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
Haemodynamic changes induced by hepatic vascular occlusion techniques.
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Was ist “ALPPS”?

Schritt 1: Portalvenenligatur + in situ split

1 week

>30% of total liver

Schritt 2: Hypertrophie des Leberrests

Entfernung des deportalisierten Lappens

Associating Liver Partition and Portal Vein Ligation for Staged Hepatectomy

Clavien Ann Surg 2012
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Portal vein thrombosis
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**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
**Nucleus**

- Chromatin
- Nucleoli
Mitochondria

Double membrane

Energy provided processes (oxidative phosphorylation)

Many enzymes
  Citric acid cycle
  Oxidation of fatty acids
  ADP production
  Haem synthesys
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 biosynthetic 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
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, i.e. pseudocholinesterase
- Bile acids
- Lymph (50%)
- Erythropoiesis, mainly in the foetus
Metabolism

• Carbohydrate, protein, lipids
• Bilirubin via conjugation
• Hormones (cortisol, oestrogens, vasopressin, aldosteron, 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 ..
• Thank you for your attention

• Questions?
Please follow this link:

https://www.surveymonkey.com/r/NRBK9V7