Liver

ANATOMY

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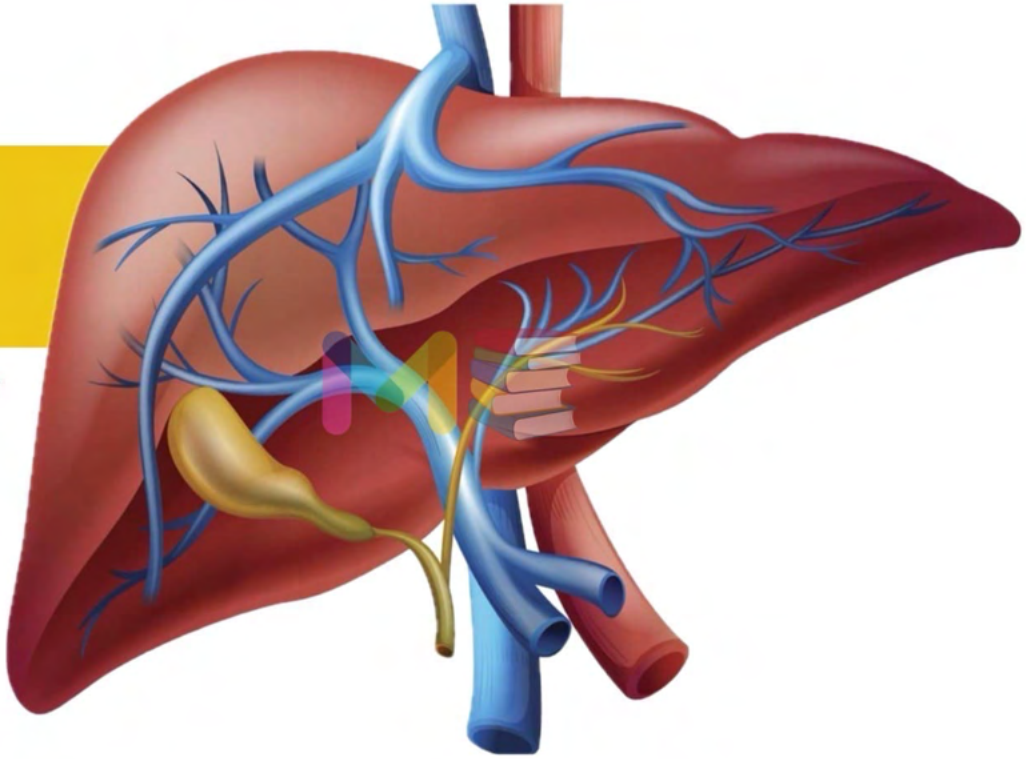


Introduction

The liver is the largest gland in the human body. The liver is found in the superior right quadrant of the abdomen and weighs approximately 1.5 kilograms. Its main functions are detoxification, metabolism (carbohydrates, proteins, lipids, hormones), nutrient storage (e.g., iron and vitamins), synthesis of coagulation factors, formation of bile, filtration, and storage of blood. The liver can be divided into 4 lobes or 8 segments. Microscopically, it is divided into hepatic lobules. Its main neurovascular bundle is found within the transverse fissure of the liver, also called the porta hepatis.

Development of the liver

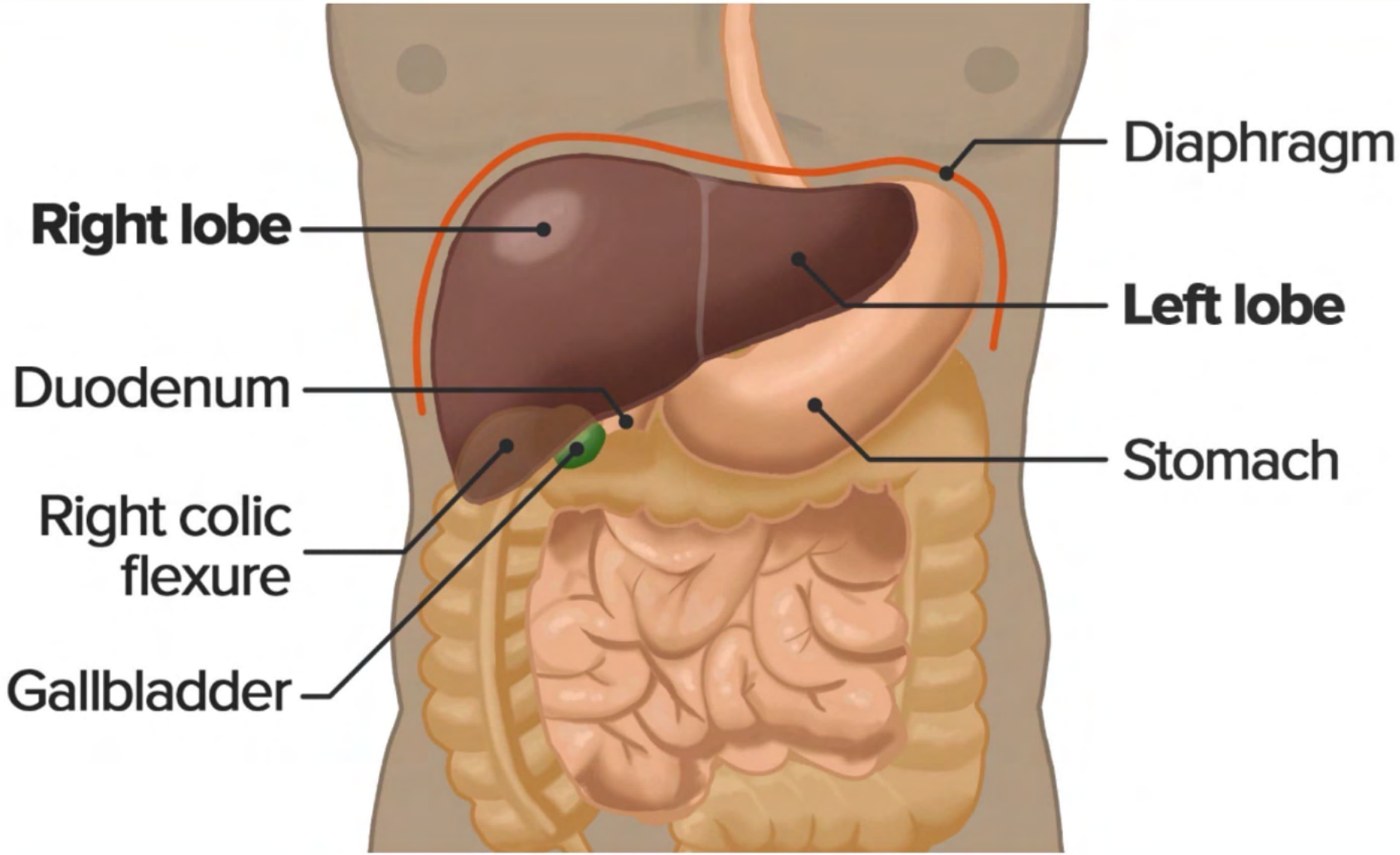
- Develops from the 3rd to 8th week during embryogenesis
  - Originates from the foregut endoderm
  - Appears as the hepatic diverticulum, which later becomes the liver and the gallbladder
- The falciform ligament is called the ventral mesentery during the fetal period.
- The round ligament contains the umbilical vein during gestation, which is the main fetal blood source (see table below).

Location

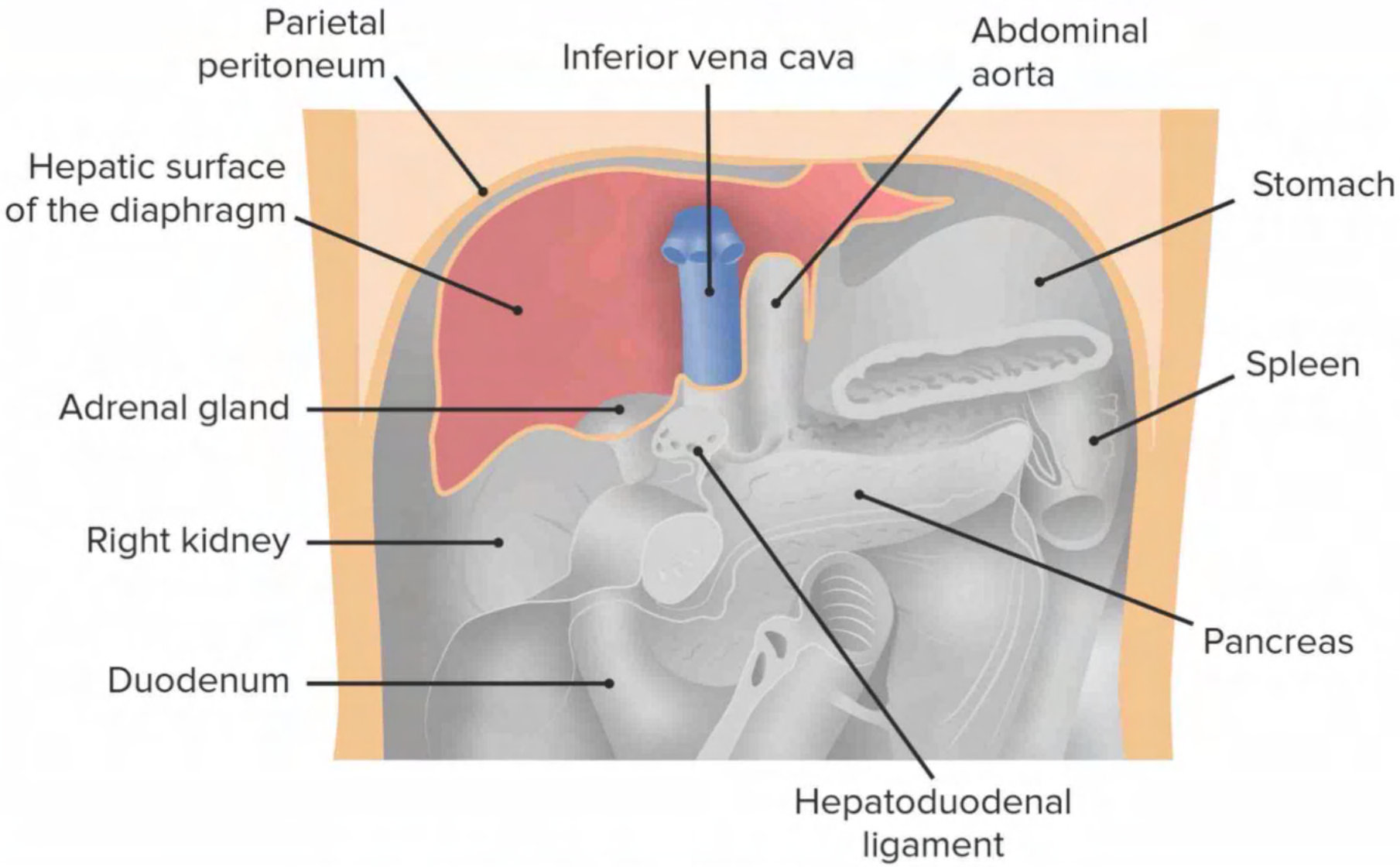
The liver is the largest gland in the body. It extends from the right to the left hypochondriac region (¾ of the liver is in the right superior quadrant).

