**Physiology of the liver**

Ozougwu, Jevas C. Ph.D

Physiology and Biomedical Research unit, Department of Biological Sciences, College of Basic and Applied Sciences, Rhema University, Nigeria.

*Corresponding Author: Ozougwu, Jevas C, Physiology and Biomedical Research unit, Department of Biological Sciences, College of Basic and Applied Sciences, Rhema University, Nigeria.

**ABSTRACT**

In this paper the functions of the liver was summarized which includes firstly, Secretion of bile, the liver assists intestinal digestion by secreting 700 to 1200 ml of bile per day. Bile is an alkaline, bitter-tasting, yellowish green fluid that contains bile salts (conjugated bile acids), cholesterol, bilirubin (a pigment), electrolytes and water. It is formed by hepatocytes and secreted into the canaliculi. Bile salts, which are conjugated bile acids, are required for the intestinal emulsification and absorption of fats. Secondly, Metabolism of bilirubin which is a byproduct of destruction of aged red blood cells and gives bile a greenish black color and produces the yellow tinge of jaundice. Also Vascular and hematologic functions,because of its extensive vascular network, the liver can store a large volume of blood. The amount stored at anyone duration depends on pressure relationships in the arteries and veins. Moreover, the liver has hemostatic functions, It synthesizes prothrombin, fibrinogen, and clotting factors. Vitamin K, a fat-soluble vitamin, is essential for the synthesis of other clotting factors. Because bile salts are needed for reabsorption of fats, vitamin K absorption depends on adequate bile production in the liver. Furthermore Metabolism of nutrients, the liver plays essential roles in the metabolism of fat, protein and carbohydrates. Also, Metabolic detoxification, the liver alters exogenous and endogenous chemicals (e.g. drugs), foreign molecules, and hormones to make them less toxic or less biologically active. This process, called metabolic detoxification, diminishes intestinal or renal tubular reabsorption of potentially toxic substances and facilitates their intestinal and renal excretion. In this way alcohol, barbiturates, amphetamines, steroids and hormones (including estrogens, aldosterone, antidiuretic hormone, and testosterone) are metabolized or detoxified, preventing excessive accumulation and adverse effects. Also, Storage of minerals and vitamins, the liver stores certain vitamins and minerals, including iron and copper, in periods of excessive intake and releases them in periods of need. The liver can store vitamins B₁₂ and D for several months and vitamin A for several years. The liver also stores vitamins E and K. Iron is stored in the liver as ferritin, an iron-protein complex and is released when needed for red blood cell production. Finally, the liver has immunologic functions as the liver contain cells involved in adaptive and innate immunity.

**Keywords:** Liver, Physiology, Functions, Lobule, Hepatocytes.

**INTRODUCTION**

The liver is the largest solid organ, the largest gland and one of the most vital organs that functions as a centre for metabolism of nutrients and excretion of waste metabolites [1]. Its primary function is to control the flow and safety of substances absorbed from the digestive system before distribution of these substances to the systemic circulatory system [2]. A total loss of liver function could leads to death within minutes, demonstrating the liver’s great importance [3], in view of this, this study was undertaken to review the physiology of the liver with a view to keep it functioning at its optimum and maintaining good health so as to avoid liver damages such as fatty liver, liver fibrosis and cirrhosis.

**Origin of the Liver**

The cells that will eventually make up the adult liver originated during embryogenesis from the ventral foregut definitive endoderm [4]. The different developmental stages of the liver involves establishment of competence for liver formation, after which liver specification, hepatic bud formation, growth and finally differentiation will occur [5]. During the development of the liver, as well as certain duration after partus, the metabolic profile of the young liver is far from that of the adult.
Phenotype. Prior to birth, and shortly thereafter, many metabolic changes occur in the liver [6]. These allow the organism to adapt to uptake of nutrients from food, but also change its ability to metabolize xenobiotics. As the organism matures, with duration an adult pattern of metabolic enzymes develops. During the development of the hepatocellular carcinoma, frequently the gene expression pattern of the hepatocytes reverts to a more fetal-like stage [7]. In certain cases this leads to the expression of metabolic enzymes otherwise found only during embryogenesis. This partly fetal-like expression pattern is also noticeable in many human hepatoma cell lines that are often used for *in vitro* toxicology studies.

