the liver to be detoxified. Chronic consumption of alcohol results in the secretion of pro-inflammatory cytokines (TNF-alpha, Interleukin 6 [IL6] and Interleukin 8 [IL8]), oxidative stress, lipid peroxidation, and acetaldehyde toxicity.

RISK FACTORS

- **Quantity of alcohol taken:**Consumption of 60–80g per day (about 75–100 mL/day) for 20 years or more in men, or 20g/day (about 25 mL/day) for women significantly increases the risk of hepatitis and fibrosis by 7 to 47%.
- **Pattern of drinking:** Drinking outside of meal times increases up to 3 times the risk of alcoholic liver disease.
- **Gender:** Women are twice as susceptible to alcohol-related liver disease, and may develop alcoholic liver disease with shorter durations and doses of chronic consumption.
- **Hepatitis C infection:** A concomitant hepatitis C infection significantly accelerates the process of liver injury.
- **Genetic factors:** Genetic factors predispose both to alcoholism and to alcoholic liver disease. ***Polymorphisms*** in the enzymes.

- **Iron overload (Hemochromatosis)**
- **Diet:** Malnutrition, particularly vitamin A and E deficiencies, can worsen alcohol-induced liver damage by preventing regeneration of hepatocytes.

SYMPTOMS :

Symptoms vary, based on how bad the disease is. You may not have symptoms in the early stages. Symptoms tend to be worse after a period of heavy drinking.

Digestive symptoms include:

Pain and swelling in the abdomen
Decreased appetite and weight loss
Nausea and vomiting
Fatigue
Dry mouth and increased thirst
Bleeding from enlarged veins in the walls of the lower part of the esophagus.

Skin problems such as:

Yellow colour in the skin, mucus membranes, or eyes (jaundice)
Small, red spider-like veins on the skin
Very dark or pale skin
Redness on the feet or hands
Itching

Brain and nervous system symptoms include:

Problems with thinking, memory, and mood
Fainting and light headedness
Numbness in legs and feet


Stages of liver damage
Healthy Liver
Fatty Liver
Liver Fibrosis
Cirrhosis
Deposits of fat lead to liver enlargement
Scar tissues forms
Growth of connective tissue destroys liver cells
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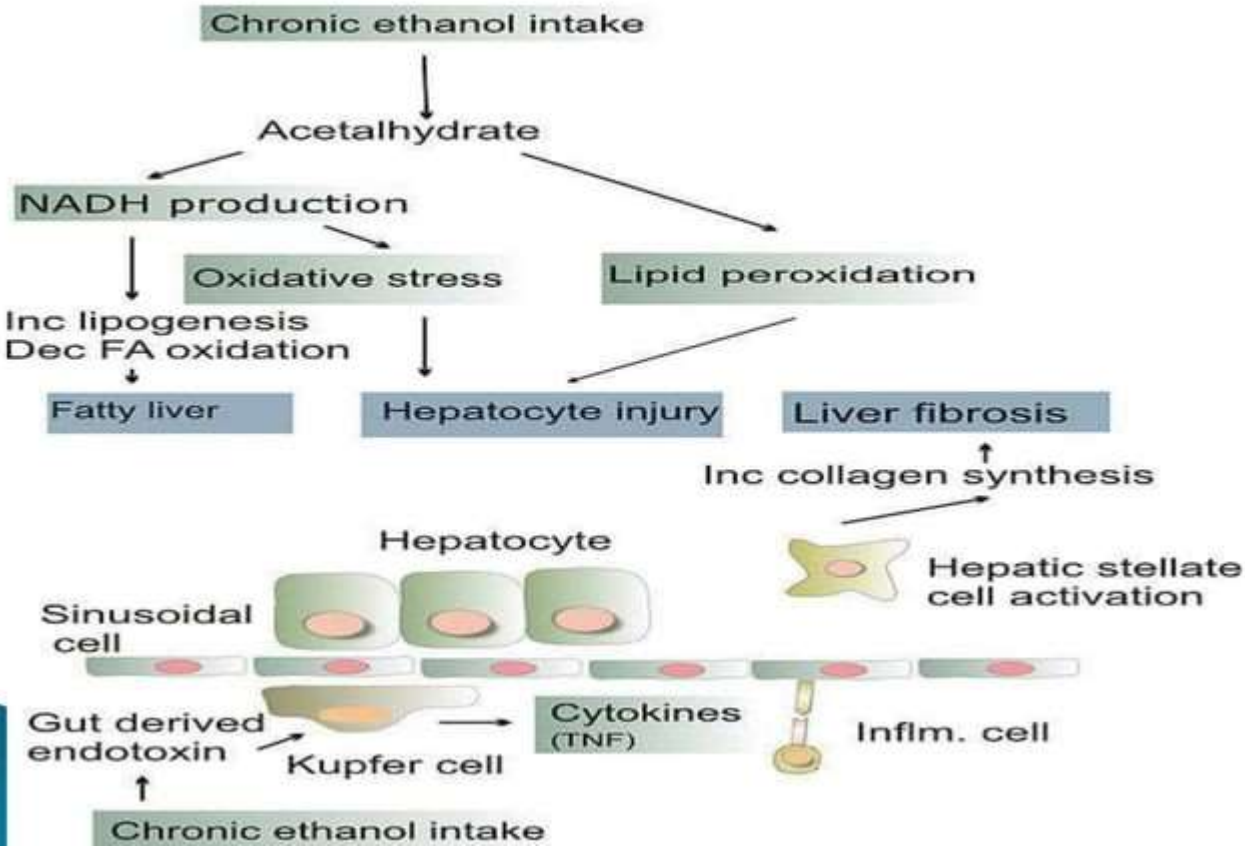
PATHOPHYSIOLOGY



