

**!! JAY AMBE !!**

**18. PATHOPHYSIOLOGY OF CIRRHOSIS &  
ALCOHOLIC LIVER DISEASE**

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## 18. CIRRHOSIS & ALCOHOLIC LIVER DISEASE

### CIRRHOSIS

**“Cirrhosis is a late stage of scarring (fibrosis) of the liver caused by many forms of liver diseases and conditions, such as hepatitis and chronic alcoholism”**

### WHAT IS CIRRHOSIS OF THE LIVER?

The liver is the largest solid organ in the body. It performs many important functions, including:

- Making blood proteins that aid in clotting, transporting oxygen, and helping the immune system.
- Storing excess nutrients and returning some of the nutrients to the bloodstream.
- Manufacturing bile, a substance needed to help digest food.
- Helping the body store sugar (glucose) in the form of glycogen.
- Ridding the body of harmful substances in the bloodstream, including drugs and alcohol.
- Breaking down saturated fat and producing cholesterol.

Cirrhosis is a slowly developing disease in which healthy liver tissue is replaced with scar tissue. The scar tissue blocks the flow of blood through the liver and slows the liver's ability to process nutrients, hormones, drugs and natural toxins (poisons). It also reduces the production of proteins and other substances made by the liver. Cirrhosis eventually keeps the liver from working properly.

### SYMPTOMS

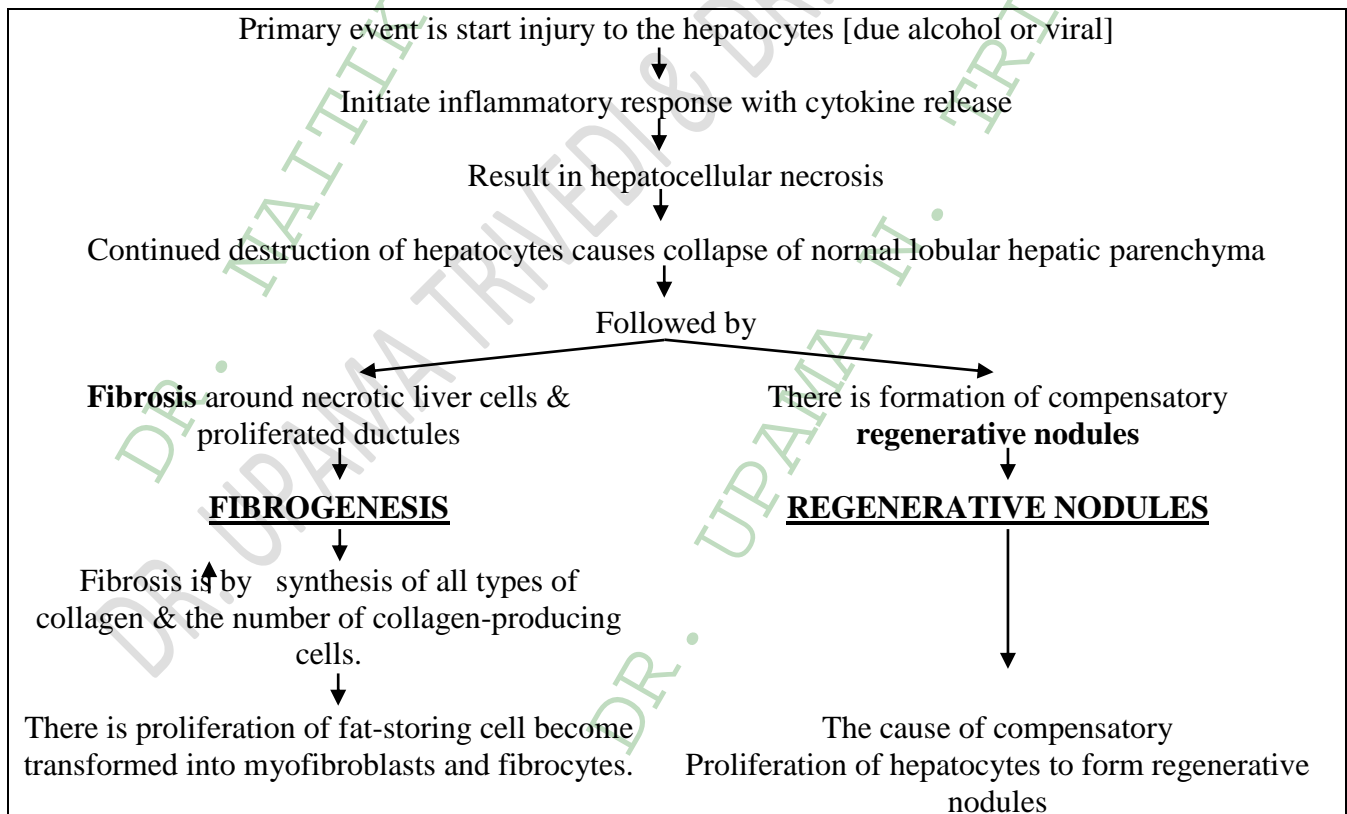
Cirrhosis often has no signs or symptoms until liver damage is extensive. When signs and symptoms do occur, they may include:

