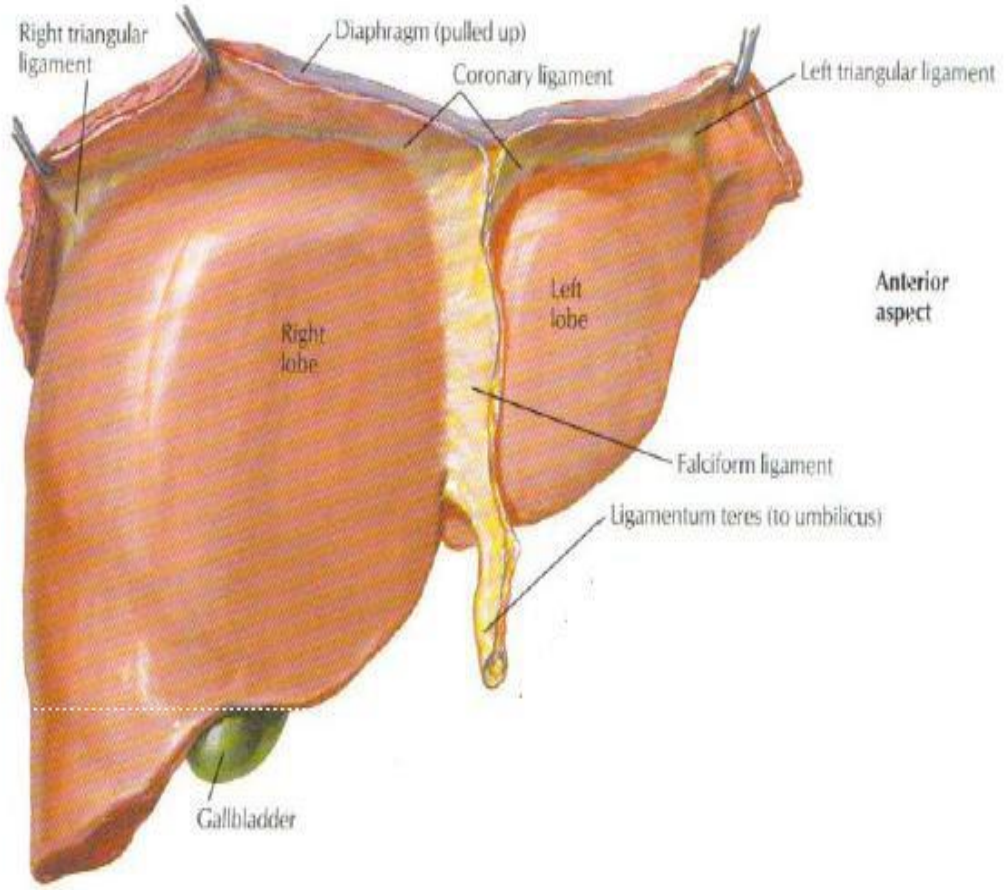
Structure of liver

- The Liver is the largest organ in the body weighing about 1.5 Kg in adults; representing 2% of the TBW)
- It is situated in the right upper quadrant of the abdomen.
- It is covered by Glisson's capsule, a visceral continuation of the peritoneum.