**General Description of the Liver**

The liver weighs approximately 1500g and accounts for approximately 2.5% of adult body weight [8]. The surface of the liver is smooth and dome shaped, where it is related to the concavity of the inferior surface of the diaphragm. (Figure 1) The liver lies mainly in the right upper quadrant of the abdomen where it is hidden and protected by the thoracic cage and diaphragm. (Figure 1) The liver lies mainly in the right upper quadrant of the abdomen where it is hidden and protected by the thoracic cage and diaphragm. The normal liver lies deep to the ribs 7 – 11 on the right side and crosses the midline towards the left nipple [8]. [2] explained that the liver is divided into 4 lobes: right, left, caudate, and quadrate. The right and left lobes are the largest, while the caudate and quadrate are smaller and located posteriorly. Two ligaments are visible anteriorly. Superiorly, the falciform ligament separates the right and left lobes. Inferior to the falciform ligament is the round ligament, which protrudes from the liver slightly. Also visible anteriorly on the most inferior portion of the right lobe is the gallbladder. Posteriorly, many more interesting structures are visible. [2] reported that the caudate lobe is located superiorly, approximately between the right and left lobes. Adjacent to the caudate lobe is the sulcus for the inferior vena cava. Just inferior to the caudate lobe is the porta hepatis, where the hepatic artery and hepatic portal vein enter the liver. The portal vein carries nutrient laden blood from the digestive system. Inferior to the porta hepatis is the bile duct which leads back to the gallbladder. [2] also explained that the hepatic vein, where post-processed blood leaves the liver, is found inferior and adjacent to the sulcus for the inferior vena cava. The liver is held in place by a system of mesenteries posteriorly, and is also attached to the diaphragm via the falciform ligament. Additionally, most of the liver is covered by visceral peritoneum.

*Figure 1.* Diagram of the liver showing the right and left lobes and its posterior and anterior views. Source: Encyclopedia Britannica, 2010

**Histology of the Liver**

The basic functional unit of the liver is the liver lobule (Figure 2, Figure 3). A single lobule is about the size of a sesame seed and is roughly hexagonal in shape. [2] explained that the primary structures found in a liver lobule include:

- Plates of hepatocytes which forms the bulk of the lobule
- Portal triads at each corner of hexagon
- Central vein
- Liver sinusoids that run from the central vein to the portal triads
- Hepatic macrophages (Kupffer cells)
- Bile canaliculi (“little canals”) – formed between walls of adjacent hepatocytes
Physiology of the liver

- Space of Disse – a small space between the sinusoids and the hepatocytes

The portal triads consist of three vessels: a hepatic portal arteriole, a hepatic portal venule, and a bile duct. The blood from the arteriole and the venule both flow in the same direction – through the sinusoids toward the central vein, which eventually leads to the hepatic vein and the inferior vena cava. Secreted bile flows in the opposite direction – through the bile canaliculi away from the central vein, toward the portal triad, and exiting via the bile duct. As blood flows through the sinusoids and the space of disse toward the central vein, nutrients are processed and stored by the hepatocytes, and worn out blood cells and bacteria are engulfed by the Kupffer cells [2].

**Figure 2.** Cellular architecture of the liver. (A) The schematic shows an adult liver (red), with the gall bladder and extra hepatic ducts (green), in relation to the stomach and intestine (yellow). The extra hepatic duct system consists of the hepatic ducts (hd), which drain bile from the liver into the common hepatic duct (chd) to the gall bladder via the cystic duct (cd) and into the duodenum through the common bile duct (cbd). (B) A schematic of the cellular architecture of the liver showing the hepatocytes (pink) arranged in hepatic plates separated by sinusoid spaces radiating around a central vein. Bile canaliculi on the surface of adjoining hepatocytes drain bile into the bile ducts (green), which run parallel to portal veins (blue) and hepatic arteries (red) to form the “portal triad”.