- Fatigue
- Easily bleeding or bruising
- Loss of appetite
- Nausea
- Swelling in your legs, feet or ankles (edema)
- Weight loss
- Itchy skin
- Yellow discoloration in the skin and eyes (jaundice)
- Fluid accumulation in your abdomen (ascites)
- Spiderlike blood vessels on your skin
- Redness in the palms of the hands
- For women, absent or loss of periods not related to menopause
- For men, loss of sex drive, breast enlargement (gynecomastia) or testicular atrophy
- Confusion, drowsiness and slurred speech (hepatic encephalopathy)

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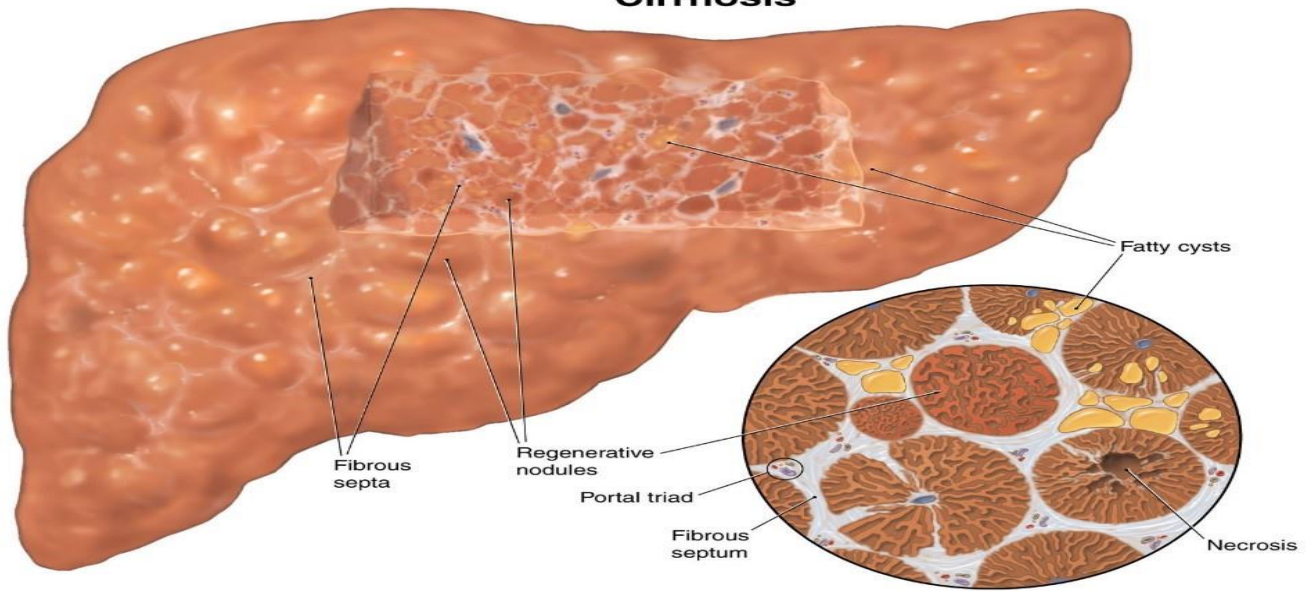
### PATHOPHYSIOLOGY OF CIRRHOSIS