- Immediately adjacent to the inferior surface of the diaphragm → location is breath-dependent (rises during exhalation, lowers during inhalation)
- Superior limit: height of the 5th intercostal space during exhalation
- Inferior limit: curve of the right costal arch during inhalation
- Surfaces: diaphragmatic and visceral
  - Intraperitoneal except for the bare area, porta hepatis, and gallbladder fossa
  - Enclosed in the Glisson capsule (external layer of fibrous connective tissue)
- Weight: 1.5 kg (average)

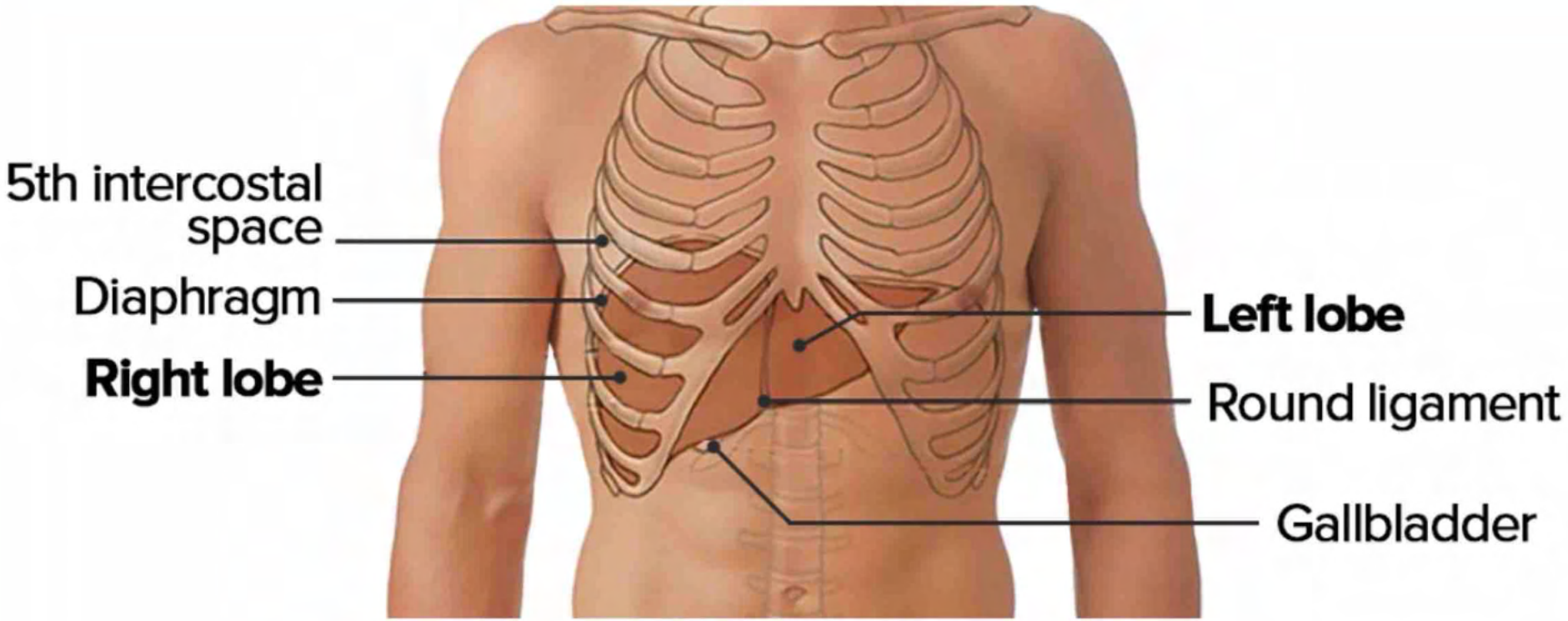
Location


Diaphragm
Right lobe
Left lobe
Duodenum
Stomach
Right colic flexure
Gallbladder

Location


Parietal peritoneum
Inferior vena cava
Abdominal aorta
Hepatic surface of the diaphragm
Stomach
Spleen
Adrenal gland
Right kidney
Pancreas
Duodenum
Hepatoduodenal ligament

Location


5th intercostal space
Diaphragm
Right lobe
Left lobe
Round ligament
Gallbladder

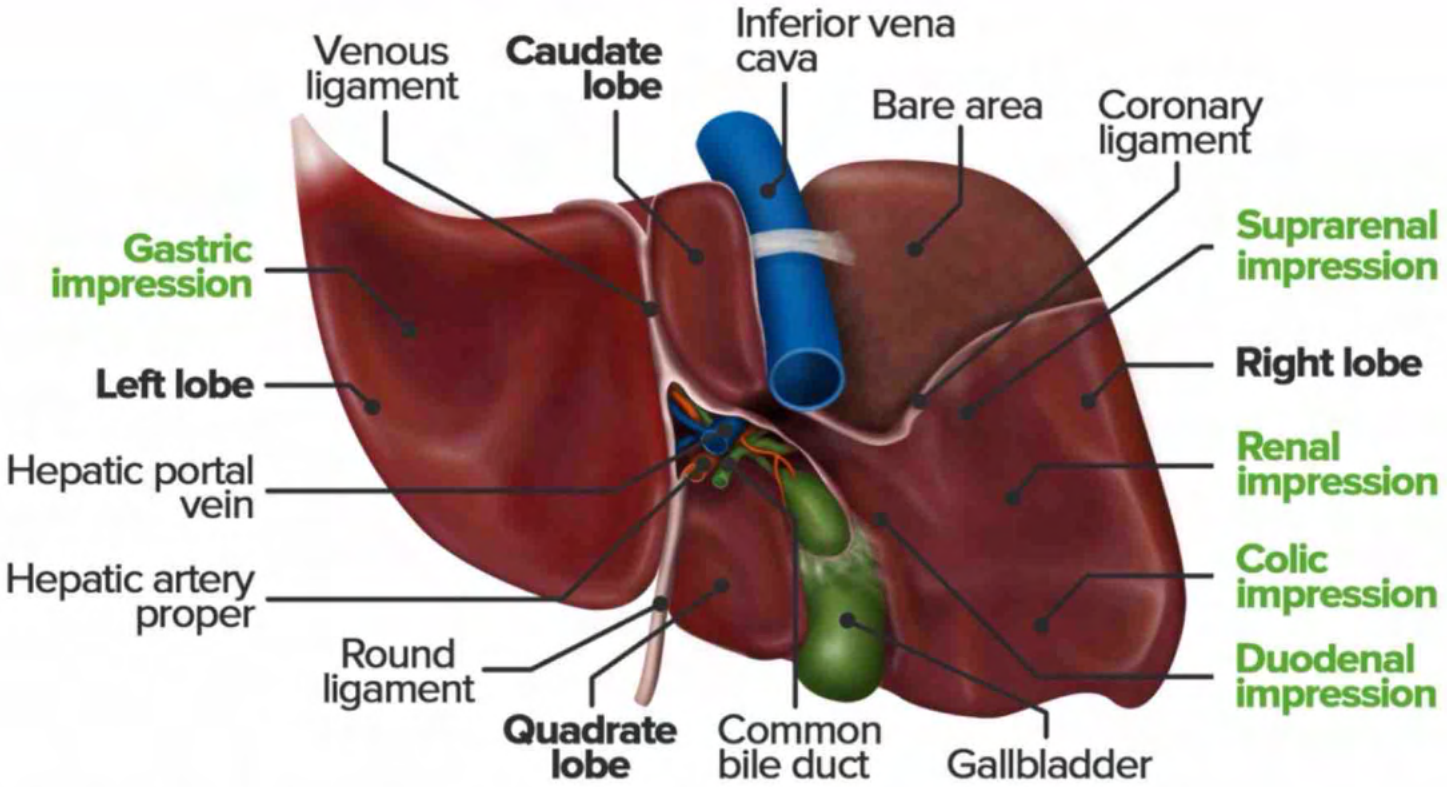
Four lobes

- Superficially divided by fissures and ligaments
- Functionally determined by the left and right branches of the hepatic vein and Cantlie's line (an imaginary line that crosses the gallbladder fossa and inferior vena cava)
  - Right lobe: largest
  - Left lobe: separated from the right by the falciform ligament on the diaphragmatic surface
  - Caudate lobe: between the venous ligament and groove for the inferior vena cava (IVC)
  - Quadrate lobe: between the round ligament and the gallbladder fossa

Impressions of adjacent structures and organs

- Gastric: left lobe, anterior to the esophageal impression
- Colic: inferior margin of the right lobe (right colic flexure)
- Duodenal: right lobe, lateral to the gallbladder (1st segment of the duodenum)
- Renal: center of the right lobe (superior pole of the right kidney)
- Suprarenal: superior to the renal impression (right adrenal gland)

Impressions of adjacent structures and organs

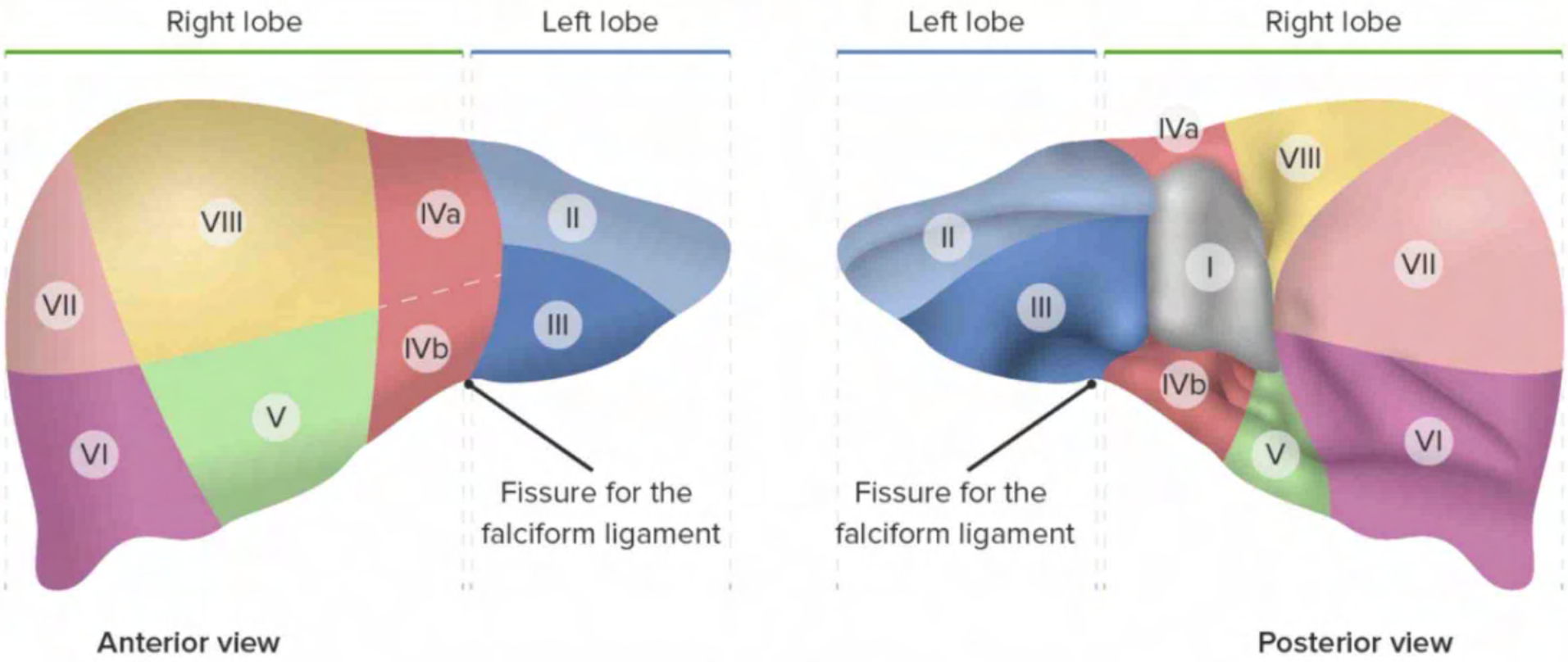


Inferior view of the visceral surface of the liver. Note the uneven structure that results from impressions of the neighboring organs. The colic impression is caused by the colon's hepatic flexure; the descending portion of the duodenum forms the duodenal impression.