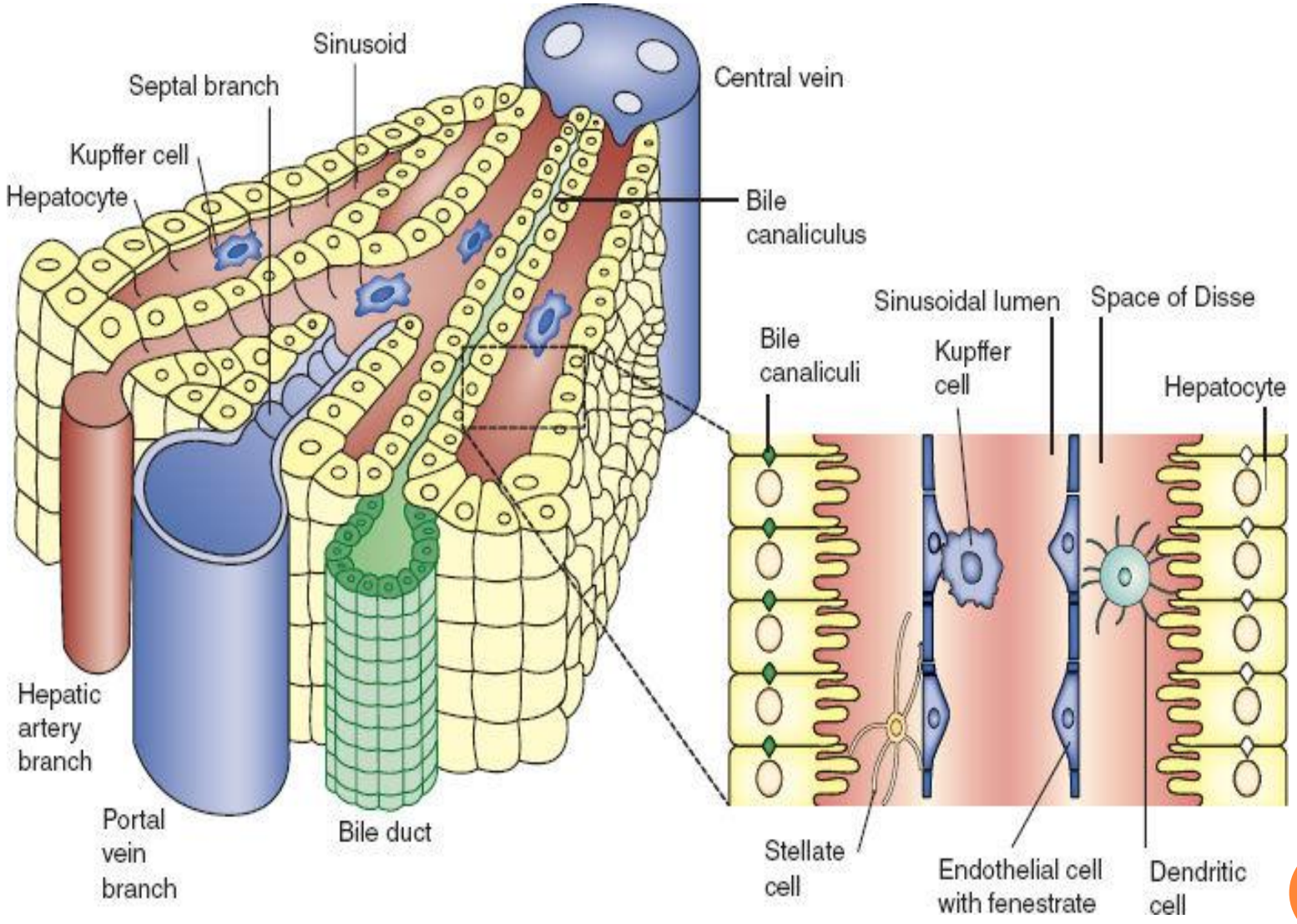
HEPATIC LOBES

- The two major lobes, right and left, and 2 accessory lobes, quadrate and caudate

- The right lobe is six times larger than left Lobe.



Liver anatomy



MICROSCOPIC STRUCTURE

- Functionally the liver consists of 3 systems;
- Liver Cell (Hepatocytes) Systems →
  arranged in hexagonal and pentagonal units
  called hepatic lobules.
- Biliary System.
- Blood Circulatory System.