- Cirrhosis, also known as liver cirrhosis or hepatic cirrhosis, is a condition in which the liver does not function properly due to long-term damage.
- A chronic degenerative disease characterized by replacement of normal liver tissues with diffuse fibrosis that disrupts the structure and function of liver.
- This damage is characterized by the replacement of normal liver tissue by scar tissue.
- Typically, the disease develops slowly over months or years.
- It represents the irreversible end-stage of several diffuse diseases causing hepatocellular injury and is characterized by the following 4 features:
  1. It involves the entire liver.
  2. The normal lobular architecture of hepatic parenchyma is disorganised.
  3. There is formation of nodules separated from one another by irregular bands of fibrosis.
  4. It occurs following hepatocellular necrosis of varying etiology so that there are alternate areas of necrosis and regenerative nodules.



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### Cirrhosis



### COMPLICATIONS

Cirrhosis can lead to several other conditions, some of which are life-threatening. These include:

**Ascites or edema:** Ascites is a buildup of fluid in the abdomen, and edema is a buildup of fluid in the legs. They can be treated with a low-salt diet and water pills. In severe cases, the fluid may have to be drained repeatedly. Surgery is sometimes needed.

**Varices and portal hypertension:** These are large, swollen veins in the esophagus and stomach. They can increase pressure in a blood vessel called the portal vein that carries blood from the spleen and bowel to the liver. Varices can rupture, causing severe blood loss and clots.

**Hepatic encephalopathy:** This refers to high levels of toxins in the blood where the liver is no longer successfully filtering them all.

**Hepatocellular carcinoma:** This is the most common type of liver cancer. It is the third-leading cause of cancer mortality across the globe.

**Hepatopulmonary syndrome (HPS):** Doctors define HPS as a combination of liver disease, dilated blood vessels in the lungs, and abnormalities in the exchange of gases. It is linked to an increase in the mortality rate of people waiting for a liver transplant.

**Coagulation disorders:** Cirrhosis can cause problems with blood clotting, leading to potentially fatal bleeds and clots.

### ALCOHOLIC LIVER DISEASE

**“Alcoholic liver disease is a result of overconsuming alcohol that damages the liver, leading to a buildup of fats, inflammation, and scarring. It can be fatal.”**

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### FAST FACTS ON ALCOHOLIC LIVER DISEASE

- Alcoholic liver disease is the main cause of chronic liver disease in Western nations and the third most common cause of liver transplants.
- Abstaining from drinking alcohol is the only way a person has a chance of recovery.
- Jaundice and tremors are symptoms of alcoholic liver disease.
- Treatment options include medication, lifestyle changes, and surgery.
- The recommended daily limits are no more than one drink a day for women and no more than two drinks a day for men.

