Functions of the Liver

Physiologic anatomy of the liver

- ❖ The basic unit is the lobule (50,000 to 100,000).
- ❖ Each liver lobule is organized around a central vein that empties into hepatic vein & then into vena cava.
- ❖ At the periphery of the lobule, blood enters the sinusoids from branches of portal vein & hepatic artery.
- ❖ In the sinusoids blood flows toward the center of the lobule between plates of hepatocytes that are 1 or 2 cells thick.
- ❖ The venous sinusoids are lined by 2 types of cells:
    a) Typical endothelial cells
    b) Large Kupffer cells (Tissue macrophages, Reticuloendothelial cells) capable of phagocytizing bacteria & foreign matter in the blood.
- ❖ There are large pores in the endothelial lining of the sinusoids, (1 µm in diameter), that allow protein molecules to pass through with the lymph.
- ❖ Each hepatocyte is in direct contact with sinusoidal blood which accounts for liver's ability to clear the blood of certain compounds.
- ❖ The average transit time for blood across the liver lobule from the portal venule to the central hepatic vein is about 8.4 sec.
- ❖ Biliary canaliculi lie between adjacent hepatocytes & drain into biliary ducts at the periphery of the lobule.

Blood Flow through the liver

- ➢ The liver has a dual blood supply.
- ➢ About 1100 ml of blood flows from the portal vein into liver sinusoids each min.
- ➢ An additional 350 ml flows into the sinusoids from hepatic artery.
- ➢ The total average hepatic blood flow is about 1450 ml/min (30 % of CO).
- ➢ This explains why the liver is one of the important blood reservoirs in the body.

Pressure & resistance in the hepatic vessels

♣ The pressure in the hepatic vein leading from the liver into vena cava = 0 mm Hg.
♣ The pressure in the portal vein leading into the liver = 9 mm Hg.
♣ The resistance to blood flow through liver sinusoids is normally low.

Portal hypertension

♣ Increase in portal pressure to 20 – 30 mm Hg.
♣ It is due to constriction or obliteration of hepatic vascular channels.
♣ Collateral channels to systemic circulation enlarge and the vessels become tortuous.
♣ Causes may be
    * Fibrosis of the liver parenchyma.
    * Liver cirrhosis.
    * Hepatic schistosomiasis.

Effects of high hepatic vascular pressure HVP

♦ When HVP rises 3 to7 mm Hg above normal, fluid transude into the lymph & through the outer surface of liver capsule into the abdominal cavity.
♦ The fluid is pure plasma containing 80 to 90% proteins > plasma proteins.
♦ At higher HVP (10 to 25 mm Hg), the sweating from the surface of the liver causes severe ascites.
♦ The high protein content of ascitic fluid also creates an osmotic gradient which attracts more water.
♦ Hypoproteinemia due to hepatocyte damage also contributes to ascites formation.

Effects of high capillary pressure in the GIT

Blockage of portal flow into or through the liver causes very high capillary pressure in the entire GIT that may result in:

❖ Edema of the gut wall.
❖ Transudation of fluid through the serosa of gut into abdominal cavity.

❖ Ascites (less lightly to occur because collateral vascular channels develop rapidly from portal to systemic veins).

Functions of the liver

The liver, the largest gland in the body, has many complex functions that can be grouped under 5 subheadings:

1- Vascular functions
2- Inactivation of various substances
3- Secretory function
4- Synthesis function
5- Metabolic functions

1- Vascular functions

a) Storage of blood.
Since the hepatic blood flow is 30 % of blood volume, it is one of the most important reservoirs of blood in the body.
In the case of strenuous exercise or hemorrhage, part of hepatic blood is diverted towards the exercising muscles or vital organs.

b) Antigen clearance. The liver filters blood coming from gut.

c) Hepatic tissue macrophage system:
Kupffer cells which line the inner surfaces of liver sinusoids are highly phagocytic, they can remove 99% of bacteria or other antigens contained in the blood arriving from the gut.