Eight segments (Couinaud classification)

- Based on a transverse plane through the bifurcation of the main portal vein
  - Exception: Caudate lobe receives blood flow from both vascular branches.
- 8 functionally independent segments, each with its own vascular inflow, outflow, and biliary drainage
- Segment I is the caudate lobe and can only be seen from the posterior view.
- Segments can be surgically resected without affecting the viability of the remaining liver.

Eight segments (Couinaud classification)



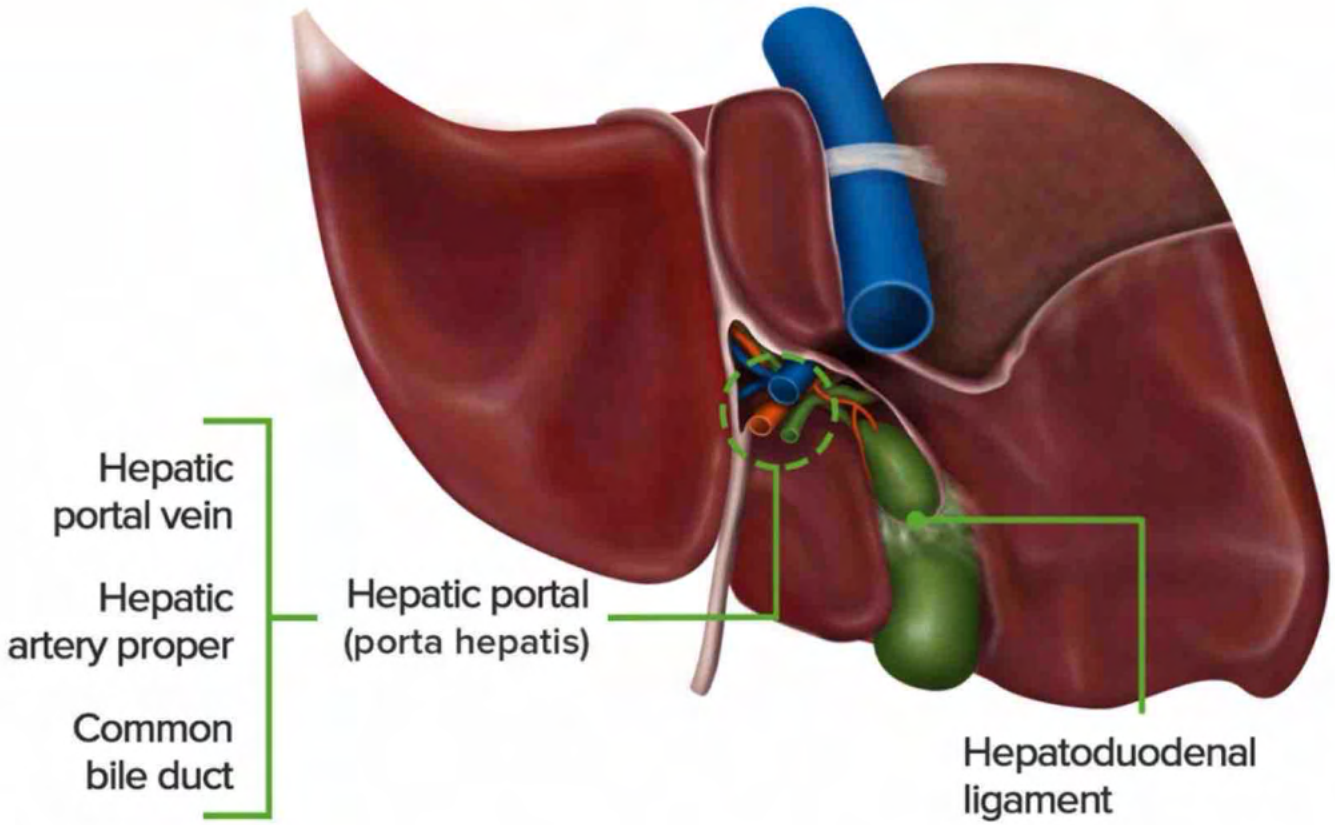
Eight hepatic segments according to the Couinaud classification system.

Porta hepatis

The porta hepatis (also called the hepatic portal) is a transverse fissure that separates the caudate and quadrate lobes and serves as a passageway for the following:

- Common hepatic bile duct (exits the liver, located anteriorly and laterally)
- Hepatic artery proper (enters the liver, located anteriorly and medially)
- Hepatic portal vein (enters the liver, located posteriorly, between the duct and artery)
- Hepatic nerve plexus (contains postganglionic sympathetic innervation from the celiac plexus and preganglionic parasympathetic innervation from the vagus nerve)
- Lymphatic vessels of the liver

Porta hepatis



Inferior view of the visceral surface of the liver, featuring the hepatic portal and surrounding hepatoduodenal ligament.

Ligaments of the liver

Definition: Ligaments of the liver are double layers of visceral peritoneum that fix the position of the liver by attaching it to the surrounding structures.

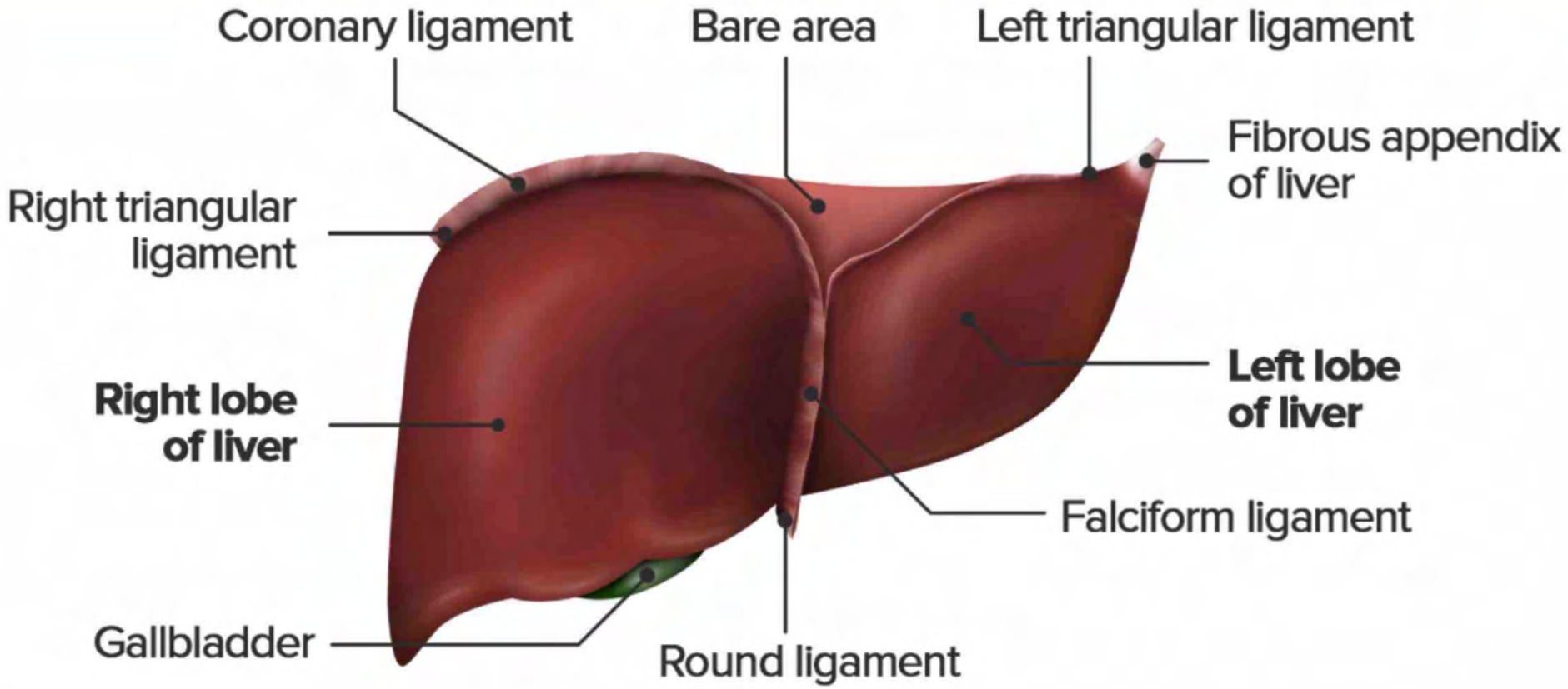
Table: Ligaments of the liver

Coronary ligaments (anterior and posterior)	Peritoneal reflection from the diaphragm to the liver Demarcates the bare area (surface of the liver with no peritoneal covering)
Falciform ligament	Peritoneal reflection from the umbilicus to the liver Remnant of the embryonic ventral mesentery Its free edge contains the round ligament of the liver.
Hepatoduodenal ligament	Portion of the lesser omentum Extends from the porta hepatis to the superior part of the duodenum contents: hepatic artery proper, portal vein, common hepatic duct
Hepatogastric ligament	Extends from the liver to the lesser curvature of the stomach contents: gastric arteries