### SYMPTOMS

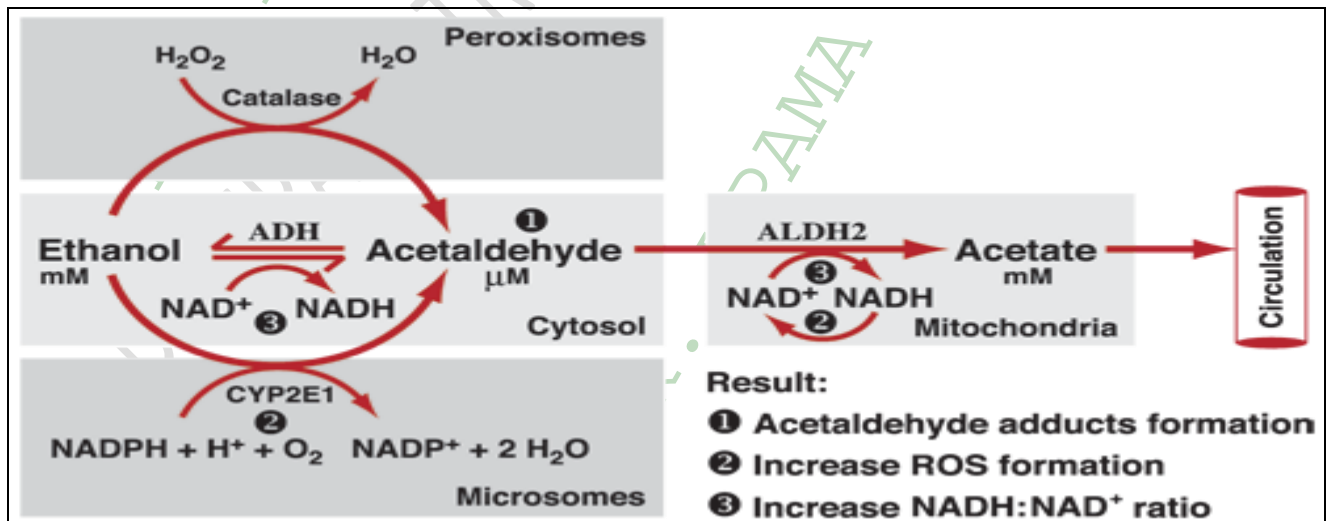
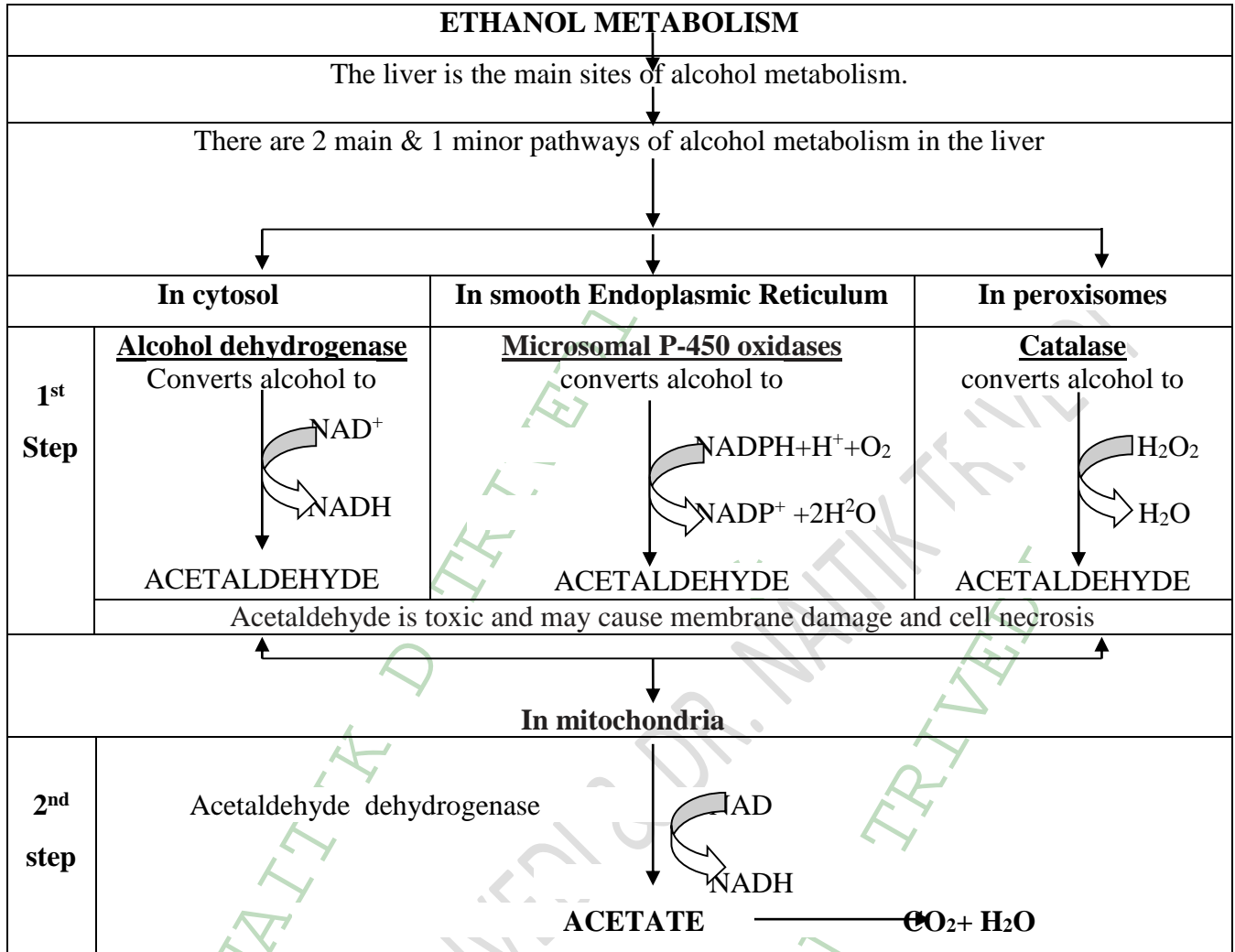
- nausea
- loss of appetite
- jaundice
- fatigue
- abdominal discomfort
- red hands or feet
- dark bowel movements
- fainting
- unusual agitation
- increased thirst
- swelling in the legs and abdomen
- weight loss
- darkening or lightening of the skin
- mood swings
- confusion
- bleeding gums
- enlarged breasts (in men)

