Practical Toxicology

Lab 3

Introduction to Toxicology

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Liver FunctionIn

In the liver three main functions occur: storage, metabolism, and biosynthesis.

- Glucose is converted to glycogen and stored; when needed for energy, it is converted back to glucose..
- Fat, fat-soluble vitamins, and other nutrients are also stored in the liver.
- Fatty acids are metabolized and converted to lipids, which are then conjugated with proteins synthesized in the liver and released into the blood stream as lipoproteins.
- The liver also synthesizes numerous functional proteins, such as enzymes and blood-coagulating factors.
- In addition the liver, which contains numerous xenobiotic metabolizing enzymes, is the main site of metabolism.

SUSCEPTIBILITY OF THE LIVER

- The liver, the largest organ in the body, is often the target organ for chemically induced injuries

Several important factors are known to contribute to the liver's susceptibility:

1. Most xenobiotics enter the body through gastrointestinal (GI) tract and , after absorption, are transported by the hepatic portal vein to the liver: thus the liver is the first organ perfused by chemicals that are absorbed in the gut.
2. 2. The high concentration in the liver of xenobiotic metabolizing enzymes , primarily the cytochrome P450-dependent monooxygenase system.

TYPES OF LIVER INJURY

The types of injury to the liver depend on:

- the type of toxic agent,
- the severity of intoxication,(dose , time)
- the type of exposure, whether acute or chronic.

Factors influencing susceptibility to hepatotoxicity

Age

Nutritional status.

Gender-

Pregnancy Duration

total dose of drug

Drug-drug interactions

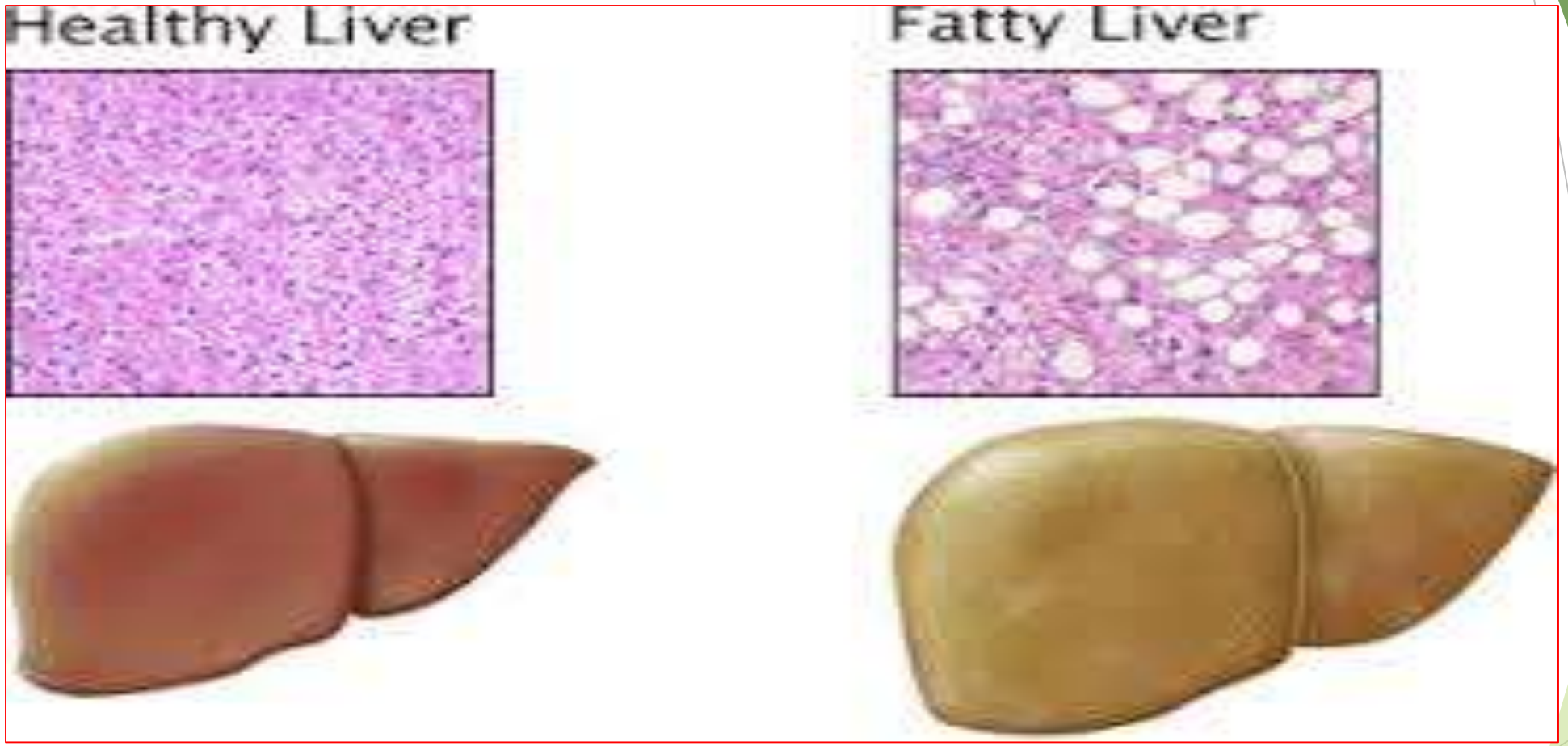
- **TYPES OF LIVER INJURYI.**
- Fatty Liver "steatosis".
- Necrosis.
- Cholestasis.
- Hepatitis.
- Cirrhosis.
- Carcinogenesis

