Digestive System, Vertebrate
Anatomy and physiology
Organ function
Liver

Hepatocytes occupy about 80 percent of the volume of the liver, and their **cytoplasm** (the area surrounding the nucleus) contains many **mitochondria,** which provide the energy needed for the many synthetic and metabolic functions of the liver cell**.**

The **cytoplasm** also contains a series of long tubules, called the **endoplasmic reticulum**, which contains many enzymes essential to liver function**.** Some of the membranes of the **endoplasmic reticulum** appear granular, or rough, owing to the presence of **ribosomes,** which are responsible for forming specific polypeptide (protein) chains from single amino acids**.**

The **non-ribosomal, or smooth, endoplasmic reticulum** is the site where **cytochromes (combinations of heme from hemoglobin with various proteins)** and certain enzymes undertake the important hepatic functions of

drug and hormonal metabolism,
cholesterol synthesis, and
conjugation with carbohydrate moieties of **bilirubin** and other fat-soluble metabolic and foreign compounds, thereby making them soluble in water**.**

The **Golgi apparatus**, a series of tubular structures between the **endoplasmic reticulum** and the **canaliculus**, acts as a transport station for newly made proteins and other hepatocytic products before they are conveyed to other parts of the cell or out of the cell entirely**.**

Lysosomes, another important cytoplasmic constituent, are responsible for the intracellular storage of pigments, such as iron or copper, and for the digestion of certain contents, such as glycogen or foreign particles.

The nucleus of the **hepatocyte** has no apparent functions that distinguish it from nuclei of other cells. The nucleus guides replication of the cell and transmits genetic material in the form of **messenger ribonucleic acid (mRNA)** from **deoxyribonucleic acid (DNA)** to organelles located in the cytoplasm.

The **major functions of the liver** are
to participate in the metabolism of protein, carbohydrate, and fat**;**
to synthesize **cholesterol** and **bile acids;**
to initiate the formation of **bile;**
to engage in the transport of **bilirubin; and**
to metabolize and transport certain drugs**.**

Dietary amino acids from ingested protein are circulated to the **hepatocytes** of the liver, where they are

either cycled into the production of specific human proteins**,**
or used as a source of energy after having had the amino group removed **(deamination)** and converted into glucose through a process called **gluconeogenesis.**

The **ammonia** released from amino acids in the process of **gluconeogenesis** is converted into **urea** only in the **hepatocyte** by way of a special enzyme-controlled metabolic process called the **urea cycle.**

Except for the **immunoglobulins (gamma globulins),** which are produced in the **spleen** and **lymphoid tissue**, **hepatocytes** are the major source for the production of all **blood proteins.** These include

albumin, proteins essential to the coagulation of blood**,**
certain enzyme inhibitors such as alpha1-antitrypsin**,**
lipoproteins, and
the transport proteins such as
thyroxine-binding globulin**,**
ceruloplasmin (copper)**,**
transferrin (iron), and
transcobalamin (vitamin B12).

The stability of these proteins is quite variable; albumin, for example, has a half-life of more than 15 days, while some of the blood coagulation factors are functional for only seven hours.

The **liver** controls the transport and storage of **energy-producing carbohydrates.** **Glucose,** which is one of the two monosaccharide components of **table sugar (sucrose)** and **milk sugar (lactose)** and is the sole building block of **dietary polysaccharides,** such as **starch,** is combined with phosphate in the liver cell and

either transported to peripheral tissues for metabolic purposes
or stored in the hepatocyte as **glycogen**, a complex polysaccharide**.**

Specific enzyme systems are present in the **hepatocyte** for these conversions, as well as for the translation of other **dietary monosaccharides (fructose from sucrose and galactose from lactose) into glucose.**

The **hepatocyte** is also able to convert certain amino acids and **products of glucose metabolism (pyruvate and lactate)** into **glucose** through **gluconeogenesis.**

The **liver** also plays a central role in **metabolizing fat** by converting **stored fatty acids** to their energy-releasing form, **acetylcoenzyme A (acetyl CoA),** when **hepatic glucose** and **glycogen stores** are exhausted or unavailable for metabolic purposes (as in **diabetic ketoacidosis).**

The **liver** also plays a role in the formation of **storage fats (triglycerides)** whenever dietary carbohydrates, protein, or fat exceeds the requirements of tissues for **glucose** or the needs of the **liver** for **glycogen.** The liver also synthesizes cell membrane components (phospholipids) and proteins (lipoproteins) that carry lipids (fats and cholesterol) in the blood.