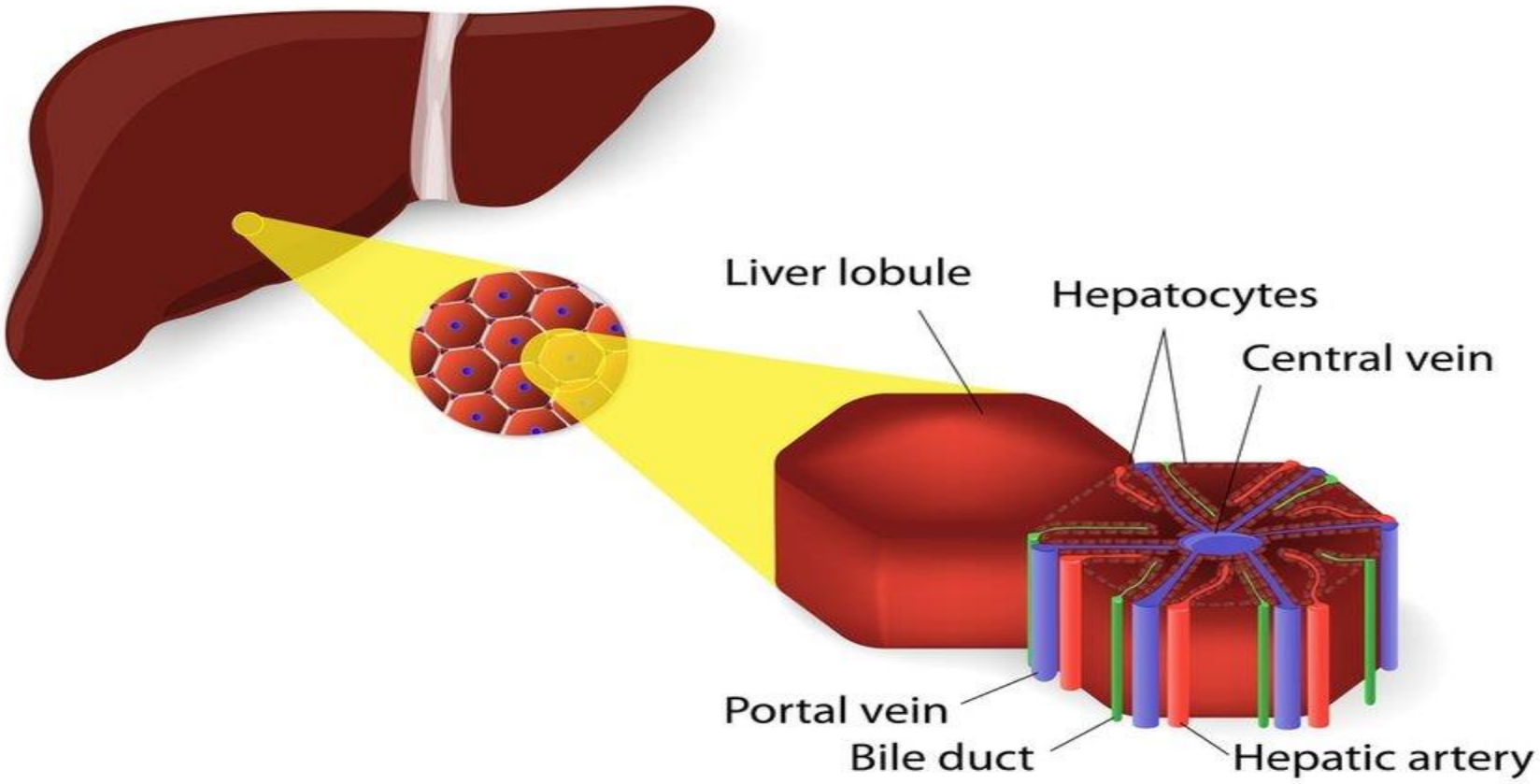
Hepatic Lobule

- The hepatic lobule is the structural unit of the liver which is hexagonal or pentagonal in shape

