

Liver functions, anatomy and diseases



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Introduction

The Anatomy and function of the Liver

Anatomy is the science of the structure and shape of entities. It is important for the knowledge of hepatic anatomy and surgery.

The liver is one of the largest organs of the human body – after the skin it is the second largest. The liver is the largest gland in the human body, with an average weight of 1500g. The transverse measurements ranges between 20 and 22, 5cm, its vertical measurements (close to its right/lateral surface) between 15 and 17, 5cm and its antero-posterior diameter between 10 and 12, 5cm. Its measurement, from opposite the vertebral column, is reduced to roughly 7, 5cm. It is found underneath the diaphragm -in the right upper abdomen, mid abdomen as well as in parts of the left upper abdomen.

The shape of the liver generally has the form of a wedge or a prism. According to Synnington the shape resembles that of a “ right-angled triangular prism with the right angle rounded off.” Its base faces the right and its apex to the left, the colour of the liver is dark reddish brown it has a soft degree of density, it contains a large amount of vessels and is very brittle .

In an adult, it is smaller than in a fetus. In the later (side) it contributes roughly one thirty-six of the body weight. In the former (side) it contributes roughly one-eighteenth of the body weight.

The liver has three surfaces namely the superior (Facies superior), inferior (Facies inferior/ visceral surface) and posterior (Facies posterior). The posterior surface is divided from the superior surface by a sharp margin. The superior surface attaches itself to the diaphragm as well as the anterior abdominal by the falciform ligament (ligamentum falciform hepatis). The falciform ligament separates the liver into a right lobe (lobus hepatis dexter) and a left lobe (lobus hepatis sinister). The right lobe is larger than the left. Five fossae divide the inferior and posterior surfaces into four lobes. The fossae are arranged like the letter "H". The left limb of the H is divided into what is known as the left sagittal fossa (fossa sagittalis sinistra/longitudinal fissure) consisting off the fossa of the umbilical vein and the fossa for the ductus venosus. The right limb of the H consists of the fossa for the gall-bladder (fossa vesicæ felleæ) and the fossa for the inferior vena cava (fossa venæ cavæ). The two limbs of the H surfs as a transverse fissure- the porta (porta hepatis/transverse fissure).

The superior surface is part of is part of the left and right lobe. This surface is convex. The middle part is found behind the xiphoid process and it makes contact with the abdominal wall. It is entirely concealed by peritoneum, with the exception of the line of attachment of the flaciform ligament.

The inferior surface is concave. It is aimed downward, backward as well as to the left. The surface is infused in peritoneum- the only parts that are without it, is where the gall-bladder and the liver attaches as well as at the porta hepatis.

The posterior surface has a curved surface and is broad on the right, but narrow on the left.

The diaphragm is attached with a triangular and coronary ligament that intertwine connective tissue, it leads to the intimate connection of the inferior vena cava that is connected with hepatic veins that holds up the posterior part of the liver. The abdominal viscera fill the abdomen, where the muscular walls are in a state of tonic contraction.

The superior surface of the liver fits under the diaphragm surface, so that the pressure is enough to hold the diaphragm. The lax falciform ligament creates no support for the lateral displacement and the latter creates negative pressure that is held up in the thorax

(Gray, Henry. Anatomy of the Human Body. PHILADELPHIA: Lea & Febiger, 1918; Bartleby. com, 2000. www.bartleby.com/107/. [DATE of Printout].)

Functions of the liver

The liver receives blood from two main sources: 30% is received from the hepatic arteries and 70% is received from the hepatic portal vein. The hepatic portal vein receives blood from the stomach, intestines, pancreas and spleen; which is then carried to the liver through the porta hepatis.

All nutrients are absorbed by the small intestine, all nutrients reaches the liver by this route except for lipids. Arterial blood bound for the liver exists the aorta and the celiac trunk. These arteries deliver oxygen and other materials to the liver. (SALADIN, p. 975-977)

Digestion

Liver produces bile; which is a mixture of water, bile salts, cholesterol and pigments of bilirubin. Bile is produced by hepatocytes in the liver. Bile passes through the bile ducts and is stored in the gallbladder. Fats are emulsified by bile. Large fat clumps are turned into smaller pieces which makes it easy for the body to digest. Old worn out red blood cells are destroyed by Kupffer cells in the liver. Kupffer cells pass their components to the hepatocytes. Haemoglobin is the red oxygen-carrying pigment of red blood cells, haemoglobin is metabolized into heme and globin components. Energy for the body comes from globin protein.