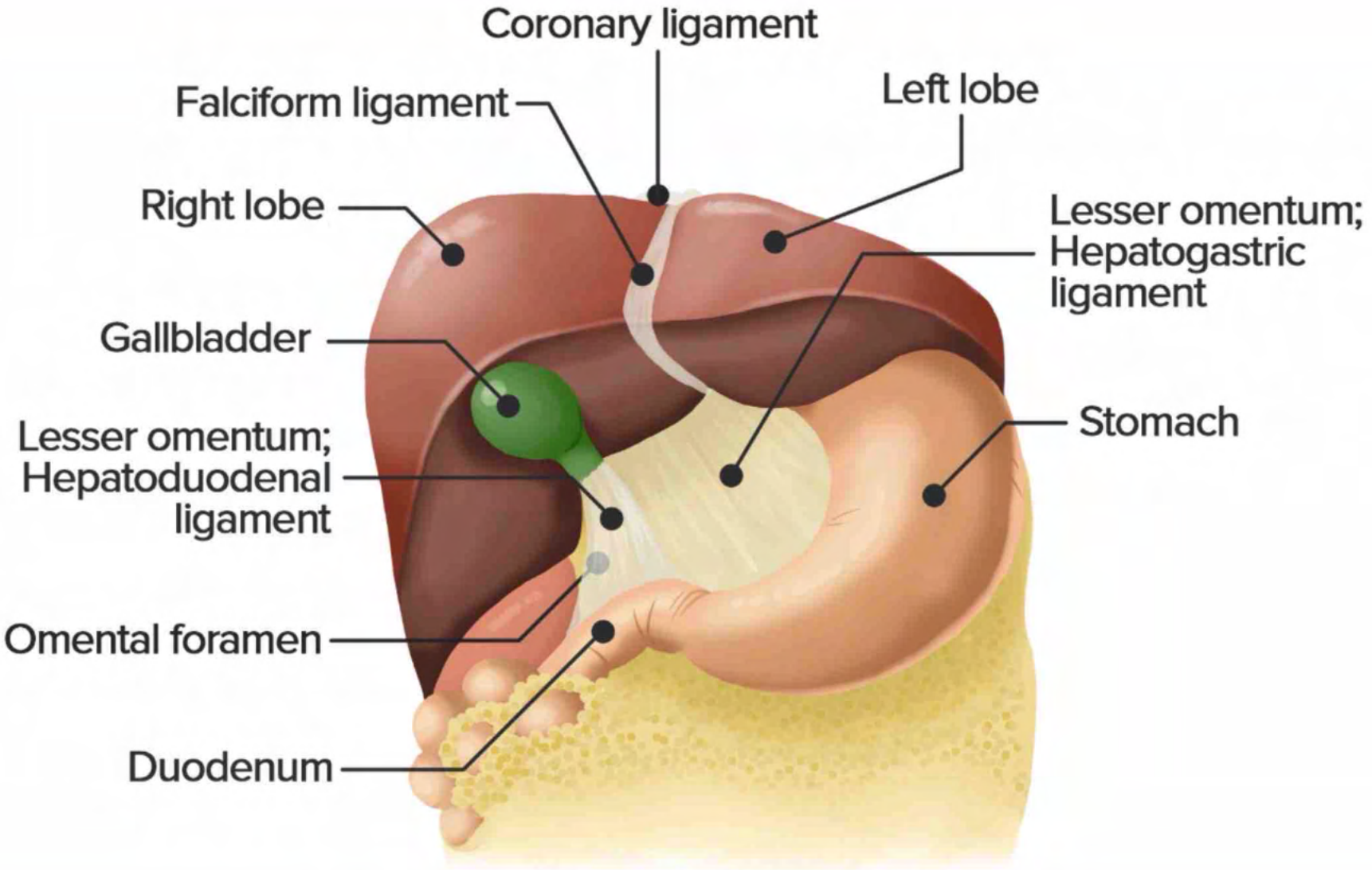
Table: Ligaments of the liver

Round ligament (also known as *ligamentum teres*)	Remnant of the intra-abdominal portion of the umbilical vein Extends from the umbilicus to the liver on the free edge of the falciform ligament
Triangular ligaments	Formed by the fusion of the anterior and posterior folds of the coronary ligament 1 left and 1 right; both extend from the liver to the diaphragm
Venous ligament (also known as *ligamentum venosum)*	Remnant of the ductus venosus Extends from the remnant of the intra-abdominal portion of the umbilical vein to the inferior vena cava
Left fissure	Impressions of the round and venous ligaments
Right fissure	Impressions of the gallbladder and the inferior caval vein