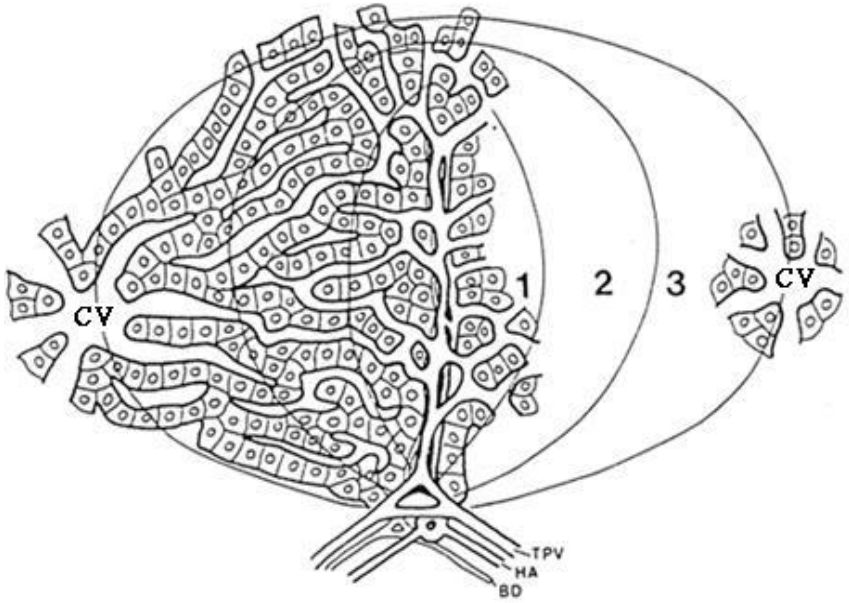
- Each lobule consists of radiating columns(2 or more rows of cells) of hepatocytes around a central vein and surrounded by 4 to 6 portal tracts (bile duct, branches of the hepatic artery and portal vein, along with nerves and lymphatic's).

- The human liver contains about 50000-1000000 lobules.