Metabolism

Liver is responsible for metabolizing carbohydrates, lipids and proteins into biologically useful materials. Blood entering the liver through the hepatic portal vein is rich in glucose from digested food. Some of this glucose is absorbed by hepatocytes. The glucose is stored as the macromolecule glycogen. Homeostasis is maintained by the absorption and release of glucose by the hepatocytes, it helps protect the body from spikes and drops that can be dangerous in the blood glucose level. Hepatocytes absorb and metabolise fatty acids to produce energy in the form of ATP. Through gluconeogenesis the hepatocytes convert glycerol and other lipid components into glucose. Cholesterol is a lipid which can also be produced by hepatocytes and gets excreted from the body as a component of bile. Amino acids is a component from dietary proteins. Amine groups are removed from the amino acids, by the hepatocytes, which is further

converted into ammonia and urea. Urea can be excreted in urine as a waste product. Urea is less toxic than ammonia.

Detoxification

Hepatocytes cells of the liver monitor the contents of the blood and toxic substances are removed before they reach the rest of the body. Alcohol and drugs are metabolised into their inactive metabolites by the enzymes in hepatocytes cells.

Storage

Nutrients, vitamins and minerals obtained from the blood passing through the hepatic portal system are stored in the liver. Homeostasis of blood glucose is maintained by the storage of nutrients. Vitamins such as A, D, E, K and B12 is stored in the liver. Minerals such as iron and copper are stored in the liver.

Production

Vital protein components of blood plasma such as prothrombin, fibrinogen and albumins are produced by the liver. Prothrombin and fibrinogen proteins are factors involved in the formation of blood clots. Albumins maintain the isotonic environment of blood.

Immunity

Bacteria, fungi, parasites, worn out red blood cells and cellular debris are captured and digested by Kupffer cells. Large volumes of blood are cleaned very quickly by Kupffer cells due to the large volumes of blood passing through the hepatic portal system.

(www.innerbody.com/image_digeov/card10-new2.html)

American journal of Physiology: Gastrointestinal and Liver Physiology :
physiology and pathophysiology of apoptosis in epithelial cells of the liver;
pancreas and intestine. By Blake. A. Jones ; Gregory. J. Gores.

Published 1 December 1997 (vol. 273. no. 6, G1174-G1188)

Definition and description of the disease

Fatty liver disease

“ Non-alcoholic fatty liver disease (NAFLD) is a clinical and pathological syndrome.” (Zeng, et al., 2008) The main feature of NAFLD is the swelling of the (liver cells) hepatocytes because of pathological factor, alcohol excluded, that injure the liver. NAFLD is ranged from fatty liver alone to steatohepatitis, steatonecrosis and non-alcoholic steatohepatitis (NASH). (NASH) is only a stage in non-alcoholic fatty liver disease. NAFLD may have the potential to progress into cirrhosis and liver failure.” Liver -biopsy features include steatosis, mixed inflammatory cell-infiltration, hepatocytes ballooning and necrosis, glycogen nuclei, Mallory’s hyaline and fibrosis.” (Angulo, 2002)

According to Jansen (2004) NASH is an under diagnosed liver disease characterized by steatosis, necroinflammation and fibrosis. NASH can possibly develop into cirrhosis and hepatic cellular carcinoma. NASH incorporate mixed acute and chronic lobular inflammation, zone 3 perisinusoidal fibrosis and ballooning (Brunt, et al., 1999).

Alcoholic liver disease.

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Alcoholic liver disease (ALD) includes a variety of spectrum of injury that can be from simple steatosis to frank cirrhosis. There are 3 groups of histological stages of ADL. Fatty liver or simple steatosis, alcoholic hepatitis and chronic hepatitis with hepatic fibrosis or cirrhosis. ALD can be caused by different types of factors including dose, duration and type of alcohol consumption and risk factors like obesity iron overload ect.

Fatty Liver Disease Symptoms

Non-alcoholic fatty liver disease causes no signs or symptoms that can be noticed but when it is noticed, it show signs of:

Fatigue Pain in the right upper abdomen Weight loss. Inflammation and scarring of the liver Possible progression to liver failure.