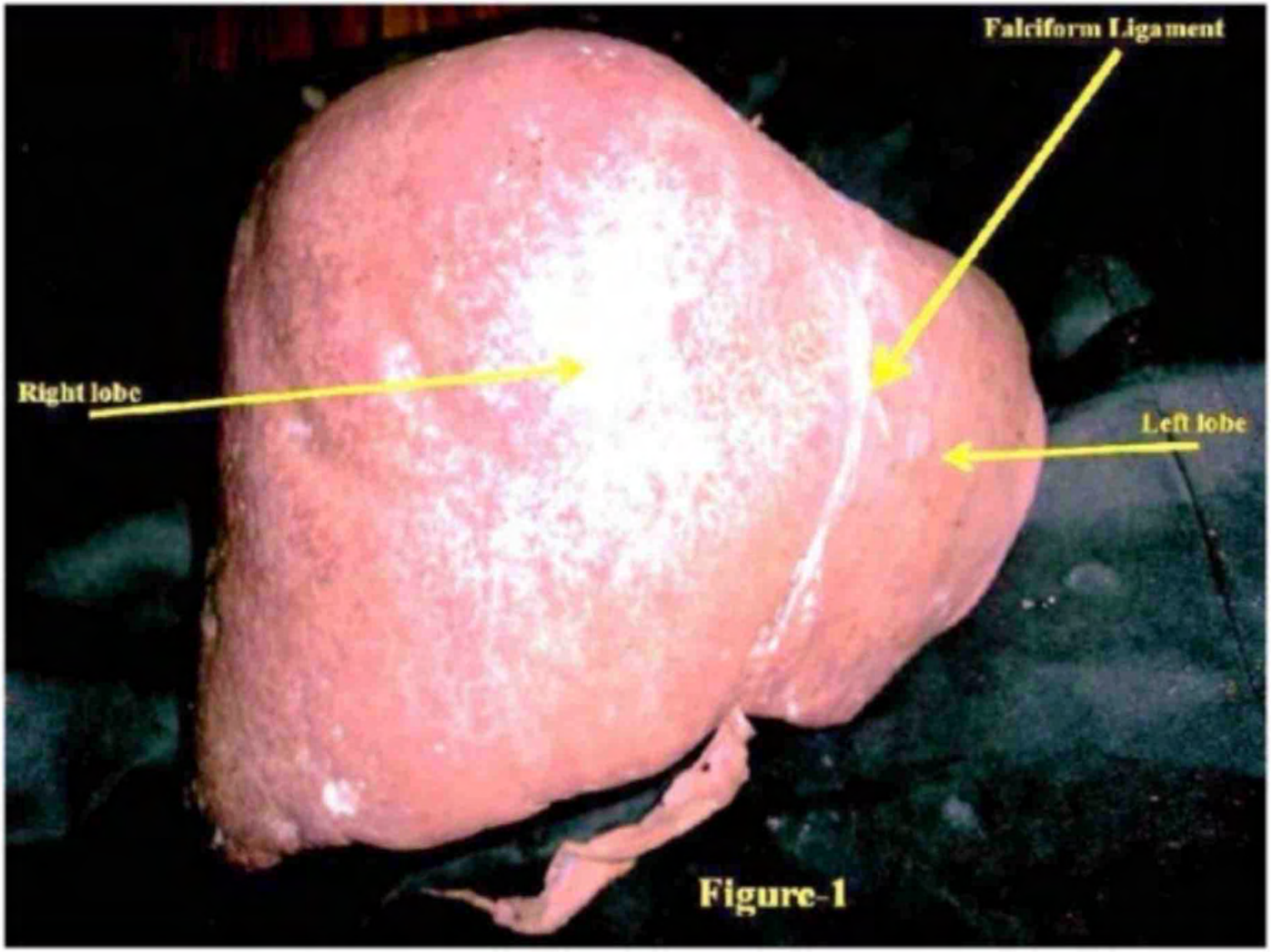
Ligaments of the liver



Ligaments of the liver



Ligaments of the liver



Ligaments of the liver

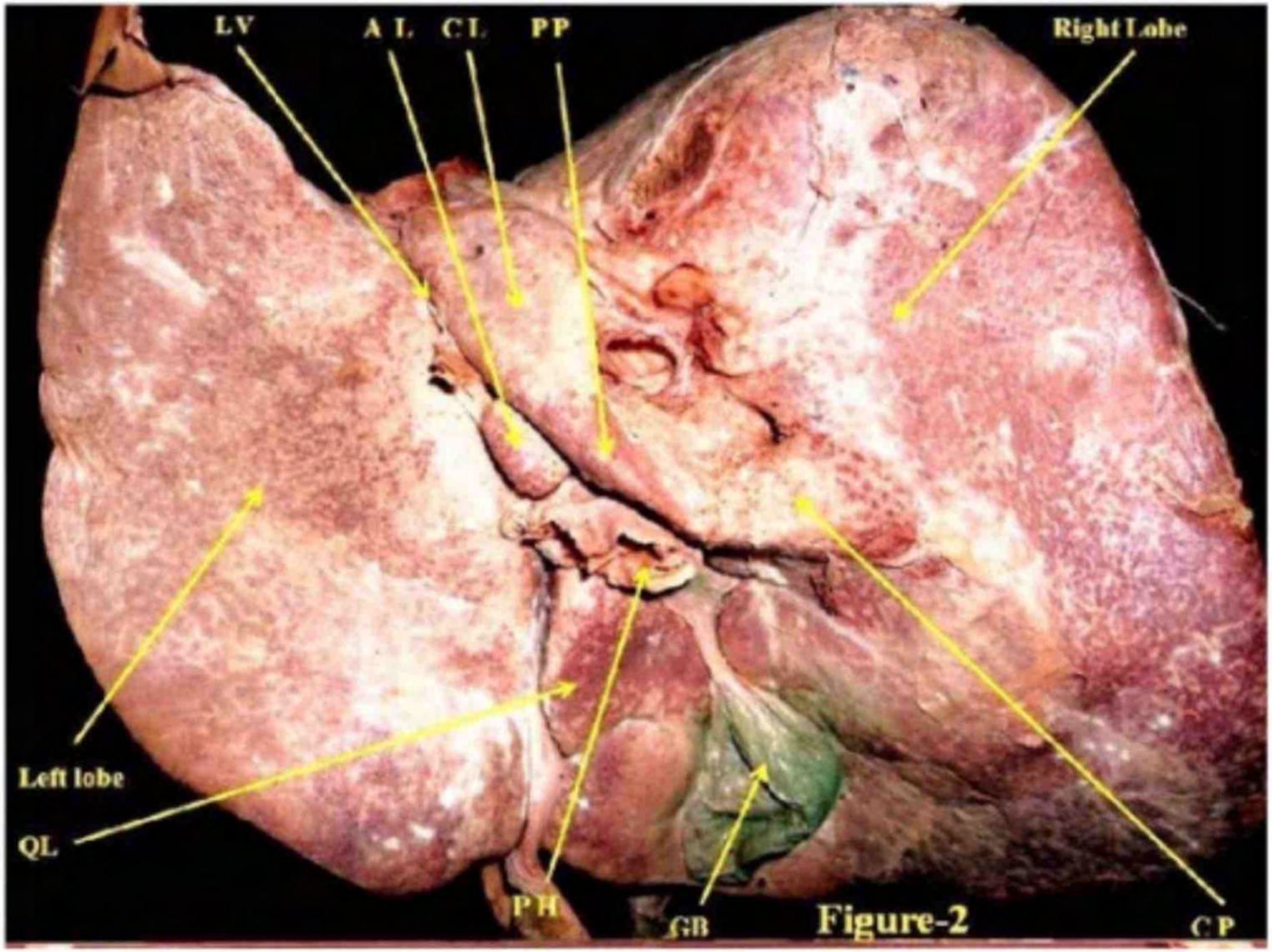


Figure-2

Hepatic (classical) lobule

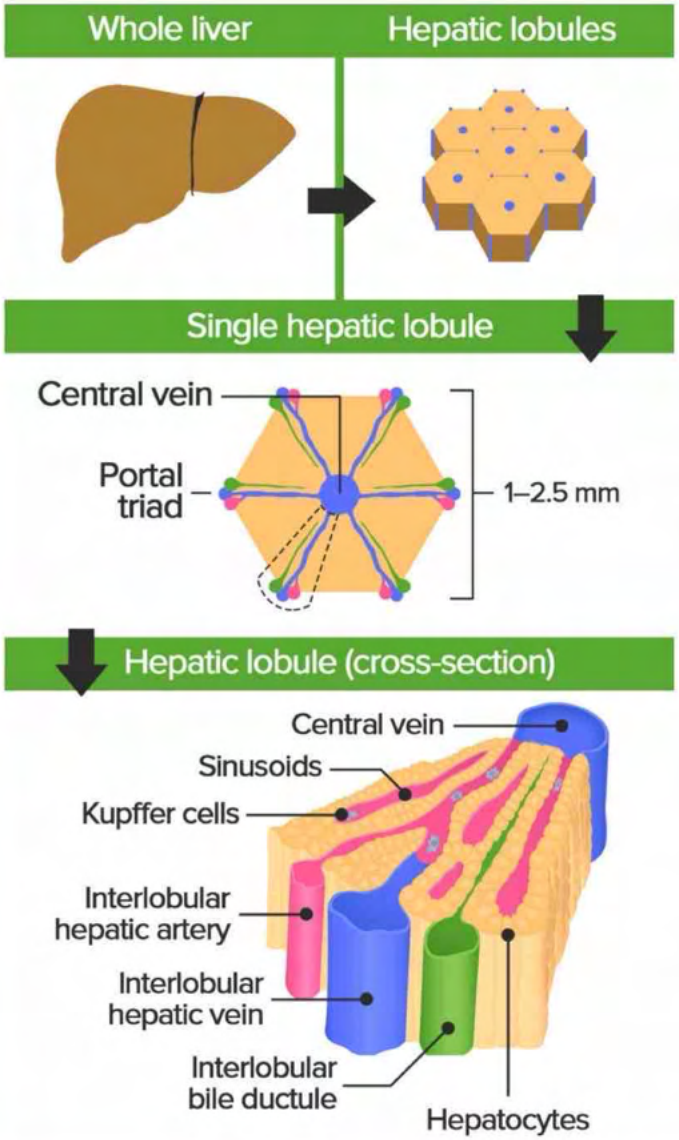
■ Small hexagonal units of the liver, measuring 1–2.5 mm each, separated by thin strands of connective tissue

■ Central vein: Each lobule has a vein in the center that receives mixed blood from the sinusoids (via branches from the portal vein and hepatic artery), drains into the hepatic veins, and leaves the liver via the IVC.

■ Portal triad: cluster of vessels located at the 6 vertices of each hepatic lobule:

- Interlobular branch of the portal vein: supplies the lobule with deoxygenated blood, rich in nutrients
- Interlobular branch of the hepatic artery proper: supplies the lobule with oxygenated blood
- Interlobular bile duct: drains the bile from the biliary ductules in the opposite direction of blood flow
- Additionally: lymphatic vessels and a branch of the vagus nerve

Hepatic (classical) lobule



Schematic diagram of the architecture of the liver, featuring the hepatic lobule. The portal triads at the corners consist of branches of the portal vein, hepatic artery proper, and a bile duct. The branch of the portal vein carries nutrient-rich, but deoxygenated blood from the small intestine, the branch of the hepatic artery supplies the hepatocytes with oxygenated blood. The bile duct drains bile from the hepatocytes towards larger ducts and the gall bladder.

Portal vein lobule

- The portal vein lobule is a lobule viewed from a 2nd perspective, with the portal triad in the center and the central veins at the 3 vertices
- Shaped like a triangle
- Functional unit for bile transport
- Bile is drawn to the center of the triangle, into the interlobular bile duct.

Hepatic acinus

■ The hepatic acinus is a lobule viewed from a 3rd perspective, with the central veins and portal triads at the 4 vertices.

■ Diamond-shaped

■ Functional unit for blood exchange

■ Blood moves from the triads to the vein through 3 zones:

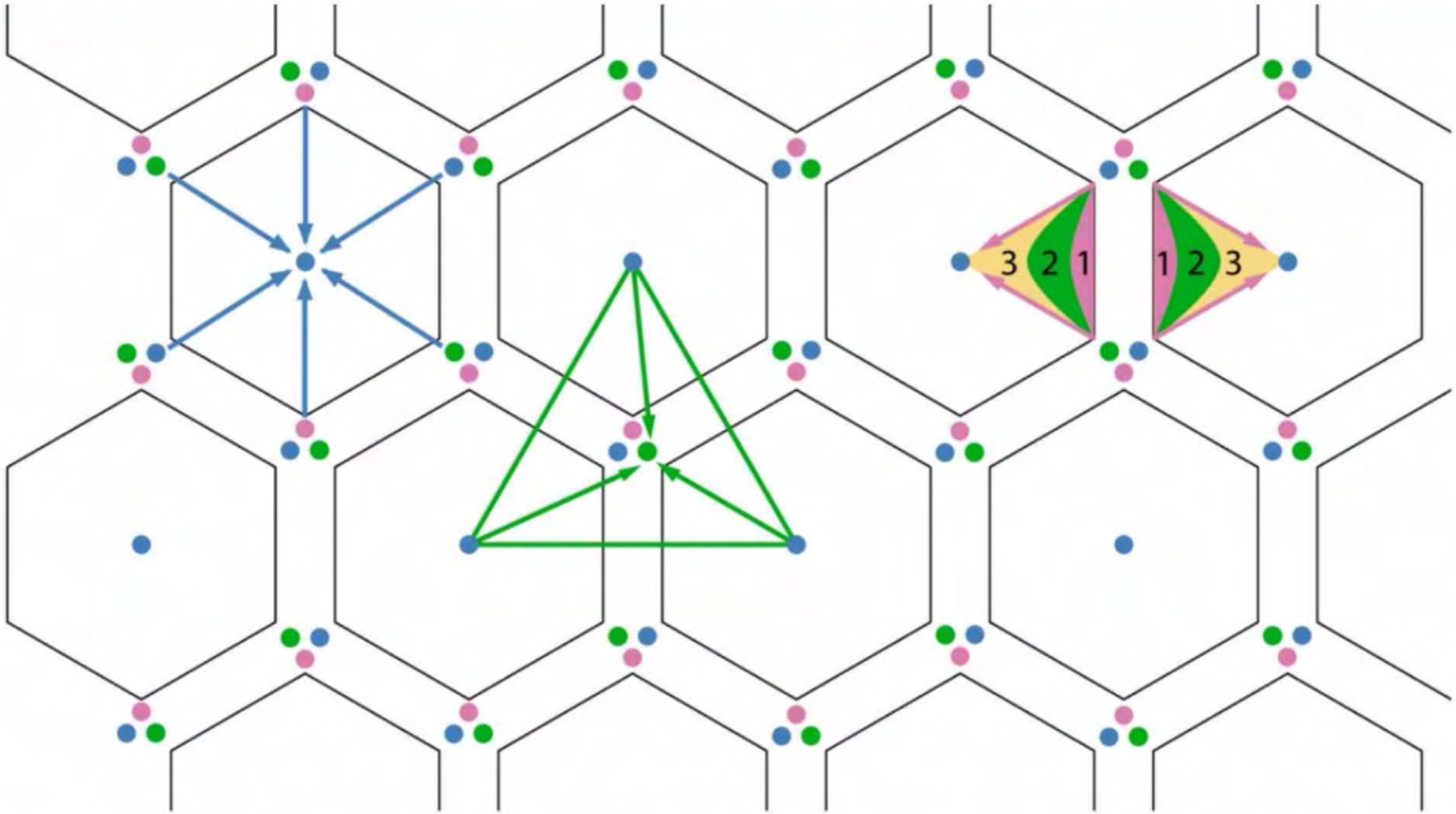
▪ Zone 1: the periphery of the hepatic lobule, highest nutrient/oxygen levels

▪ Zone 2: transitional zone

▪ Zone 3: the center of the hepatic lobule, lowest nutrient/oxygen levels

- Most sensitive to ischemic damage

Hepatic acinus



Schematic diagram of the 3 types of hepatic units. Note the portal triads located at the vertices of the hexagonal units and the 3 histological zones within the hepatic acinus.