**Source:** Zorn, 2013.

**Figure 3.** Diagram Showing Liver Lobules.

**Source:** [9]
The liver is the first site of passage for venous blood arriving from the intestines via vena porta [10]. The areas around the influx blood vessels are named periportal. The areas surrounding efflux blood vessels are the perivenous. The periportal area is highly complex and consists of a dense matrix containing collagen where afferent blood vessels are found, together with bile ducts, nerve and lymph [10]. Spaces within the matrix contain a variable cell population, such as fibroblasts, hematopoietic cells and inflammatory cells. Also found here are epithelial cells of the bile ducts, endothelial cells of the blood vessels, and smooth muscles of arteries and veins [11]. The liver lobule consists mainly of plates of hepatocytes and sinusoids, with a light matrix of collagen to form a network between the two. Kupffer cells, as well as fat storing stellate cells are found here. (Figure 4) These types of cells reside mainly in the tissue space between the hepatocyte and the sinusoids. Terminal bile ductules connect here to the bile canaliculi between hepatocystic plates [11]. The walls of the hepatic sinusoid are lined by three different cell types: the sinusoidal endothelial cells, kupffer cells and stellate cells. Additionally, pit cells, the liver specific natural killer (NK) T cells are often present in the sinusoidal lumen [12]. The main parenchymal mass is normally that of hepatocytes. In rat, the hepatocytes make up about 60 % of liver cell count and the remaining 40 %, non-parenchymal cells only make up for about 6 -7 % of the liver volume while the remaining volume of approximately 23 % is formed by extracellular spaces [13]. The liver is made up of many different cell types. Four main cell types will be discussed for the purpose of this paper, namely:

- Hepatocytes
- Endothelial cells
- Kupffer cells (liver resident macrophages)
- Stellate cells (liver fat storing cells). (Figure 5)

**Hepatocytes**

Hepatocytes represent 60 % of the liver’s cells and about 80 % of the liver’s total cell mass. Most of the liver’s synthetic and metabolic capabilities stem from the work of hepatocytes [2]. Hepatocytes are arranged in plates only a single cell thick [9]. (Figure 5) Blood flowing toward the hepatic vein within the space of Disse passes both exposed surface areas of the hepatocyte plates and toxins and nutrients within the blood are extracted by the hepatocytes. Hepatocytes are large and rich in organelles such as endoplasmic reticulum and Golgi apparatuses. They contain many and large mitochondria, as well as lysosomes and peroxisomes [14]. The main function of hepatocytes is to participate in lipid, carbohydrate and protein metabolism. They also produce serum proteins such as albumin and coagulation factors [15]. Furthermore, hepatocytes produce and secrete bile as well as detoxify and excrete cholesterol, steroid hormones and xenobiotic drugs. Numerous xenobiotics are metabolized by the mixed-functions of monooxidases found in hepatocytes [16]. Structure and function of the hepatocytes within the liver lobule differs greatly depending...
on proximity to periportal or perivenous areas. Periportal type of hepatocytes are often smaller, but have larger mitochondria, and a larger Golgi apparatus as compared to the perivenous type. Perivenous hepatocytes on the other hand have larger endoplasmic reticulum. Functionally, periportal hepatocytes are more involved in gluconeogenesis, while perivenous are involved in glycolysis [10]. Additionally, perivenous hepatocytes are dormant with respect to P 450-dependent hydroxylation reactions [17] and glutamine synthetase [18].

**Endothelial Cells**

The sinusoidal endothelial cells line the walls of the hepatic sinusoid and perform a function of filtration due to the presence of fenestrae [10]. (Figure 5) These cells also demonstrate large endocytic capacity for extracellular matrix components and immune complexes. In general they engulf smaller size particles and may play a role in clearance of viruses, but do not possess phagocytic function [19]. They may also function as antigen presenting cells and secrete certain cytokines and eicosanoids [12].

**Kupffer Cells**

The liver harbors large amounts of kupffer cells, which represent the largest tissue resident macrophage population of the body [20]. (Figure 5) They are located within the sinusoid and are in constant contact with gut-derived particles that lead to low but constant amount of activation of these monocyte derived cells. Upon activation they are able to secrete a vast range of inflammatory mediators such as cytokines, reactive oxygen species, eicosanoids and nitric oxide [12]. Kupffer cells have receptors that enable them to bind cells covered with immunoglobulins or bind to complement receptors and subsequently phagocytose cell [21]. Kupffer cells are even actively phagocytic in vitro and contain high levels of peroxidase, acid phosphatase and glucose 6-phosphate dehydrogenase [22].