Symptoms of hepatotoxicity

can include rash, stomach pain, nausea and vomiting, fatigue, dark-colored urine, light-colored bowel movements, jaundice (yellow skin and eyes), loss of appetite, and fever.

Fatty Liver "steatosis“

- Fatty liver refers to the abnormal accumulation of fat in hepatocytes.
- At the same time there is a decrease in plasma lipids and lipoproteins.
- lipid accumulation is related to disturbances in either the synthesis or the secretion of lipoproteins.
- Although many toxicants may cause lipid accumulation in the liver, the mechanisms may different.
- Chemical or Drug inducers Fatty Liver . CCL4, Chloroform, Aflatoxins, Ethanol .


Healthy Liver
Fatty Liver

- Necrosis: Cell necrosis is a degenerative process leading to cell death .
- Cell death occurs along with rupture of the plasma membrane , and is preceded by a number of morphologic changes such as cytoplasmic edema, accumulation of triglycerides, and dissolution of organ clles and nucleus.
- Chemical or Drug inducers. CCI4, Chloroform, Ethanol, Bromobenzene, Digoxins,Acetaminophen.

Cholestasis

Is the suppression of bile flow. It is an acute injury. Intrahepatic or extra-hepatic factors produce inflammation or block the bile ducts results in:

- retention of bile salts &bilirubin accumulation . leading to jaundice
- Chemical or Drug inducers, Estrogens, Anabolic steroids, Paraquat , Chlorpromazine, Erythromycin.