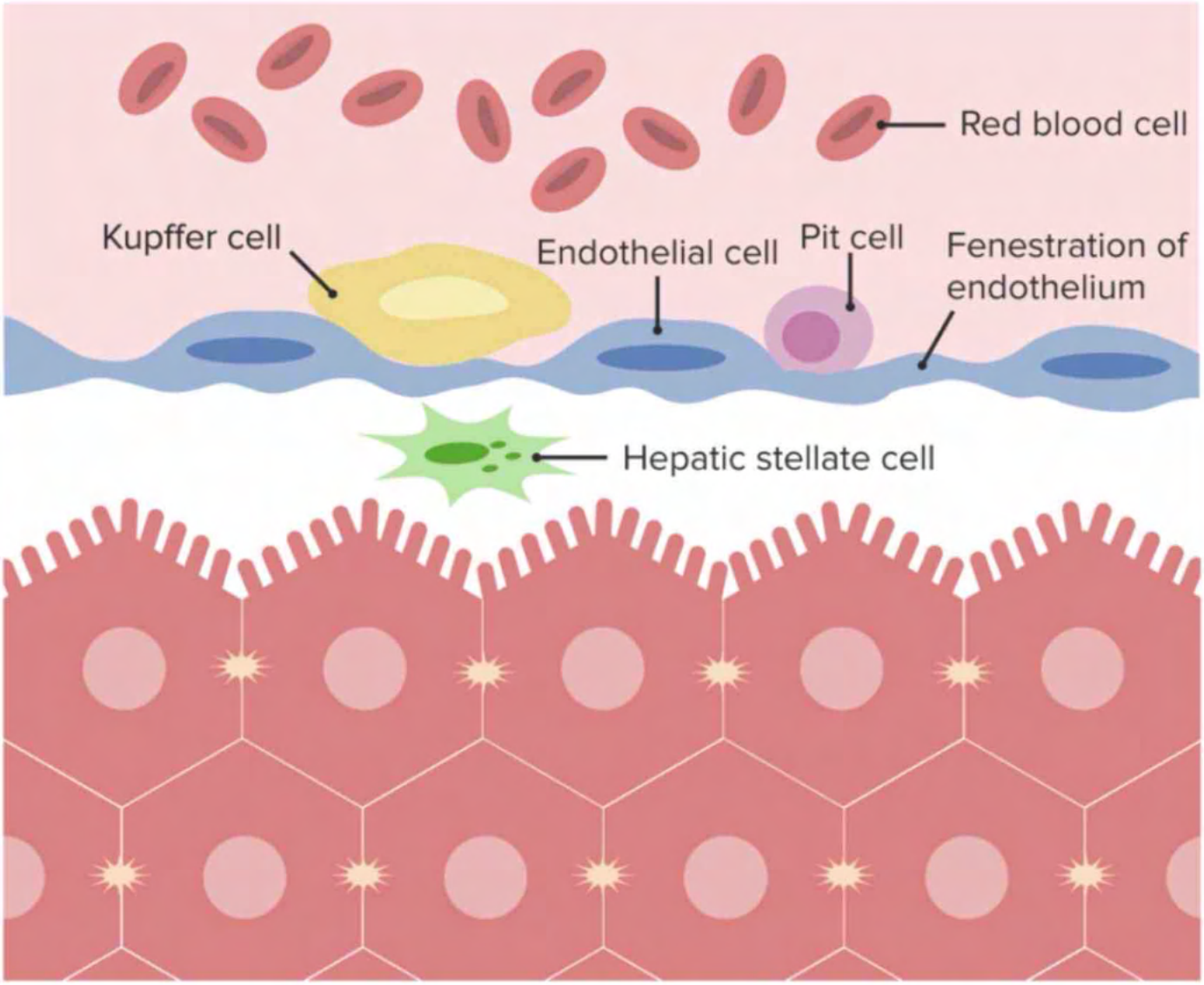
Hepatocytes

- Polyhedral cells organized into plates separated by sinusoids
- Shape and number of the nuclei vary
- Each cell has an apical biliary pole, which drains into one or more bile canaliculi, and a basolateral blood pole, which receives blood from the sinusoids.

Sinusoids

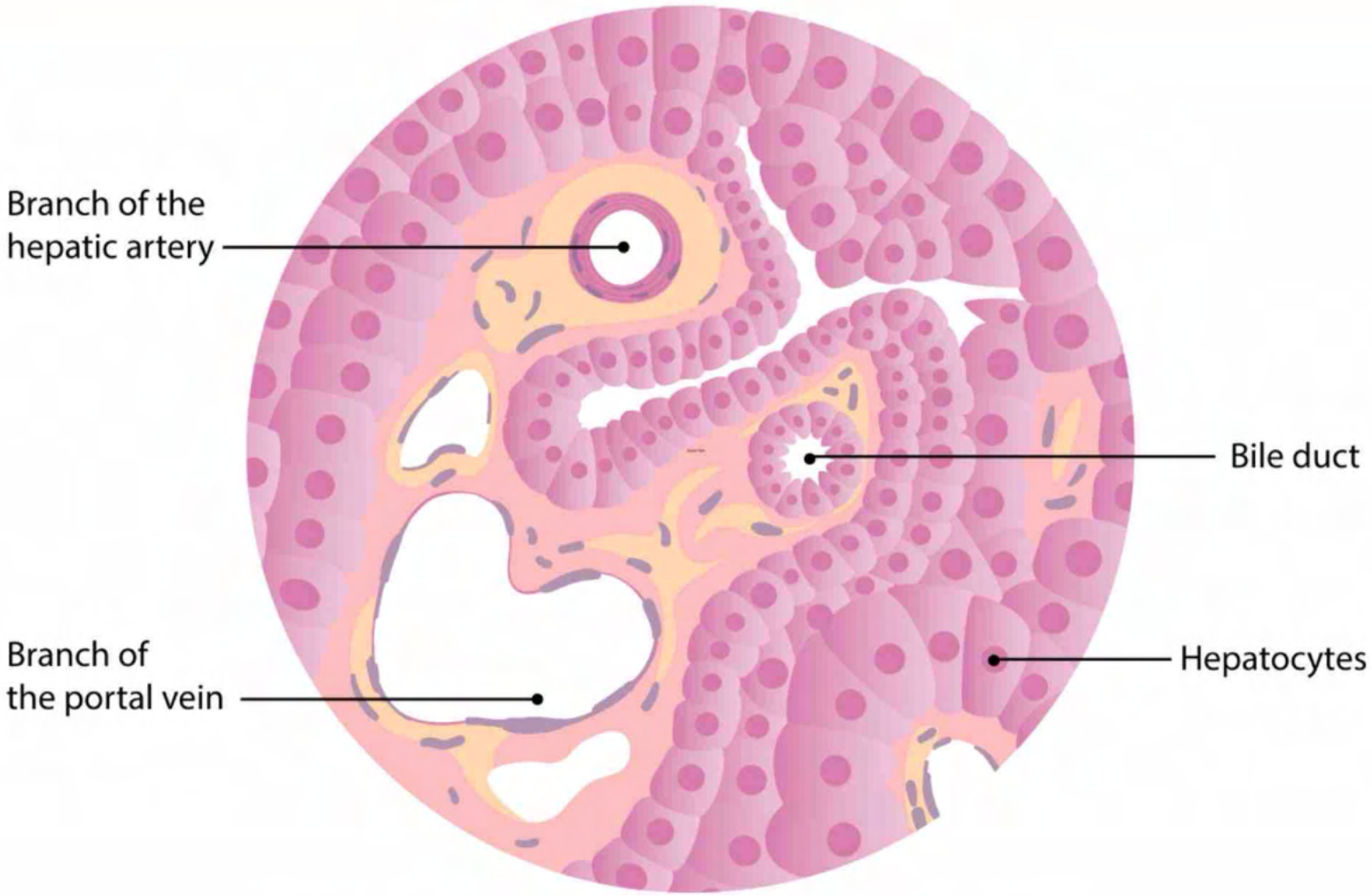
- Capillaries with discontinuous endothelium between hepatocyte plates
- Receive oxygen-rich blood from the interlobular arteries and nutrient-rich blood from the interlobular veins and conducts in toward the central veins
- Kupffer cells: specialized macrophages between the endothelial cells, which phagocytose old or damaged erythrocytes
- Pit cells: liver-specific natural killer cells that adhere to the endothelium, are dependent on Kupffer cells, and have tumor cell-lysing capability
- Perisinusoidal or space of Disse: space filled with blood plasma that lies between the sinusoids and hepatocytes
  - Contains Stellate or Ito cells: store vitamin A and play a role in collagen production (important in the development of cirrhosis)

Sinusoids

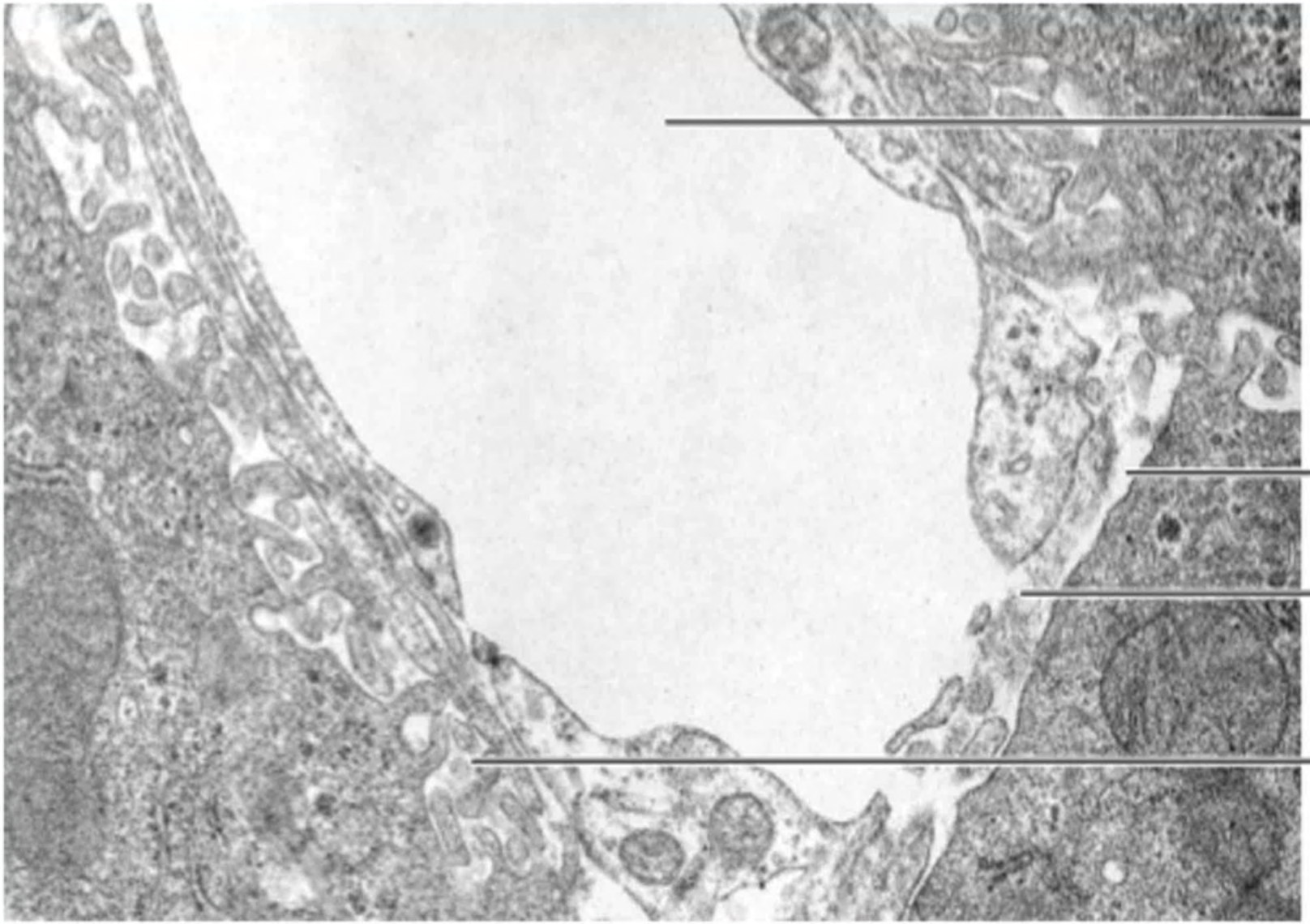


Schematic representation of a sinusoid and plate of hepatocytes separated by the space of Disse. Note the specialized cells of the liver: Kupffer, Pit, and Stellate cells.