**Stellate Cells**

The liver plays a central role in uptake and storage of vitamins A (Retinol) and stores about 95 % of retinoids found in the body. The fat storing perisinusoidal cells of the liver, stellate cells are the main vitamin A storing cells (Figure 5). They harbor large amounts of retinol and retinyl palmitate in lipid droplets within their cell cytoplasm [23]. They are located in the space of Disse (between hepatocytes and sinusoid) and generally protrude to come into contact with several sinusoids [23]. Additionally, they function to control the turnover of extracellular matrix and regulate sinusoid contractility. The stellate cells may become activated under stressful conditions and transformed into myofibroblast – like cells which play a key role in inflammatory fibrotic response [12]. When activated, stellate cells not only proliferate, but also produce increased amounts of extracellular matrix per cell. Transforming growth factor beta (TGF β) is one of the most important signals to activate stellate cells, which leads to a higher transcriptional rate of mRNAs coding for extracellular matrix components such as collagen I, fibronectin and proteoglycans [10]. Lipid peroxidation products are also an important stimulus, whose effect may be augmented in oxidative stress conditions [24].

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**Figure 5.** Diagram showing main cell types of Liver - hepatocytes, endothelial cells, Kupffer cells and Stellate cells. Source: Tissupath specialist pathway services, Retrieved 2017. www.Tissupath.com.au
Physiology of the liver

FUNCTIONS OF THE LIVER

The liver has numerous functions best grouped into secretion of bile, metabolism of bilirubin, vascular and hematologic functions, metabolism of nutrients, metabolic detoxification and storage of minerals and vitamins. (Table 1)

Table.1. Summary Of Major Functions Of The Liver

<table>
<thead>
<tr>
<th>Secretion of Bile</th>
<th>Metabolism of Bilirubin</th>
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<td>Metabolism of Nutrients</td>
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<td>Vascular and Hematologic Functions</td>
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<td>Metabolic Detoxification</td>
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<td>Storage of Minerals and Vitamins</td>
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<td>Endocrine functions</td>
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<td>Immunological/ Protective Functions</td>
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[25] and [8] explained the functions of the liver as follows:

Secretion of Bile

The liver assists intestinal digestion by secreting 700 to 1200 ml of bile per day. Bile is an alkaline, bitter-tasting, yellowish green fluid that contains bile salts (conjugated bile acids), cholesterol, bilirubin (a pigment), electrolytes and water. It is formed by hepatocytes and secreted into the canaliculi. Bile salts, which are conjugated bile acids, are required for the intestinal emulsification and absorption of fats. Having facilitated fat emulsification and absorption, most bile salts are actively absorbed in the terminal ileum and returned to the liver via the portal circulation for resecretion as follows:

- Bile has two fractional components: the acid-dependent fraction and the acid-independent fraction. Hepatocytes secrete the bile acid-dependent fraction of the bile. This fraction consists of bile acids, cholesterol, lecithin (a phospholipid), and bilirubin (a bile pigment). The bile acid-independent fraction of the bile, which is secreted by the hepatocytes and epithelial cells of the bile canaliculi, is a bicarbonate-rich aqueous fluid that gives bile its alkaline pH.

- Bile salts are conjugated in the liver from primary and secondary bile acids. The primary bile acids are cholic acid and chenodeoxycholic (chenic) acid. These acids are synthesized from cholesterol by the hepatocytes. The secondary bile acids are deoxycholic acid and lithocholic acid. These acids are formed in the small
intestine by the action of intestinal bacteria, after which they are absorbed and flow to the liver.

- Both forms of bile acids are conjugated with amino acids in the liver to form bile salts.
- Conjugation makes the bile acids more water soluble, thus restricting their diffusion from the duodenum and ileum.

Metabolism of Bilirubin

Bilirubin is a byproduct of destruction of aged red blood cells. It gives bile a greenish black color and produces the yellow tinge of jaundice.

- Aged red blood cells are taken up and destroyed by macrophages of the mononuclear phagocyte system, primarily in the spleen and liver (in the liver these macrophages are Kupffer cells). Within these cells hemoglobin is separated into its component parts—heme and globin. The globin component is further degraded into its constituent amino acids, which are recycled to form new protein. The heme moiety is converted to biliverdin by the enzymatic cleavage of iron. The iron attaches to transferrin in the plasma and can be stored in the liver or used by the bone marrow to make new red blood cells. The biliverdin is enzymatically converted to bilirubin in the macrophage of the mononuclear phagocytic system and then is released into the plasma. In the plasma, bilirubin binds to albumin and is known as unconjugated bilirubin or free bilirubin, which is lipid soluble.