STRUCTURE OF LIVER LOBULE



LIVER ACINUS

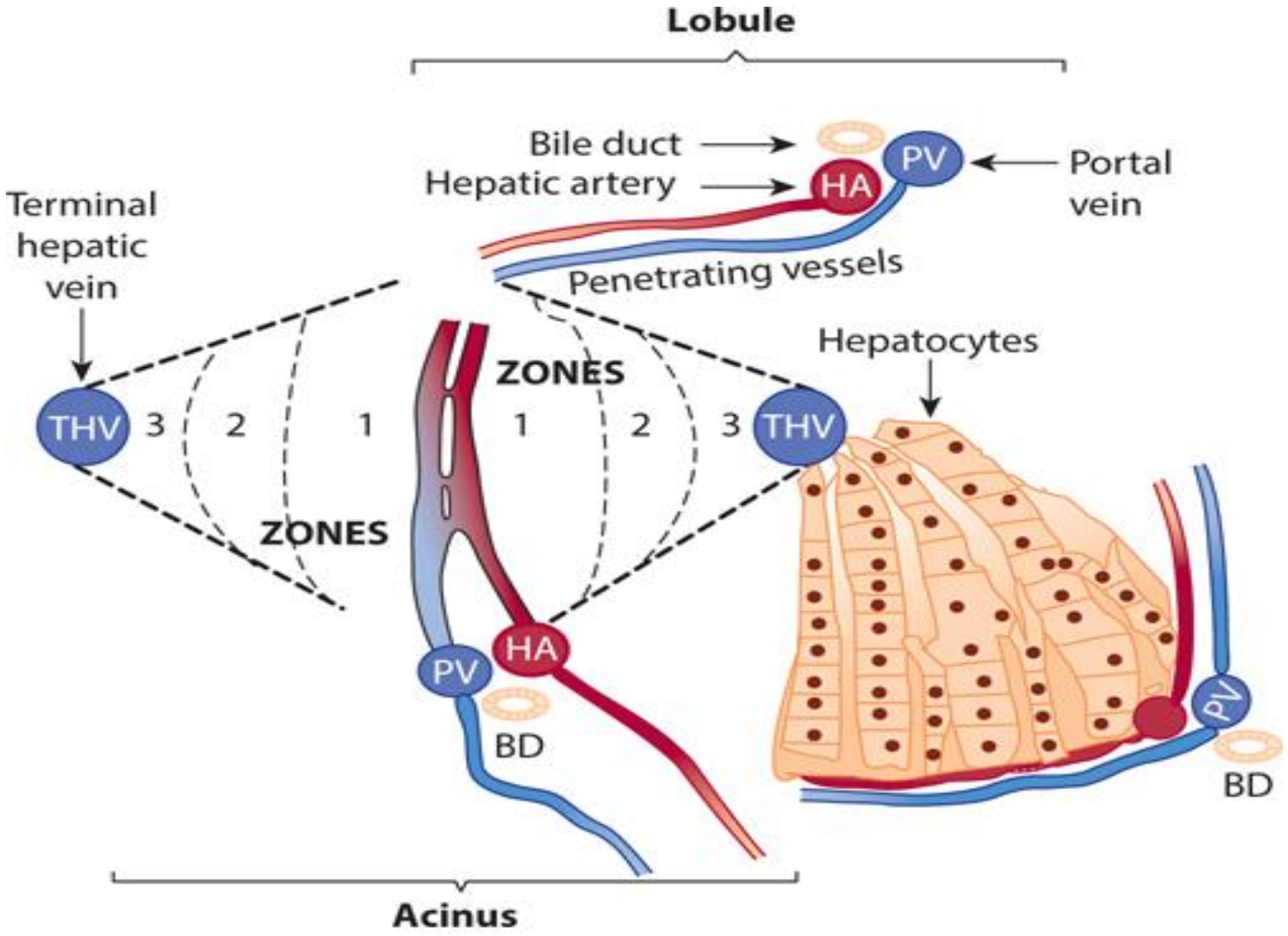


- The acinus is a diamond – shaped mass of liver parenchyma from 2 adjacent hepatic lobules.

- It is subdivided into 3 zones;

- Zone 1 cells form the most active core of the acinus and are the last to die and the first to regenerate.

- Zone 3 cells are the most prone to toxic, viral injury.



Source: Curtis D. Klaassen, John B. Watkins III: *Casarett & Doull's Essentials of Toxicology*, 3rd Edition: www.accesspharmacy.com

ULTRASTRUCTURE OF HEPATOCYTES

- Hepatocytes represent 94 % of liver parenchyma.
- Hepatocytes are covered by specific membranes which have 3 surfaces :

1) Sinusoidal (70 % of surface area) for exchange of material between the Disse space and intracellular compartment (endo and exocytose).

2) Canalicular membrane (15 %) for exchange with the biliary canaliculi.

3) Lateral membrane (15%) separated from neighboring hepatocytes by tight junctions and involved in intercellular transport between hepatocytes.

- Mitochondria account for 17% of the cell volume with about 2200 per hepatocyte (highly metabolic cells).

- The hepatocytes in zone 1 have more mitochondria whereas the zone 3 hepatocytes have fewer mitochondria.

- Peroxisomes are 1 to 2% of the hepatocyte volume and are vital in hydrogen peroxide metabolism.

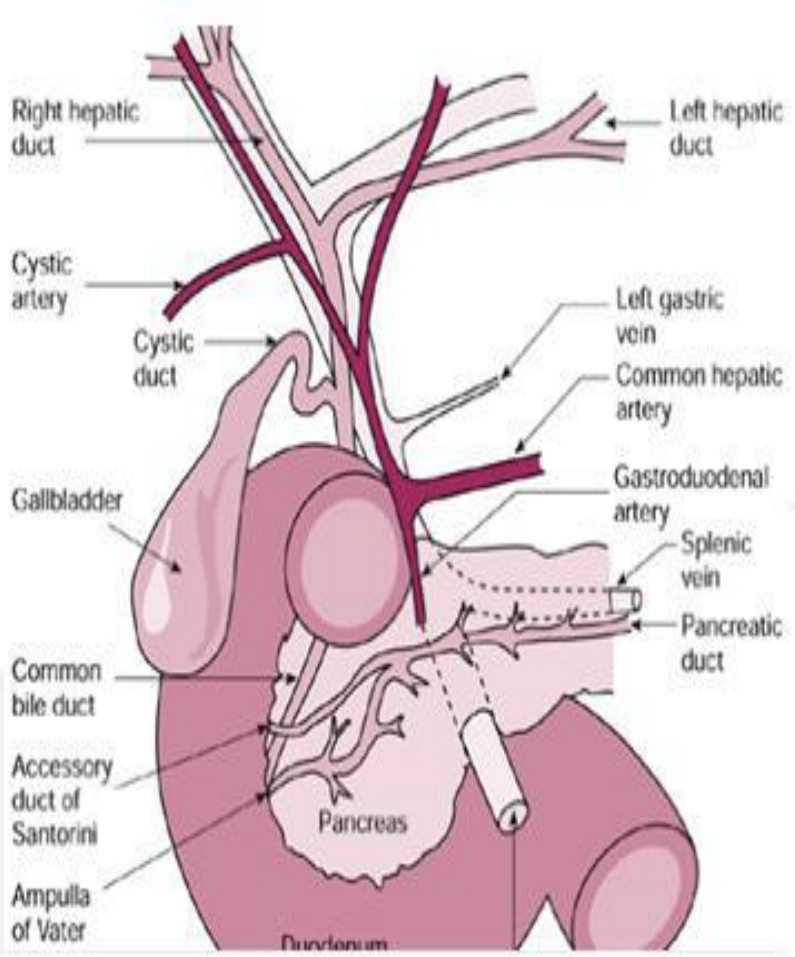
- Peroxisomes are more numerous in zone 3 and play an important role in oxidation of fatty acids and detoxification.