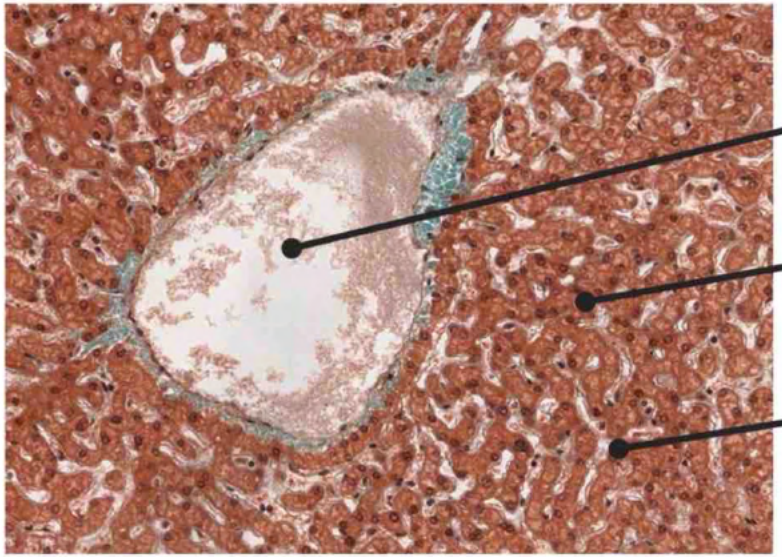
Sinusoids

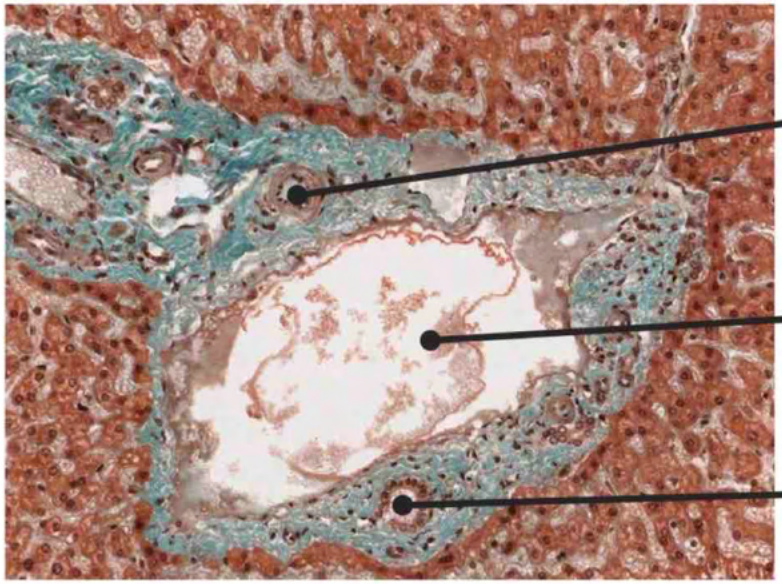

Branch of the hepatic artery
Bile duct
Branch of the portal vein
Hepatocytes

Sinusoids



Sinusoids


Central vein
Hepatocytes
Sinusoids


Hepatic artery
Portal vein
Bile duct

Blood supply

The liver has a special dual blood supply that provides a mix of oxygenated, deoxygenated, and nutrient-rich blood.

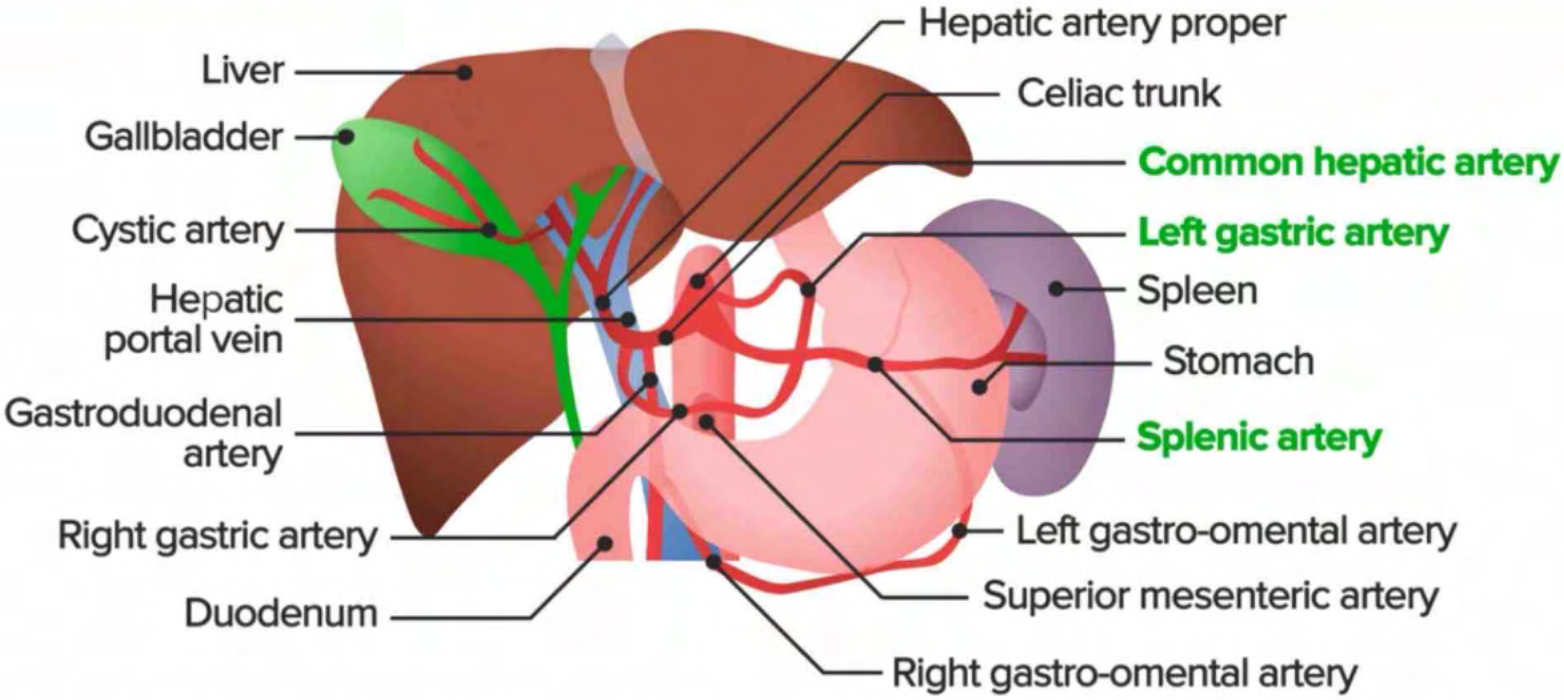
■ Hepatic artery proper (HAP): supplies 25% of the liver's blood supply and carries oxygenated blood

- Abdominal aorta → celiac trunk → common hepatic artery →HAP

■ Portal vein: supplies 75% of blood supply, carries oxygen-poor, nutrient-rich blood drained from the abdominal organs

- Formed most commonly by the union of the splenic and superior mesenteric veins
- Additional tributaries: inferior mesenteric, cystic, and left and right gastric veins

Blood supply



Overview of the abdominal arterial blood supply. The celiac trunk is the 1st major branch of the abdominal aorta. It supplies the liver, stomach, spleen, pancreas, and parts of the esophagus and duodenum with oxygenated blood. The celiac trunk gives off the left gastric artery, splenic artery, and the common hepatic artery. The common hepatic artery divides into the hepatic artery proper, gastroduodenal artery, and right gastric artery, all of which can be seen here.

Venous drainage

■ Sinusoids → central vein of each lobule → hepatic veins → IVC

■ Portosystemic anastomoses: alternative routes of circulation ensuring venous drainage of abdominal organs even if blockage occurs in portal system. Anastomosis between:

- The left gastric veins and the lower esophageal veins
- The superior rectal veins and the inferior and middle rectal veins
- The paraumbilical veins and the small epigastric veins
- The intraparenchymal hepatic branches of the right division of the portal vein and the retroperitoneal veins
- The omental and colonic veins with the retroperitoneal veins
- The ductus venosus and the IVC

Venous drainage

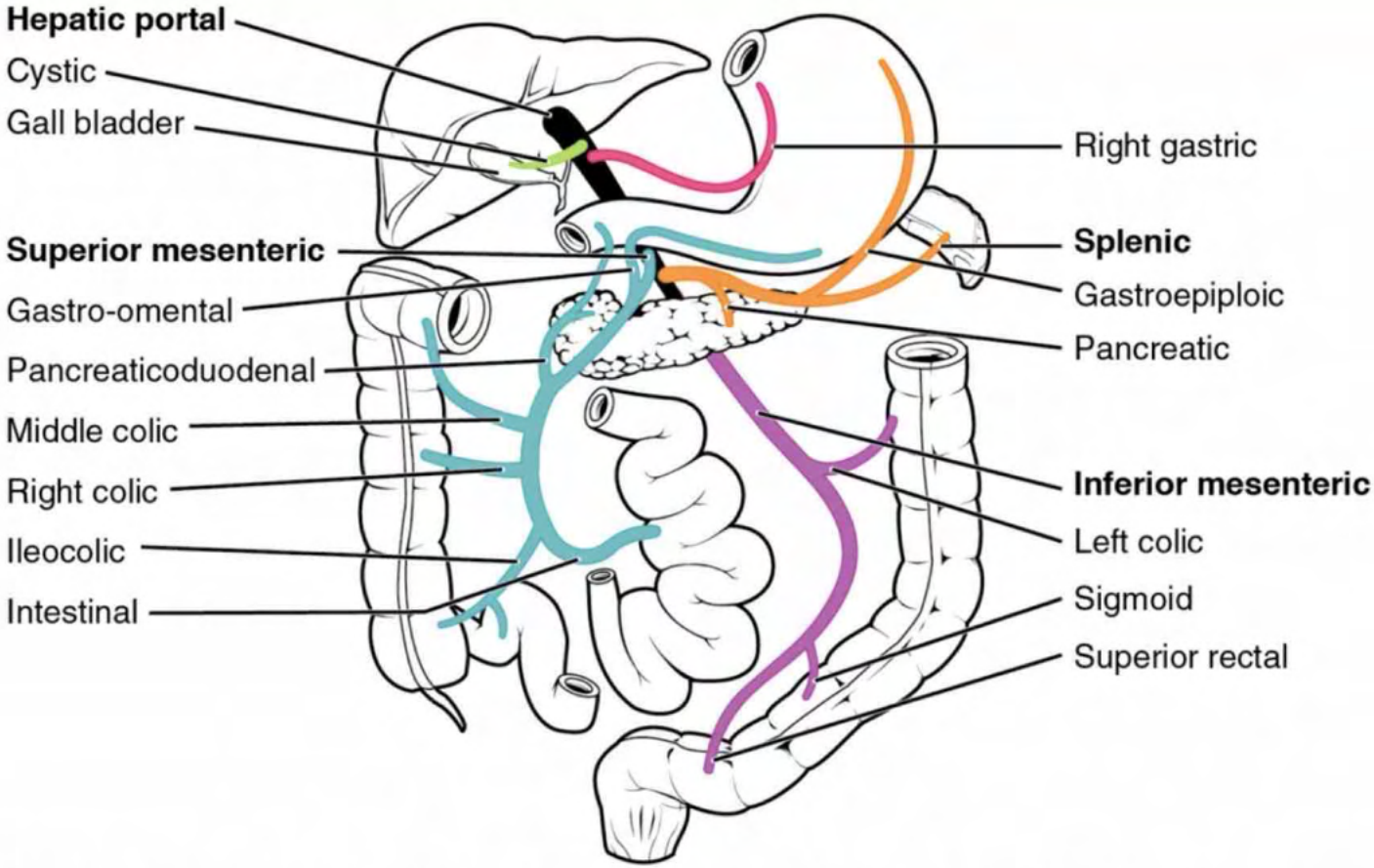


Diagram of the venous portal system. The hepatic portal vein is formed most commonly by the union of the splenic vein and superior mesenteric veins. Other tributaries include the inferior mesenteric, cystic, and the left and right gastric veins. As a whole, the portal system collects the venous drainage of the spleen, stomach, gallbladder, small and large intestines, and pancreas.