- In the liver, unconjugated bilirubin moves from plasma in the sinusoids into the hepatocyte. Within hepatocytes, it joins with glucuronic acid to form conjugated bilirubin, which is water soluble. Conjugation transforms bilirubin from a lipid-soluble substance that can cross biologic membranes to water-soluble substance that can be excreted in the bile. When conjugated bilirubin reaches the distal ileum and colon, it is deconjugated by bacteria and converted to urobilinogen. Most of the urobilinogen is then excreted in the urine, and a small amount is eliminated in feaces.

Vascular and Hematologic Functions

Because of its extensive vascular network, the liver can store a large volume of blood. The amount stored at any one duration depends on pressure relationships in the arteries and veins.

- The liver can also release blood to maintain systemic circulatory volume in the event of hemorrhage.
- Kupffer cells in the sinusoids of the liver remove bacteria and foreign particles from the portal blood. Because the liver receives all of the venous blood from the gut and pancreas, the Kupffer cells play an important role in destroying intestinal bacteria and preventing infections.
- The liver also has hemostatic functions. It synthesizes prothrombin, fibrinogen, and clotting factors. Vitamin K, a fat-soluble vitamin, is essential for the synthesis of other clotting factors. Because bile salts are needed for reabsorption of fats, vitamin K absorption depends on adequate bile production in the liver.

Metabolism of Nutrients

- Fats: Fat is synthesized from carbohydrate and protein, primarily in the liver. Fat absorbed by lacteals in the intestinal villi enters the liver through the lymphatics, primarily as triglycerides. In the liver the triglycerides can be hydrolyzed to glycerol and free fatty acids and used to produce metabolic energy adenosine triphosphate (ATP), or they can be released into the bloodstream as lipoprotein. The lipoproteins are carried by the blood to adipose cells for storage. The liver also synthesizes phospholipids and cholesterol, which are needed for the hepatic production of bile salts, steroid hormones, components of plasma membranes and other special molecules.
- Proteins - The plasma proteins, including albumins and globulins (excluding gamma-globulin), are synthesized by the liver. The liver also synthesizes several non essential amino acids and serum enzymes including aspartate aminotransferase, alanine aminotransferase, lactate dehydrogenase and alkaline phosphatase.
Carbohydrates: The liver contributes to the stability of blood glucose levels by releasing glucose during states of hypoglycemia (low blood sugar) and taking up glucose during states of hyperglycemia (high blood sugar) and storing it as glycogen (glycogenesis) or converting it to fat. When all glycogen stores have been used, the liver can convert amino acids and glycerol to glucose.

Metabolic Detoxification

The liver alters exogenous and endogenous chemicals (e.g., drugs), foreign molecules, and hormones to make them less toxic or less biologically active. This process, called metabolic detoxification, diminishes intestinal or renal tubular reabsorption of potentially toxic substances and facilitates their intestinal and renal excretion. In this way, alcohol, barbiturates, amphetamines, steroids and hormones (including estrogens, aldosterone, antidiuretic hormone, and testosterone) are metabolized or detoxified, preventing excessive accumulation and adverse effects. Although metabolic detoxification is usually protective, in some durations the products of metabolic detoxification become toxins. Those of alcohol metabolism, for example, are acetaldehyde and hydrogen. Excessive intake of alcohol over a prolonged period causes these end products to damage the hepatocytes. Acetaldehyde damages cellular mitochondria, and the excess hydrogen promotes fat accumulation. This is how alcohol impairs the liver’s ability to function.