- Also hepatocytes contains;
- Lysosomes are electrondense cytoplasmic organelles responsible for degrading biological material using acid hydrolases.
- The endoplasmic reticulum constitutes 19% of the cell volume and is the site of protein synthesis.
- The Golgi apparatus.

BILIARY SYSTEM

- Bile secreted through the canalicular membrane of the hepatocyte collects in biliary canaliculi.

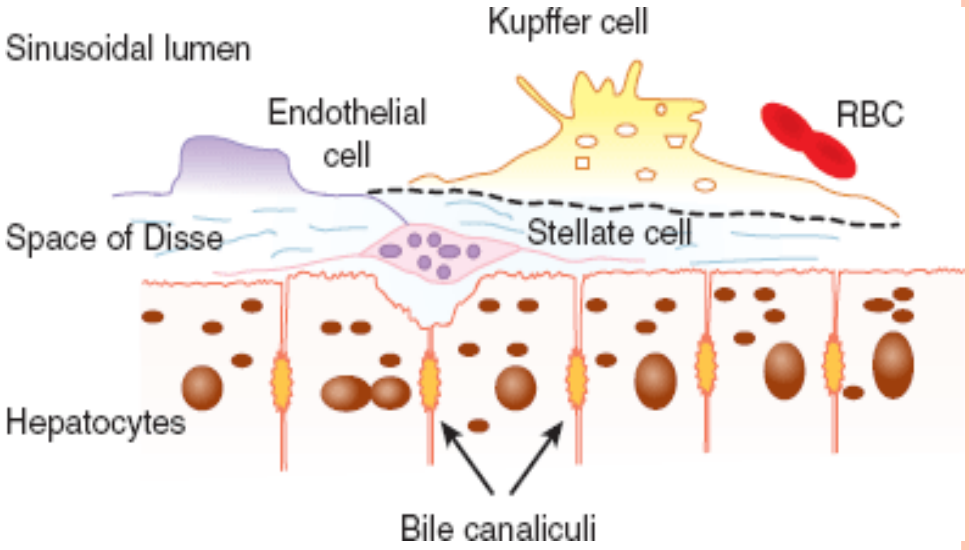
- These small biliary canaliculi form channels continuous with the short duct of Hering that join the cholangioles.
These cholangioles then merge into larger bile ducts.



HEPATIC VASCULAR SYSTEM

- The liver receives about 1.5 L blood / minute from 2 sources;
- The portal vein is formed by the confluence of the superior mesenteric vein and the splenic veins
- The hepatic artery arises from the coeliac trunk
- These vessels pour their blood into the sinusoids which drain into central veins and these coalesce forming hepatic veins which drain into the inferior vena cava.

BLOOD SINUSOIDS



Liver Sinusoidal cells

- Sinusoids are specialized capillaries without a basement membrane and lined with endothelial lining cells through which proteins of low molecular weight may percolate into the space of Disse.
- The sinusoidal endothelial cells lack a basement membrane and are perforated by abundant small fenestrae (average diameter 100 nm) in clusters called sieve plates.

Hepatic sinusoid lining cells

There are 4 types of hepatic sinusoid lining cells.