Symptoms of ALD may show up more often after binge drinking.

### PATHOPHYSIOLOGY OF ALCOHOLIC LIVER DISEASE

- ❖ Alcoholic liver disease is the result of excessive alcohol consumption over a long period of time. It is a severe and fatal consequence of alcohol abuse.
- ❖ Alcohol abuse over the years leads to the replacement of healthy liver tissue with scar tissue..
- ❖ The liver is one of the most complex organs in the human body, with over 500 functions. These include filtering out blood toxins, storing energy, making hormones and proteins, and regulating cholesterol and blood sugar.
- ❖ Alcoholic liver disease is the term used to explain the spectrum of liver injury associated with acute and chronic alcoholism.
- ❖ There are three sequential stages in alcoholic liver disease:
  1. **Alcoholic Steatosis (Fatty Liver),**
  2. **Alcoholic Hepatitis**
  3. **Alcoholic Cirrhosis.**

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### PATHOPHYSIOLOGY OF ALCOHOLIC LIVER DISEASE

Alcohol dehydrogenase and acetaldehyde dehydrogenase cause the reduction of nicotinamide adenine dinucleotide (NAD) to NADH (reduced form of NAD).

The altered ratio of NAD/NADH promotes fatty liver through the inhibition of gluconeogenesis and fatty acid oxidation.

Cyto P450 which is upregulated in chronic alcohol use, generates free radicals through the oxidation of NADPH to NADP

Chronic alcohol exposure also activates hepatic macrophages, which then produce (TNF-alpha)

TNF-alpha induces mitochondria increase reactive oxygen species.

This oxidative stress promotes hepatocyte necrosis and apoptosis

Free radicals initiate lipid peroxidation, which causes inflammation and **FIBROSIS**.

Inflammation is also incited by acetaldehyde that, when bound covalently to cellular proteins, forms adducts that are antigenic

The effect of acetaldehyde dehydrogenase can include

#### **HEPATIC STEATOSIS**

Initial microvesicular droplets of fat accumulate in the hepatocyte cytoplasm

Then macrovesicular droplets of fat displacing the nucleus to the periphery

Fat cysts may develop & rupture of fat-containing hepatocytes.

lipogranulomas consisting lymphocytes, macrophages and some multinucleate giant cells may be found

#### **ALCOHOLIC HEPATITIS**

**Necrosis:** Single or small clusters of Hepatocytes undergo ballooning degeneration and necrosis.

**Mallory bodies or alcoholic hyaline found in hepatocyte** swollen and ballooned hepatocytes.

The areas of hepatocellular necrosis and regions of Mallory bodies are associated with an inflammatory infiltrate

**Fibrosis:** Most cases of alcoholic hepatitis are accompanied by pericellular and perivenular fibrosis,

#### **ALCOHOLIC CIRRHOSIS**

It begins as micronodular cirrhosis (nodules less than 3 mm diameter, wt is 2 kg

then liver shrinks to less than 1 kg in weight,

becomes non-fatty, having macronodular cirrhosis (nodules larger than 3 mm in diameter),

resembling post-necrotic cirrhosis

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