The adult liver is the main organ responsible for detoxifying and metabolizing a variety of exogenous as well as endogenous compounds, rendering them more hydrophilic, which often affects their potency and level [10]. The enzymes responsible for the actions are primarily produced in hepatocytes and mainly divided into two groups phase I and phase II. The phase I enzymes are predominantly from the P-450 family of genes, whose general function is to add polar groups, such as hydroxyl groups, to lipophilic molecules thus rendering them more hydrophilic [26]. The main function of the phase II enzymes is to covalently attach a water soluble moiety to the polar group added by the phase I enzymes. Usually such molecules are sugars or peptides, such as glucuronic acid or glutathione. This usually renders the compound less reactive. Examples of phase II enzymes are glutathione-S-transferase and UDP-glucuronosyl transferase. If the phase II reaction is impaired for some reasons or the phase I reaction is induced, this may leave the organism with an excess of reactive molecules from the phase I reaction, which can be detrimental. This can occur in the case of drug induced hepatotoxicity, when reactive metabolites of the parent compound are formed, which subsequently negatively affects cellular functions [27].

Storage of Minerals and Vitamins

The liver stores certain vitamins and minerals, including iron and copper, in durations of excessive intake and releases them in durations of need. The liver can store vitamins B₁₂ and D for several months and vitamin A for several years. The liver also stores vitamins E and K. Iron is stored in the liver as ferritin, an iron-protein complex and is released as needed for red blood cell production.

The Immunologic Function of the Liver

The liver is the main hematopoietic organ during certain stages in fetal development and continues to be a hematopoietic organ even after birth. It can produce all leukocytes lineages from resident hematopoietic stem cells [28, 29]. The portal tract of the liver contains many different cells of hematopoietic origin, as well as hematopoietic stem cells [11]. The liver contains cells involved in adaptive and innate immunity.

Innate Immunity of the Liver

In comparison to other organs, the liver is particularly rich in cells of the innate immune system. The main cell types here are kupffer cells and NK T cells. NK T cells are not strictly part of innate immunity but functionally somewhere in between adaptive and innate. Of hepatic lymphocytes, approximately 30 % are NK cells, indicating the great contribution of NK cells to liver immunity. This may be compared to the approximately 15% that the two cell types combined contribute to in peripheral blood lymphocytes [30]. NK cells are one of the main producers of liver INFγ in response to lipopolysaccharide (LPS), which partly depends on the activation of NK cells by IL-12 derived from activated Kupffer cells. They show high cytotoxic level towards tumor cells, with the help of the trail-ligand, which is up regulated by IL-2. Kupffer cells are derived from circulating monocytes and play a particularly important role in initiating inflammation in the liver. Kupffer cells differ in properties depending if they are periportal or perivenous. Periportal cells are larger and more active in phagocytosis,
miring their function as the first line of defense of the body towards gut derived bacteria entering the blood stream and reaching the liver via the vena porta [31]. Perivenous kupffer cells on the other hand, are smaller and produce larger amounts of nitric oxide, as well as prostaglandins [32]. Ex vivo culture of kupffer cells have shown that the perivenous type secretes more than double the amount of TNF α upon LPS stimulation. Kupffer cells are one of the main cell types to secrete cytokines, which then regulate the function not only of the kupffer cells themselves but also that of other cell types such as the NK cells. Stimulation of kupffer cells by bacteria and bacterial LPS leads to production of IL-12 [33], as well as TNFα. Other cytokines known to be produced by kupffer cells upon LPS stimulation include IL-6, TGF β, IL-1β and IL-8 [34]. Cytokines derived from kupffer cells have in turn been proven to stimulate hepatocytes to further increase chemotactic response by secretion of IL-8 [35]. Thus kupffer cells and NK cells hence mainly secrete Th1 type cytokines that activate the immune system. Immunosuppressive cytokines such as IL-10 may instead be secreted by stellate cells and regulatory T cells (but also by kupffer cells and NK cells) [36].