Symptoms consists of four (4) stages namely Simple fatty liver disease (steatosis), Non-alcoholic Fatty liver Disease (NAFLD), Fibrosis And Cirrhosis.

1. Simple fatty liver (Steatosis)- There are no clear symptoms and it can only be discovered by an abnormal blood test result.
2. Non-alcoholic Steatohepatitis (NASH)- It is the most aggressive form of this condition, it causes the liver to become inflamed creating a dull or aching pain in the top right abdomen, covering the lower side of the ribs. There may be no signs of any symptoms at all and it can only be discovered by specialized testing.
3. Fibrosis- Constant inflammation in the liver which leads to the formation of scar tissue.

4. Cirrhosis- Over a long period of time, it creates inflammation which can lead to the loss of liver function- which may lead to creating primary cancer.

ALCOHOL-RELATED (ARLD)

It shows no symptoms until the liver has already been severely damaged and it causes symptoms such as: Feeling sick, weak or tired Loss of weight Loss of appetite Jaundice- the yellowing of the eyes and skin The swelling of the stomach and ankles Confusion or drowsiness The excretion or the vomiting of blood.

Alcohol related fatty liver disease is constantly diagnosed because of other conditions or other tests.

PATHOPHYSIOLOGY AND ETIOLOGY OF FATTY LIVER DISEASES:

Fatty Liver Disease encompasses two over head segments, namely Alcoholic Liver Disease and Non Alcoholic Liver Disease.

ALCOHOLIC LIVER DISEASE (ALD)

Alcoholic Liver Disease (ALD) encompasses the manifestations of the liver that is caused by the over consumption of alcohol (ethanol). It includes Fatty Liver, Alcoholic Hepatitis, and Chronic Hepatitis with liver cell fibrosis or cirrhosis.*1

Ethanol metabolization takes place in the liver. There are two main pathways of alcohol metabolism, namely alcohol dehydrogenase and cytochrome P-450 (CYP) 2 E1. The first pathway works as follows: Firstly ethanol is

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metabolized by Alcohol dehydrogenase (ADH) into Acetaldehyde in the cytoplasm. The second phase occurs in the smooth Endoplasmic reticulum of mitochondria, where Acetaldehyde is further metabolized by Aldehyde dehydrogenase into acetate. Acetate is then finally oxidized into carbon dioxide (CO₂) and water. CYP 2E1 also converts ethanol into acetaldehyde (O'Shea, et al., 2010).

Liver damage occurs in a few mutually related pathways:

“ Acetaldehyde can form hybrid-adducts with reactive residues acting on proteins or small molecules, mediating lipid peroxidation and nucleic acid oxidation.” (French, et al., 1984)

During further metabolization of alcohol, Nicotinamide Adenine Dinucleotide (NAD) is reduced. This causes a shift in the NADH/NAD ratio. A higher NADH (reduced form of NAD) concentration increases the production of fatty acids, while lower concentrations of NAD result in decreased fatty acid oxidation. This altered ratio impair the metabolization of carbohydrates and lipids, resulting in the diversion from gluconeogenesis to ketogenesis and fatty acid synthesis. The liver cells compound the fatty acids to glycerol to form triglycerides. These accumulating triglycerides result in fatty liver. This leads to oxidative stress, which plays a pivotal role in ALD development. (French, et al., 1984)

Furthermore, Acetaldehyde interacts through covalent binding with reactive residues of proteins found on the membranes of liver cells. This binding results in the formation of stable protein by-products which have been shown to be immunogenic. Tissue damage and ALD may be caused by this, because <https://assignbuster.com/liver-functions-anatomy-and-diseases/>

the neo-antigens may induce an immune reaction with anti-body production. CYP 2 E 1, when exposed to chronicle alcohol use generates free radicals through the oxidation of Nicotinamide Adenine Dinucleotide phosphate (NADPH) to NADP (O'Shea, et al., 2010). This exposure activates hepatic macrophages, also known as Kupffer cells, which leads to Tumor Necrosis factor-alpha (TNF-alpha). The production of reactive oxygen species (ROS) is increased by the mitochondria, which in turn was induced by the TNF-alpha. This also promotes oxidative stress, which leads to hepatocytes necrosis and apoptosis. Many alcoholics have a condition of malnutrition. The deficiency in anti-oxidants, such as vitamin E, only worsens the necrosis and apoptosis. Free radicals initiate the oxidative degradation of lipids, which causes inflammation and liver tissue becomes scarred.