FATTY CHANGE

- Fatty change, or steatosis is the accumulation of fatty acids in liver cells.
- Alcoholism causes development of large fatty globules (macro vesicular steatosis) throughout the liver and can begin to occur after a few days of heavy drinking.
- Alcohol is metabolized by alcohol dehydrogenase (ADH) into acetaldehyde

- Aldehyde dehydrogenase (ALDH) into acetic acid, which is finally oxidized into carbon dioxide (CO_2) and water (H_2O).

- A higher NADH concentration induces fatty acid synthesis while a decreased NAD level results in decreased fatty acid oxidation.

- triglycerides accumulate, resulting in fatty liver

Alcoholic fatty liver disease symptoms

- Weakness
- Nausea
- Abdominal pain
- Loss of appetite
- Malaise(generally feeling unwell)

ALCOHOLIC HEPATITIS

- Alcoholic hepatitis is characterized by the inflammation of hepatocytes. Between 10% and 35% of heavy drinkers develop alcoholic hepatitis (NIAAA, 1993).
- Development of hepatitis is not directly related to the dose of alcohol, some people seem more prone to this reaction than others. This is called alcoholic steato necrosis and the inflammation appears to predispose to liver fibrosis.
- Inflammatory cytokines (TNF-alpha, IL6 and IL8) are thought to be essential in the initiation and perpetuation liver injury by inducing apoptosis and necrosis.
- Symptoms may include *pain or tenderness in the abdomen, jaundice , spider like veins appear on the skin, malaise, fever, nausea and loss of appetite.*
- End stage there will be *hair loss, dark urine, black or pale stools, dizziness, fatigue, loss of libido, bleeding gums or nose, edema, vomiting, muscle cramps, weight loss*

CIRRHOSIS

- Cirrhosis is a late stage of serious liver disease marked by inflammation (swelling), fibrosis (cellular hardening) and damaged membranes preventing detoxification of chemicals in the body, ending in scarring and necrosis(cell death).

- Between 10% to 20% of heavy drinkers will develop cirrhosis of the liver (NIAAA, 1993).

- Acetaldehyde may be responsible for alcohol-induced fibrosis by stimulating collagen deposition by hepatic stellate cells.

- Symptoms include jaundice (yellowing), hepatomegaly, pain and tenderness from the structural changes in damaged liver architecture.

DIAGNOSIS :

LIVER FUNCTION TESTS:

These are simple, inexpensive and easy to perform but cannot be used in alone to make diagnosis which include ;

- Serum albumin levels and prothrombin time indicates hepatic protein synthesis,
- bilirubin is a marker of whole liver function, transaminase levels indicate hepatocellular injury and death.
- alkaline phosphatase levels estimate the impedance of bile flow.