Hepatitis

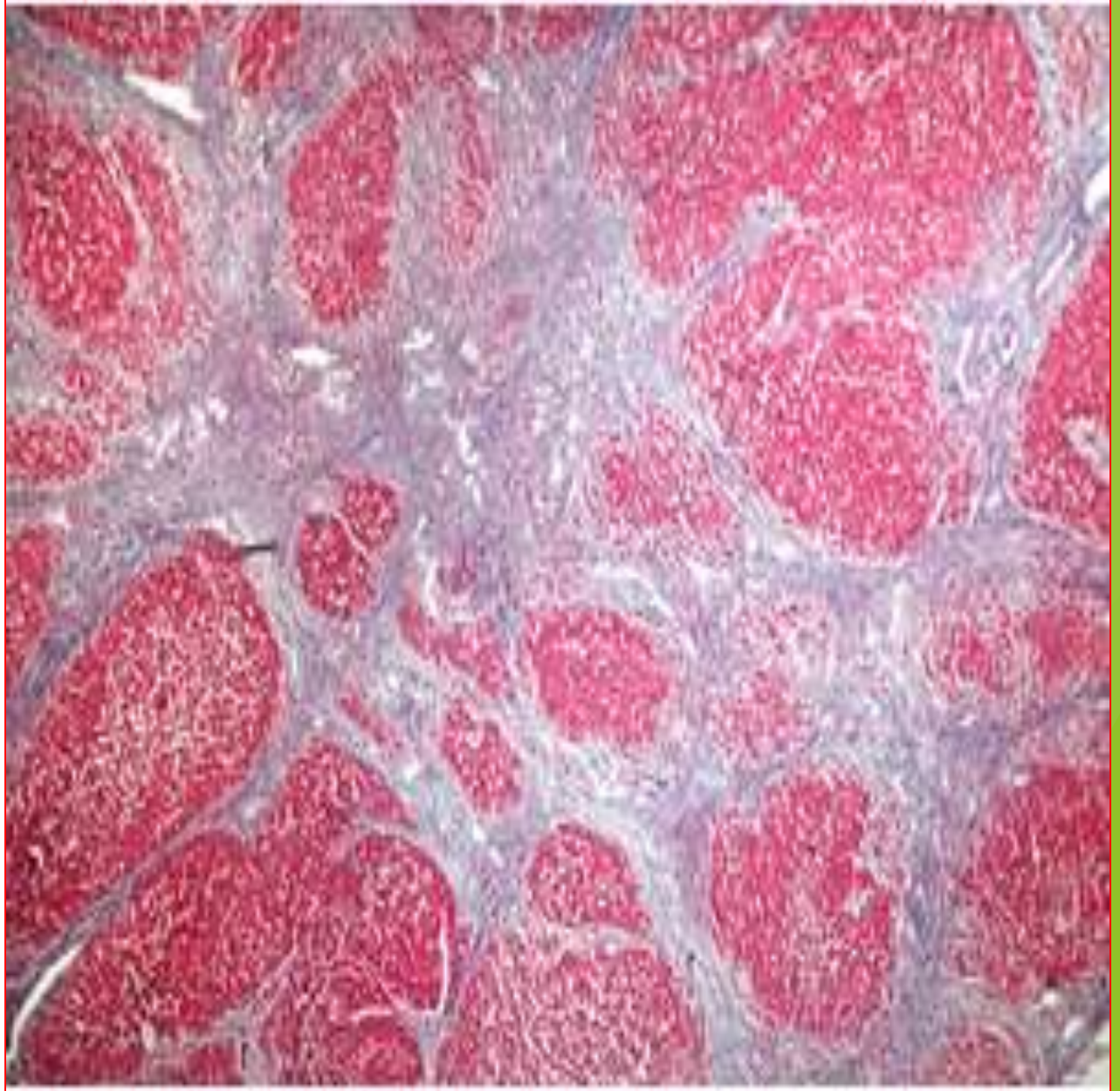
- Hepatitis is an inflammation of the liver, usually viral in origin ;however , certain drugs, can induce Hepatitis such as Non steroidal anti-inflammatory drugs (NSAIDs), ibuprofen, diclofenac, and naproxen, may also cause hepatitis.

Cirrhosis

Is a chronic liver injury results from : accumulation of collagen fibers within the liver, leading to fibrosis.

- Accumulation of fibrous material cause severe restriction in blood flow & dysfunction in liver's normal metabolic & detoxifcation processes → cirrhosis & liver failure.
- **Cirrhosis is not reversible** and is **associated with overdose of vitamin A and chronic alcoholism**.
- Chemical or Drug inducers✓ CC14, Chloroform, Aflatoxins, Ethanol, Bromobenzene, Digoxins

accumulation of excessive amounts of collagen fibers in response to damage or inflammation.



Advanced Cirrhosis

http://www.med.sc.edu/schedules/pathophys/jaundice1.htm

Diagnosis

Tests and procedures used to diagnose hepatotoxicity include:

- **Physical exam.**
- Your doctor will likely perform a physical exam and take a **medical history.** Be sure to bring to your appointment all medications you're taking, including over-the-counter drugs and **herbs**, in their original containers. Tell your doctor if you **work with industrial chemicals** or may have been exposed to pesticides, herbicides or other environmental toxins.

•**Blood tests.** Your doctor may order blood tests that look for high levels of certain liver enzymes. These enzyme levels can show how well your liver is functioning.

- **Imaging tests.** Your doctor may recommend an imaging test to create a picture of your liver using ultrasound, computerized tomography (CT) or magnetic resonance imaging (MRI). Additional imaging tests may include magnetic elastography and transient elastography.

Liver biopsy. A liver biopsy can help confirm the diagnosis of toxic hepatitis and help exclude other causes. During a liver biopsy, a needle is used to extract a small sample of tissue from your liver. The sample is examined under a microscope.

Thanks for Listening