Physiology of the liver

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General information

- The largest organ in the body
- 1200-1500g
- 1/50 TBW (1/18 TBW in children-LLL)
- HBF 1.5l/min (25% CO)
- Right lobe (RL):LL=6:1
- A double blood supply: Portal vein (70%) and Hepatic artery (30%)
- Nerve plexus-fibres from the sympathetic ganglia T7-T10, R&L vagi & phrenic nerve
- Lymphatic vessels: glands around porta hepatis, coeliac glands, diaphragm, mediastinal, thoracic VC
- The liver is completely covered with peritoneum and is kept in position with peritoneal ligaments and intra-abdominal pressure
Functional anatomy
Based on vascular and biliary anatomical landmarks

The right & left side are independent

Three plains divide liver into four sectors.

Further subdivision into segments

Hepatic and portal veins are interwined as the fingers of two hands

Coiunaud C. Etudes Anatomiques et Chirurgicales, 1957
Microanatomy

Lobule introduced by Kiernan in 1833

Hexagonal in shape

Central: tributary of the hepatic vein

Peripheral: a triad of branches of the hepatic artery, the portal vein, bile duct

The terminal branches of portal vein discharge their blood into the sinusoids and the direction of blood flow is determined by the higher pressure in the portal vein.
Portal tracts

Small connective tissue island containing triads:
P-portal vein
A-Hepatic artery
B-Bile duct

Portal vein saturation ($S_{pv}O_2$) is 85%-70% from hepatic artery

Hepatic Artery Buffer Response (HABR) is attenuated by: halothane and enflurane, minimally by sevoflurane and desflurane, not affected by isoflurane and iv anaesthetics
funcional unit Acinus-diagram


Zone 1: portal vein branch
hepatic artery
bile duct
Core from which regeneration proceed

Zone 3: hepatic veins
Suffers most from injury (viral, toxic or anoxic)
Nucleus

Chromatin

Nucleoli
Mitochondria

Double membrane

**Energy provided processes** (oxidative phosphorylation)

Many enzymes
- Citric acid cycle
- Oxidation of fatty acids
- ADP production
- Haem synthesis
Rough endoplasmatic reticulum (RER)

They synthetize:

1. Proteins: album, clotting factors and enzymes

2. Lipids: Tryglycerides from fatty acids

3. Carbohydrates: Glycogenesis, Glucose-6-phosphates

3a. Lipoproteins
Smooth endoplasmatic reticulum (SER) and peroxisomes

SER:
Bilirubin conjugation
Detoxification of many drugs and other foreign compounds (P450 system)
Synthesis of steroids, cholesterol and primary bile acids

Increased by enzyme inducers such as phenobarbital

Peroxisomes:
Complex catabolic and biosyntetic role
Enzymes include simple oxydases, beta-oxydation cycles, the glyoxalate cycle, lipid synthesis, cholesterol biosynthesis
Lysosome and

Golgi apparatus

**Lysosome** contain *hydrolytic* enzymes which, if released, could destroy the cell.

They are site of *deposition* of ferritin, lipofuscin, bile pigment, cooper and senescent organelles.

**Golgi apparatus** is regarded as a *packaging* site before excretion into the bile.

Both are *sequestering* any material that is ingested and has to be excreted, secreted or stored.

They are concerned in cholestasis.
Sinusoidal cells

Endothelial, Kupffer, stellate &pit cells

They interact via cytokines

Disse’s space contains tissue fluid which flows into lymphatics.

Endothelial cells act as a filter between sinusoidal blood and plasma within a space of Disse

Endocytosis:
Transferrin
Caeruloplasmin
HDL
LDL, VLDL
Hepatic lipase

Fenestrae size can change with alcohol, nicotine, serotonin, endotoxin and partial hepatectomy.
Kupffer cells

Responsible for removing old and damaged blood cells, bacteria, viruses, parasites & tumour cells

Activated by endotoxins, sepsis, shock, interferons & TNF

When activated, they produce cytokines, nitric oxide, TNF, interleukin (IL) IL1, IL6, IL10, interferon alpha and beta, and prostaglandins

They act alone or they stimulate other events in cytokine cascade, but also increase discomfort and sickness
Hepatic stellate cells

Fat storing cells, lipocytes, Ito cells

Long cytoplasmatic extensions, some in close contact with parenchymal cells, other reaching several sinusoids, where they may regulate blood flow and influence portal hypertension

Contain lipid droplets

With hepatic injury, they loose lipid droplets, proliferate, migrate to zone 3, Change to myofibroblast like phenotype and produce collagen

Collagenization of the space of Disse results in decreased access to protein-bound substrates to the hepatocyte
Functional units

60% hepatocytes
No basement membrane
No oncotic gradient:

- Raised CVP
- Parenchymal oedema
- Increased lymph production
- Exacerbation of ascites
- Reduced hepatic perfusion

The functional units are a low pressure system<6mmHg + IVC60
Liver functions

- Synthesis
- Metabolism
- Storage
Synthesis

- Carrier/modulator proteins such as albumin, complement, coagulation factors, transferrin, ceruloplasmin, thyroid-binding globulin, haptoglobin, globulins & alpha-1-antitripsin
- Enzymes, ie pseudochocholinesterase
- Bile acids
- Lymph (50%)
- Erythropoiesis, mainly in the foetus
Metabolism

- Carbohydrate, protein, lipids
- Bilirubin via conjugation
- Hormones (cortisol, oestrogens, vasopressin, aldosterone, thyroxine)
- Drugs via oxidation, reduction, hydrolysis, methylation, acetylation and conjugation
- Old erythrocytes
- Antigens and bacteria
Storage

• Glycogen

• Vitamins A, D, K, B12 and folate

• Blood—approximately 10-15% of the total blood volume
Hepatocyte death and regeneration

Death
- Apoptosis (‘suicide’)
  - organelles viable
  - fragmented nucleus and DNA
  - fragmented cell (apoptotic body)
  - no inflammation

Necrosis (‘murder’)
- organelles non-viable
- pyknotic chromatin
- lysis of cell membrane
- inflammation

Regeneration
- Primers
- Growth factors

Hepatocytes
- Stem cells
- Oval cells
- Bone marrow cells
Summary

• Liver is the largest organ in our body
• It has synthetic and metabolic function and acts as a storage
• There is no membrane between sinusoids and liver cells-CVP is transmitted into the liver
• Liver has significant regenerative function
• Liver function can compensate for a long time but ..