Adaptive Immunity

Adaptive immunity can be classified into humoral immunity and cell-mediated immunity, mediated principally by B and T lymphocytes, respectively. T cells promote differentiation of B cells to antibody secreting plasma cells. T cells kill infected cells and secrete cytokines such as TNF α, IFN γ and IL -6. TNF α derived from kupffer cells play an important role in stimulating activation of T cells which then elicit a cytotoxic response [37]. Intrahepatic accumulation of highly activated CD8+ T cells is part of the pathogenesis process in hepatitis, including alcoholic hepatitis [38]. NK T cells constitute a distinct subpopulation of T cells that is particularly abundant in the liver, as previously mentioned. Infact, they are not strictly a part of adaptive immune response, but can be seen as having a function in between adaptive and innate immunity. These cells produce large amounts of the Th 2 cytokine IL-4 [39] but also the Th1 cytokine IFN γ [40]. This ability of secreting both Th 1 and Th 2 type cytokines is particularly feature of NK cells. NK T cells are often present in the lumen of the sinusoid. They exhibit MHC- unrestricted killing of a variety of tumor cells, an level which is enhanced by IFN γ [12]. NK T cells have been shown to ‘crawl’ within the hepatic sinusoid, and stop upon T cell antigen receptor activation [41]. Naïve CD8+ T cells are also known to accumulate in the liver, where they may be activated, but at durations to a lesser degree than in lymph nodes. Thus, low-grade activation of T cells in liver rather leads to tolerance [42]. There is also evidence for regulatory T cells expressing IL-10 [36]. B cells have not been well studied in adult liver, however, there is a substantial B cell population showing similarities to splenic B cells. It has been shown that B cells play a role in liver fibrosis, as B cell deficient mice show significantly less fibrotic lesions after carbon tetrachloride induced liver injury. This effect is independent of antibody production. But also B cell antibody-dependent responses play a part in liver injury, as antibody production has been shown to be of importance in alcohol induced liver damage [43].

Interrelationships of the Liver with Other Organs

The liver interacts with many other organs. Following the flow of blood, the liver receives its arterial blood supply from the hepatic arteries [3]. The hepatic arteries are distal to the celiac trunk, which is distal to the abdominal aorta. Thus the liver receives its oxygenated blood supply from the heart. Nutrient laden blood from the digestive system and blood leaving the spleen enters the liver through the hepatic portal vein. Processed blood leaving the liver through the hepatic veins drains into the inferior vena cava, completing the connection to the heart. The liver affects digestion through its formation of bile, which is secreted into the small intestine [2]. The gallbladder is essentially an overflow area for the liver’s bile duct. The liver is full of lymph glands, which provide fluid drainage and immune system support. The liver synthesizes many blood proteins, showing its relation to that “organs”. The liver also has a supply of nerves, showing its relationship with the nervous system. Finally, liver disease often causes problems in the renal system, demonstrating a relationship with the kidneys [2]. The liver has many important functions in maintaining the physiologic balance of the human body.

CONCLUSIONS

In conclusion this paper summarized the functions of the liver which includes firstly, Secretion of bile, the liver assists intestinal digestion by secreting 700 to 1200 ml of bile per day. Bile salts, which are conjugated bile acids,
are required for the intestinal emulsification and absorption of fats. Secondly, Metabolism of bilirubin which is a byproduct of destruction of aged red blood cells and gives bile a greenish black color and produces the yellow tinge of jaundice. Also, Vascular and hematologic functions, because of its extensive vascular network, the liver can store a large volume of blood. The amount stored at any one duration depends on pressure relationships in the arteries and veins. Moreover, the liver has hemostatic functions. It synthesizes prothrombin, fibrinogen, and clotting factors. Vitamin K, a fat-soluble vitamin, is essential for the synthesis of other clotting factors. Because bile salts are needed for reabsorption of fats, vitamin K absorption depends on adequate bile production in the liver. Furthermore, Metabolism of nutrients, the liver plays essential roles in the metabolism of fat, protein, and carbohydrates. Also, Metabolic detoxification, the liver alters exogenous and endogenous chemicals (e.g., drugs), foreign molecules, and hormones to make them less toxic or less biologically active. This process, called metabolic detoxification, diminishes intestinal or renal tubular reabsorption of potentially toxic substances and facilitates their intestinal and renal excretion. In this way alcohol, barbiturates, amphetamines, steroids and hormones (including estrogens, aldosterone, antidiuretic hormone, and testosterone) are metabolized or detoxified, preventing excessive accumulation and adverse effects. Also, Storage of minerals and vitamins, the liver stores certain vitamins and minerals, including iron and copper, in periods of excessive intake and releases them in periods of need. The liver can store vitamins B12 and D for several months and vitamin A for several years. The liver also stores vitamins E and K. Iron is stored in the liver as ferritin, an iron-protein complex and is released as needed for red blood cell production. Finally, the liver has immunologic functions as the liver contain cells involved in adaptive and innate immunity.

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Physiology of the liver