Although the over consumption of alcohol is the primary cause of ADL, it is not always a pre-requirement for ALD development. It is important to understand the mechanisms of liver damage. When liver cells are exposed to alcohol, ATP synthesis is reduced and the activity of mitochondrial complexes is depressed. This causes energy metabolism of liver cells to be severely weaker and results in tissue damage.

Metabolization of ethanol takes place in the centrilobular area of the liver lobule. Hypoxia alters energy metabolism, therefore centrilobular hypoxia can also be responsible for liver injury.

The pathophysiology of alcoholic liver disease is very complex and further in depth investigation to understand the disease and how to treat it is being done.

NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD)

Non-Alcoholic Fatty Liver Disease is an over arching term for a variety of conditions associated with fat depositions in liver cells. NAFLD ranges from Simple fatty liver to nonalcoholic steatohepatitis (NASH), to fibrosis and cirrhosis.

The first stage of NAFLD is simple fatty liver or steatosis. It is considered harmless and only consists of a fat build up in the liver.

The second stage, Nonalcoholic steatohepatitis is more serious, but not many individuals progress to this state from simple fatty liver.

Two liver insults may lead to the development of NASH. With the first insult or “ hit”, macro-vesicular steatosis (abnormal retention of lipids within a cell) occurs as a result of an excessive amount of triglycerides accumulating in the liver. The cause of triglyceride accumulation can result from excessive importation of free fatty acids from adipose tissue.*5

The accumulating lipids in the liver cells seem to be caused by insulin resistance. Insulin resistance leads to changes in the liver’s enzymatic pathways that control free fatty acid uptake, synthesis, degradation and the secretion of free fatty acids. A crucial paradox arises: the liver maintains its liver lipid metabolism, but carbohydrate metabolism is weakened or damaged. Hepatic steatosis caused by these factors can result into diminished hepatic free fatty acid oxidation, more hepatic lipogenesis or fewer lipids are secreted from the liver. Along with insulin resistance, obesity plays an important role in the development of NAFLD.

These alterations make the liver sensitive for the second insult or “ hit”, which is an inflammatory response and further liver damage (Carey, et al., 2013). Toxic inflammatory proteins are secreted by the cytokines in the liver.*6 Hepatocyte apoptosis, an organized form of cellular death, is a leading component of the second insult of NAFLD progression.

Oxidative stress and resulting lipid peroxidation are involved in the progression of NAFLD to NASH. “ The term “ oxidative stress” is frequently used to describe the imbalances in redox couples.” *7 This metabolic reaction produce too much reactive free radicals called reactive oxygen species (ROS). This process usually occurs in the mitochondria. Lipid peroxidation can lead to changes in the cell membrane fluidity and these alterations cause tissue damage.

Fibrosis is the third stage of NAFLD. NASH develops to form fibrosis if it is not treated. Fibrosis occurs where chronicle inflammation in the liver results in the formation of fibrous scar tissue around hepatic cells and blood vessels. The liver still functions normally, because there is still enough healthy tissue.

The forth and most severe stage of NAFLD is cirrhosis. During this stage lots of scar tissue develops. This causes the liver to shrink and change morphologically. The damage caused by cirrhosis is permanent and cannot be saved or reversed. The progression of cirrhosis is slow, but it ultimately causes the liver to stop functioning.*8

Treatment and prevention

1. Basic therapy: you have to work out a strategic plan of the intake of calories and adjustment of diet constitution. Medium aerobic exercise and the changing of some life styles and behaviour.
2. Weight reduction: The most important fact of weigh reduction is not the amount of weight loss but how the weight is lost. Losing weight rapidly may increase portal inflammation and fibrosis. A relatively safe goal is to lose about 1. 6kg per week.
3. Liver transplantation: For some patients liver transplantation is recommended. Metabolic states should be examined before the transplantation. A BMI > 40kg/m² is a contraindication (Zeng, et al., 2008)
4. Abstinence: This is a very important therapeutic intervention for patients that have ALD. Abstinence helps to decrease portal pressure and lower progression to cirrhosis.