Imaging tests:

An ultrasound scan , CT scan or a MRI scan also be carried. These scans produce detailed images of liver.

- Imaging studies do not confirm the presence of alcoholic liver disease .
- Can be used to assess for hepatic parenchymal changes.
- Ultrasound, CT scan, and MRI can be used to diagnose fatty change, cirrhosis, or neoplastic diseases of the liver.

Liver biopsy:

A fine needle is inserted into body and a small sample of liver cell is taken under local anaesthesia and is examined under microscope.

➢Biopsy may be indicated in:

➢Any patient with serum aminotransferases elevations that persist for >6 months, even if the patient is asymptomatic.

➢Patients who have evidence of liver failure (eg, abnormal prothrombin time, hypoalbuminemia) in addition to elevated aminotransferases.

If a coagulopathy is present, transjugular biopsy is usually safer than percutaneous biopsy.

➢Patients in whom the diagnosis of alcoholic hepatitis is uncertain based upon clinical and laboratory findings.

➢Patients who may have more than one type of liver disease (such as alcohol and hepatitis C) in whom a liver biopsy may help determine the relative contribution of these factors .

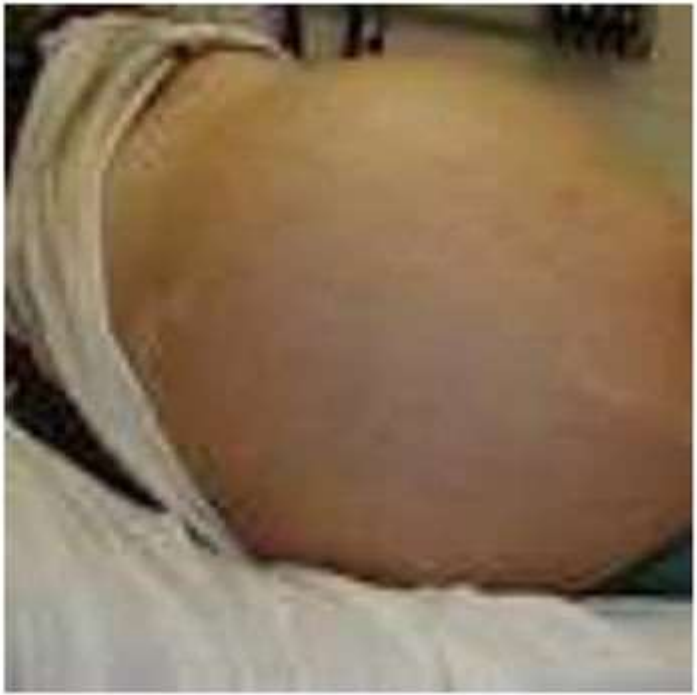
➢Patients in whom a more detailed understanding of prognosis is desired.

Endoscopy:

An endoscope is a thin long flexible tube with a light and video camera at one end this tube is passed into oesophagus and stomach and examine for varices

ASCITES

- Accumultion of fluid in the peritoneal cavity . The medical condition is also known as **peritoneal cavity fluid,peritoneal fluid excess, hydroperitoneum**
- A low salt diet may be enough to facilitate the elimination of ascites and delay reaccumulation of fluid.(60-90mEq/day).
- Mild ascites is hard to notice, but severe ascites generally lead to abdominal distension
- Amounts of upto 35 liters are possible.
- Symptoms of ascites;
  - Abdominal distension with fullness in the flanks
  - Abdominal and back pain
  - Gateroesophageal reflux



Management of cirrhotic ascites

Bed rest and sodium restriction[60-90meq/day to 1500-2000mg of salt/day]

Spironolactone : 100-400 mg/day

Furosemide : 40-160mg/day

Hydrochlorothiazide : 50mg/day

HEPATIC ENCEPHALOPATHY :

- A high level of toxins in the blood due to liver damage is known as hepatic encephalopathy.
- Symptoms of hepatic encephalopathy include:

agitation
confusion
disorientation
muscle stiffness
muscle tremors
difficulty speaking
in very serious cases, coma

MANAGEMENT

- Lactulose:

15-30ml orally 2-4 times per day.