Cholesterol is a major factor in **cell membrane structure**, and it is essential to cellular survival**. Cholesterol** is a four-ringed sterol that is absorbed from the diet or synthesized from **dietary acetyl CoA** by the **liver** and the **intestinal lining. Excess cholesterol** is a major constituent of the **bile** that is produced in the **liver** and transmitted into the **intestine.**

About half of the **hepatic cholesterol** is first converted into **bile acids**, which have the **same sterol structure as cholesterol but contain three fewer carbon atoms and an acidic side chain.** The **rate of bile flow** is **controlled in part** by the **rate of bile acid secretion** by the **hepatocyte.**

The **hepatocyte** also acts to **transport** certain **water-insoluble products** of **metabolism** and **agents foreign to the body** into the **bile** and **urine. Bilirubin** is the product of **hemoglobin metabolism** after the iron and protein fractions have been removed**. Bilirubin** is formed in the **bone marrow** and the **lymphatic tissue** and is carried to the **liver** after becoming bound to **plasma albumin.** It is released at the **hepatocytic** sinusoidal membrane and is transported to the **smooth endoplasmic reticulum** where, in **an enzymatic system**, it is conjugated with one or two molecules of **glucuronic acid,** thereby becoming soluble in water and excretable in **bile.**

Similarly, **many drugs** that are normally insoluble in water are conjugated, or joined with other substances to **detoxify** them, in **phase II reactions** in **hepatocytes** after having been **oxidized** by **cytoplasmic enzyme systems (phase I reactions). Small drug metabolites** are excreted into the **urine,** while **larger (drug) molecules** leave the body through the **bile** and the **feces.**

Biliary tract

Aside from **inorganic ions (sodium, potassium, calcium, magnesium, chloride, and bicarbonate), bile** contains **protein** and **bilirubin; the latter is responsible for its golden colour in dilute solutions and dark amber colour in concentrate.** It is richest, however, in **bile acids (derived from cholesterol in the hepatocyte), phospholipids** (largely phosphatidyl choline, or lecithin), and **cholesterol.**

Normally the **cholesterol,** which is not soluble in watery secretions, is carried in a colloidal solution in **bile** in the form of mixed aggregates of complexes containing **bile acids** and **lecithin. In the absence of adequate amounts of lecithin and bile acids, cholesterol crystallizes.**

The **liver** synthesizes **two types of primary bile acid** from **cholesterol**, called **chenodeoxycholic acid** and **cholic acid.**

In the lower intestine, **bacterial action** removes one of the **hydroxyl groups (dehydroxylation)** from **cholic acid,** changing it to **deoxycholic acid (deoxycholate). This secondary bile acid** appears in **bile** because it is absorbed from the intestine and recirculated to the **liver.**

Chenodeoxycholic acid is also **dehydroxylated** in the **(lower) intestine,** becoming ***lithocholic acid (lithocholate)***, a small amount of which is also reabsorbed and appears in normal **bile.**

Neither **deoxycholate** nor ***lithocholate*** appears to be an important factor in the incorporation of **cholesterol micelles, or vesicles,** in **bile** because they lack the important feature of carrying hydroxyl groups at both the C3 and C7 positions of the sterol nucleus.

The **total bile acid pool** at any one time measures about **three grams,** almost all of which is contained at rest in the **gallbladder.** It is maintained largely because about **95 percent** of the **bile acids** entering the intestine from the **biliary system** are **reabsorbed actively in the lower portion of the small intestine,** so that only 0.2 to 0.6 gram of bile acids is lost daily**.** This loss can be replaced readily by the normal **liver.**

Bile is formed initially in the **hepatocyte,** and the rate of formation is dependent primarily on the rate at which **bile acids** are secreted into **bile canaliculi.** A portion of the flow of **bile**, however, is related to factors other than the secretion of **bile acids.** This flow appears to be dependent on the **secretion of sodium** from the **hepatocyte** and is also partially governed by the action of **intestinal hormones** such as **secretin, cholecystokinin,** and **gastrin.**

In its passage through the **biliary tract**, **hepatic bile** is concentrated to as little as one-tenth of its original volume by the selective reabsorption of **water, chloride, and bicarbonate.** This concentration process takes place largely in the **gallbladder**, with the result that **bile** from this organ is much thicker in density and darker in colour (due to concentration of pigments) than is bile emerging from the **liver.**

Distension of the duodenum, particularly by a meal containing fat, provokes the secretion of **CCK**, a hormone that causes contractions of the muscular layer in the wall of the **gallbladder.** Bile concentration is greatly reduced if the **gallbladder** is removed, but this effect apparently does not impede the primary digestive function of **bile**, which is to **aid in the dispersion and digestion of fat in the lumen of the intestine.**