2- Inactivation of various substances

a. Removal of toxins from circulation and either broken down or excreted in bile.
b. Reduction & conjugation of adrenal & gonadal steroid hormones as estrogen, cortisol & aldosterone.
c. Chemical alteration or excretion of other hormones as thyroxin.

Therefore liver damage can lead to excess accumulation of one or more of these hormones in body fluids & over activity of the hormonal system.

3- Secretory function

The liver continuously secretes bile which after storage in gall bladder is discharged into duodenum.

4- Synthesis function e.g.

* Acute phase protein.
* Albumin.
* Coagulation factors.
* *Steroid-binding and other hormone-binding proteins.*

5- Metabolic functions

The live cells are a large chemically reactant pool having a very large rate of metabolism.

It shares substrates and energy from one metabolic system to another.

It plays a role in processing and synthesizing multiple substances that are transported to other areas of the body.

❁ *CHO metabolism*

The liver performs the following specific functions:

A- Storage of glycogen.

B- Conversion of fructose and galactose into glucose.

C- Gluconeogenesis.

D- Formation of important compounds from intermediate products of CHO metabolism.

Glucose buffer function

The liver is important for maintaining a normal blood glucose concentration:

- When the blood glucose level begins to rise too high, the live stores glucose as glycogen.
- When the blood glucose begins to fall too low, glycogen in the liver is broken down to glucose (glycogenolysis) and large amount of AA are converted into glucose (gluconeogenesis).

❁ *Fat metabolism*

Certain aspects of fat metabolism occur mainly in the liver:

- Beta oxidation of fatty acids and formation of acetoacetic acid.
- Formation of most of lipoproteins.
- Synthesis of large quantities of cholesterol and phospholipids.
- Conversion of large quantities of CHO and proteins into fat.

❁ *Protein metabolism*

The most important functions are:

- Deamination of AA before they can be used for energy or before they can be converted into CHO or fats.

- Synthesis of plasma proteins (except gamma globulins).
- Inter conversions among different AA and different compound. e.g. nonessential AA.
- Formation of urea for removal of ammonia from body fluids. In absence of this function, plasma ammonia conc. rises and results in hepatic coma.

Hepatic encephalopathy

- It is the most serious complication of hepatic failure.
- It is due to accumulation of substances toxic to brain as ammonia, phenols and amines derived from bacteria in the gut.
- Ammonia combines with glutamate in the brain where it gives rise to glutamine and leads to glutamate depletion.
- Since glutamate is the main excitatory transmitter in brain, its depletion could account for neuroinhibition of hepatic encephalopathy.

❁ *Miscellaneous metabolic functions of the liver*

A- Storage of vitamins, as vitamin A, D and $B_{12.}$

Hepatic storage protects the body from transient deficiencies of these vitamins e.g.:

- Sufficient vitamin A can be stored to prevent deficiency for as long as 10 months.
- Sufficient vitamin D can be stored to prevent deficiency for as long as 3-4 months.
- Sufficient vitamin B_{12} can be stored to prevent deficiency for at least a year & may be several years.

B- Storage of iron. Except for iron in Hb of blood, by far the greater portion of iron in the body is usually stored in the liver where it combines with apoferritin to form ferritin.

Blood iron buffer (apoferritin-ferritin system of the liver):

* When iron is available in body fluids in extra quantities, it combines with apoferritin to form ferritin and stored until needed.

* When iron in body fluids reaches a low level, ferritin releases iron.

C- Synthesis of blood substances utilized in coagulation process as fibrinogen, prothrombin, factor VII, IX and X. Vitamin K is required for these processes.

D- Removal or excretion of drugs into the bile as ampiciline, erythromycin.

E- Excretion of calcium from blood into bile.

Tests of liver function

I. Synthetic Functions:

They are assessed by determination of the concentration of plasma proteins & prothrombin time.

II. Secretory Functions:

They are assessed by determination of bile acids in serum.

III. Excretory Functions:

- The role of liver in bilirubin metabolism can be assessed by estimation of serum bilirubin & other related tests, such as determination of urinary excretion of conjugated bilirubin & urobilinogen.
- Alkaline phosphatase is normally excreted in bile. In biliary obstruction its plasma level rises.