- Antibiotics:

Metronidazole:

250mg orally 3 times daily .

Neomycin:

0.5-1g orally every 6-12 hrs for 7 days.

Rifaximin:

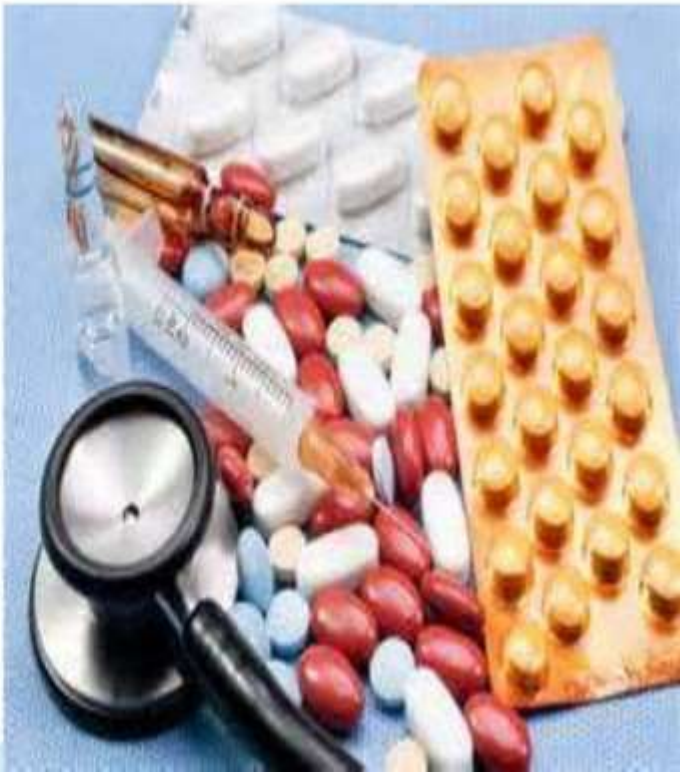
400mg orally 3 times daily.

- LOLA:

L-ornithine L-aspartate 9g orally 3 times daily

TREATMENT

- Abstinence .
- Nutrition .
- Drug therapy .
- Liver transplantation .



Alcohol Abstinence

- Abstinence is the most important therapeutic intervention for patients with ALD .
- Abstinence has been shown to improve the outcome and histological features of hepatic injury, to reduce portal pressure and decrease progression to cirrhosis, and to improve survival at all stages in patients with ALD
  - Less than 20 % of patients will demonstrate progression of liver disease after abstinence .
  - 5 year survival improves from 34 % to 60 % for those with decompensated liver disease

Nutritional diet

- Alcoholism is associated with nutritional deficiencies .
- The presence of significant protein calorie malnutrition is a common finding in alcoholics, as are deficiencies in a number of vitamins and trace minerals, including vitamins A, D, thiamine, folate, pyridoxine, and zinc .

DRUG THERAPY

- **ALCOHOLIC HEPATITIS**

  Prednisolone :

  40mg orally daily for 4 weeks; then taper the dose.

- **FOLIC ACID DEFICIENCY** :

  Folic acid :

  1mg orally daily in conjugation with improved dietary intake until repletion occurs.

- **THIAMINE DEFICIENCY :**

  THIAMINE:

  100mg orally or subcutaneously daily for 2 weeks or until repleted.

- **VITAMIN D DEFICIENCY:**

  Ergocalciferol:

  12,000 to 50,000 international units orally daily; reassess vitamin D serum levels in 2 to 3 months.

- ***VITAMIN E DEFICIENCY :***

  Vitamin E

  400 IU orally daily

- ***VITAMIN A DEFICIENCY :***

  25,000 TO 50,000 IU orally 3 times weekly.

Silymarin

- Antioxidative and antifibrotic properties.
- Believed to enhance liver regeneration and protect hapetocytes from toxicity

- Recommended dose is 140mg 2-3 times /day

Liver Transplantation

- Liver transplantation remains the only definitive therapy.
- Alcoholic hepatitis has been considered an absolute contraindication to liver transplantation.

THANK YOU