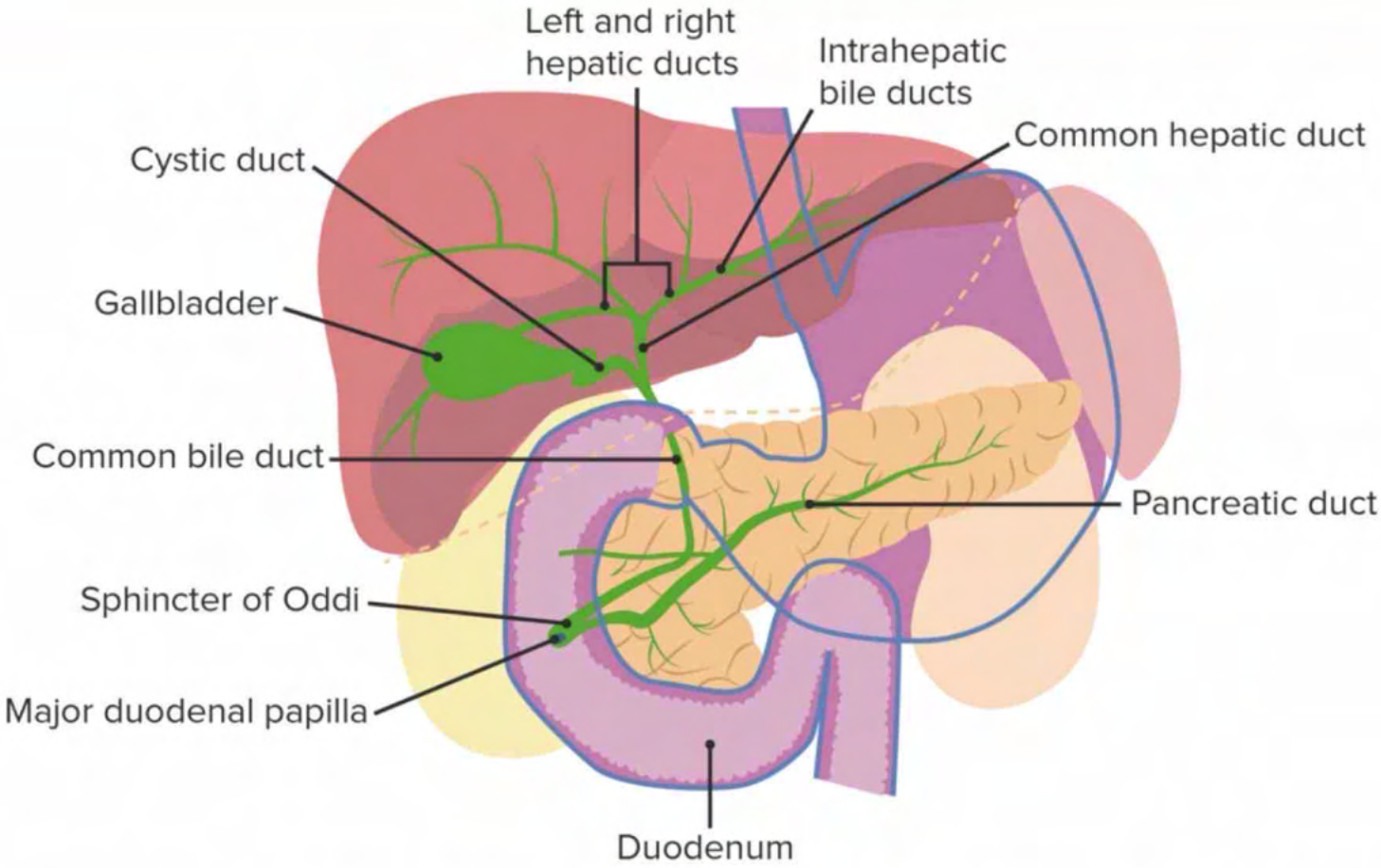
Lymphatic drainage

Hepatic lymph nodes: located around the porta hepatis → celiac cluster of lymph nodes → cisterna chyli (dilated sac that receives lymph from the gastrointestinal [GI] trunk and 2 lumbar lymphatic trunks) → thoracic duct

Innervation

- Hepatic plexus (travels with the hepatic artery and portal vein)
- Sympathetic fibers from the celiac plexus and superior mesenteric plexus
- Parasympathetic fibers from the anterior and posterior vagal trunks
- Glisson capsule innervated by the most inferior intercostal nerves
- HAP has α and β adrenergic receptors innervated by splanchnic nerves

Gallbladder and biliary tract



Bile canaliculi → intrahepatic bile ducts → left and right hepatic ducts → common hepatic duct → common bile duct → duodenum

Functions

Detoxification

The liver eliminates degradation products obtained via resorption from the GI tract. It makes fat-soluble substances water-soluble through enzymatic modification. This allows for excretion via biliary tracts or through urine.

- Cytochrome p450 system: inactivates orally administered drugs via the first-pass effect
- Degradation of ammonia into urea
- Ethanol breakdown
- Breakdown of bilirubin (glucuronidation) → excretion into bile

Metabolism

■ Carbohydrates:

- Gluconeogenesis (synthesis of glucose from amino acids, lactate, or glycerol)
- Glycogenesis (synthesis of glycogen from glucose)
- Glycogenolysis (breakdown of glycogen into glucose)
- Glycolysis (breakdown of glucose into pyruvate, producing adenosine triphosphate (ATP))

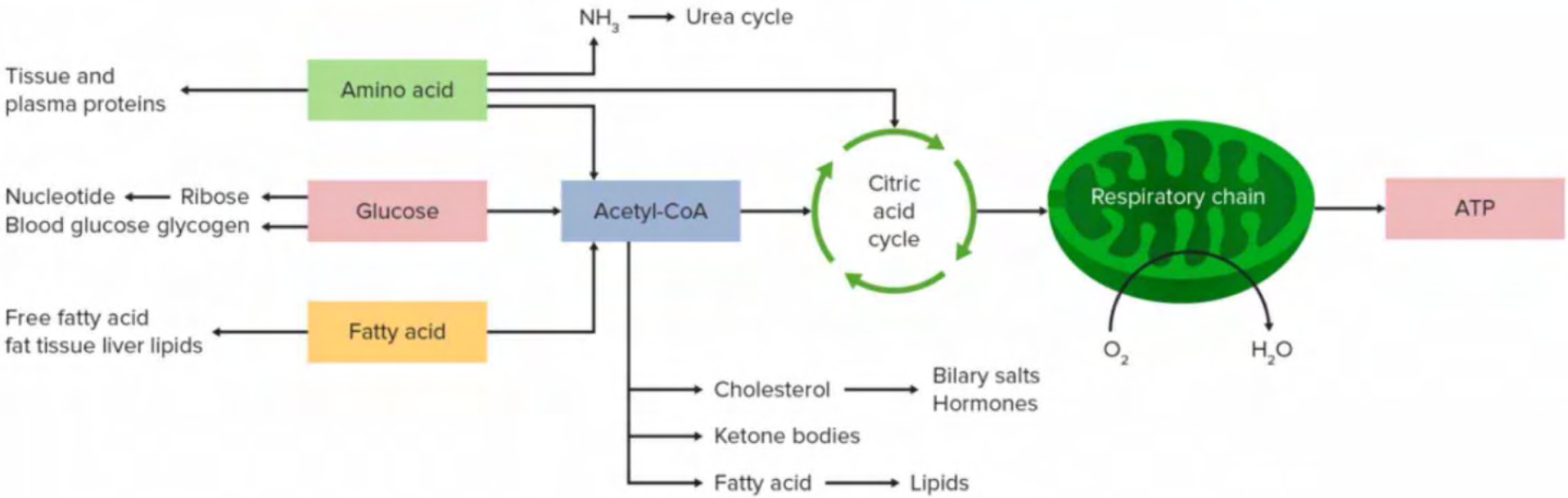
■ Proteins:

- Production of albumin; globulins; acute phase proteins; transaminases; coagulation factors I (fibrinogen), II (prothrombin), V, VII, VIII, IX, X, XI, XII, and XIII; protein C; protein S; and antithrombin
- Amino acid degradation

Metabolism

- Lipids:
  - Lipogenesis (storage of free fats as triglycerides)
  - Ketogenesis (synthesis of ketone bodies)
  - Fatty acid synthesis and degradation
  - Production of bile acids, lipoproteins, and cholesterol

The Metabolism of the Liver



Schematic diagram showing the various metabolic pathways the liver is involved in

Functions

Storage and hormone production

- **Storage**
  - Glycogen
  - Lipoproteins
  - Vitamins A, K, B12, B9 (folate), E, and D
  - Iron and copper
- **Hormone production**
  - Thrombopoietin
  - Insulin-like growth factor 1
  - Angiotensinogen

Functions

Erythropoiesis

- Site of fetal RBC production from week 6 of gestation until birth
- Extramedullary erythropoiesis may occur in adulthood after bone marrow irradiation, in various bone marrow disorders (e.g., myelofibrosis, myelodysplastic syndrome, polycythemia vera), and chronic anemias (e.g., thalassemia, sickle cell disease).

Clinical evaluation

- **Abdominal examination:** The examination of the liver is mostly based on palpation and percussion.
- **Liver function tests:** can be divided into 3 categories:

- Parameters of hepatocellular damage (transaminases, glutamate dehydrogenase, and AST/ALT ratio)
- Parameters of cholestasis (e.g., γ-glutamyl transpeptidase, alkaline phosphatase, and direct and indirect bilirubin)
- Parameters of hepatic synthesis (albumin, cholinesterase, and coagulation factors)

- **Normal abdominal imaging:** Imaging is essential for accurately detecting focal liver lesions (e.g., abscess, tumor), but is limited in detecting and diagnosing diffuse hepatocellular disease (e.g., hepatitis, cirrhosis).

Clinical relevance

Disorders

- **Neoplasms**
  - Benign liver tumors
  - Liver cancer
- **Infections**
  - Viral hepatitis
  - Bacterial infections
  - Fungal infections
  - Parasitic infections
- **Inflammatory disorders**
  - Alcoholic liver disease
  - Nonalcoholic fatty liver disease
  - Autoimmune hepatitis
  - Fitz-Hugh-Curtis syndrome (perihepatitis)
- **Hereditary disorders**
  - Hemochromatosis
  - Wilson's disease
  - Dubin-Johnson syndrome
- **Miscellaneous disorders**
  - Portal hypertension
  - Cirrhosis
  - Budd–Chiari syndrome