They make up 6 % of all liver Parenchyma. They include endothelial cells,

- Kupffer cells, hepatic stellate cells (Ito cells, fat storing cells), and pit cells (intrahepatic lymphocytes).

KUPFFER CELLS

- These cells represent part of the mononuclear phagocyte system and are adherent to the sinusoidal surface of endothelial lining cells, predominantly in a periportal distribution.
- 2 % of the total liver parenchyma cells.
- Their main function is to phagocytose a range of particulate material including cellular debris,senescent red blood cells, parasites, bacteria, endotoxin, and tumour cells.
- They secrete 10 % of erythropoietin hormone.

Hepatic stellate cells

- Stellate cells (Ito cells, fat storing cells) have a similar morphology to fibroblasts with the addition of fat droplets, and are located within the Disse space.
- These cells contain most of the body's stores of vitamin A.
- These cells are central to the process of hepatic fibrogenesis, responding to mediators released by parenchymal and Kupffer cells, causing transformation into myofibroblasts.
- Activation of stellate cells is also an important mechanism for control of sinusoidal perfusion, through cytoskeletal actin within branching cellular processes beneath the endothelium.

Pit cells

- Pit cells are large granular lymphocytes which

have natural killer cell properties with spontaneous activity against tumour cells in the absence of prior activation.

- They may also play a role in hepatic regeneration

LYMPHATICS

- The liver has a high blood flow and a highly permeable microcirculation. The consequent production of interstitial fluid, intrahepatic lymph, is formed in the perisinusoidal space of Disse between the hepatocytes and sinusoidal lining endothelium.
- Lymphatic vessels drain via the portal tracts, closely applied to the hepatic arterial branches, to the hilum and thence to the thoracic duct.
- Some interstitial fluid drains through Glisson's capsule into the peritoneum.
- The lymph flow rate in mammalian liver is approximately 0.5 ml/kg of liver per minute making up 25 to 50 per cent of thoracic duct lymph flow.

Hepatic blood flow

- Hepatic blood flow is about 1500 ml blood / minute
- It increases after feeding and with expiration.
- It decreases with standing, inspiration, and sleep.
- **Regulation of HBF:**
- **A) Autoregulation:**
- The portal venous system is passive, without pressure dependent autoregulation, and the major physiological factors controlling flow are those modulating supply to the intestines and spleen.
- Vascular autoregulation of hepatic arterial blood flow mediated by adenosine is present.

Hepatic blood flow

- **Autoregulation:**

- Changes in hepatic oxygen consumption do not seem to control hepatic blood flow.

- There is an important reciprocity between portal venous and hepatic arterial flow with a reduction in portal venous input being associated with significant compensatory decrease in hepatic arterial resistance and rise in arterial flow.

- **B) Nervous regulation :**
- Sympathetic nerve stimulation may reduce hepatic blood volume by up to 50 per cent.

SINUSOIDAL PERFUSION

- Blood pressure in sinusoids ranges from 4.8 to 1.7 mmHg, with flows of 270 to 410 ml/s.
- The unidirectional sinusoidal flow can be controlled for by either passive (haemodynamic) or active mechanisms;
- **Passive control mechanisms include:**

(i) the arterial input pressure and flow at the level of the arterio sinous twig at the origin of the sinusoid; and

(ii) changes in right atrial pressure, central venous pressure, and hepatic venous pressure that are transmitted to the sinusoid from the centrilobular veins.

SINUSOIDAL PERFUSION

- **Active control mechanisms include:**

(i) the presence of ‘functional’ sphincters at the inlet and outlet of the sinusoid due to indentations by the cell bodies of sinusoidal lining cells, which under different physiological stimuli may change dimension and alter sinusoidal perfusion.

(ii) plugging by leucocytes, which are less compressible than erythrocytes and may under physiological stimuli adhere to endothelial lining cells.

(iii) activation of Kupffer cells within sinusoids and release of other vasoactive mediators including nitric oxide, cytokines, and prostanoids.

(iv) transformation of hepatic stellate cells into activated contractile myofibroblasts that constrict the sinusoidal lumen.