• The liver and the pancreas are two large glands that originate from the entoderm of the alimentary tract. The liver is the largest gland in the body, weighing about 1.5 kg in the adult and occupies the hollow cavity of the diaphragm. The liver as the exocrine gland, secretes bile into the duodenum, and as the endocrine gland many kinds of substance that are released directly into the blood stream.

• The pancreas is also a large gland which secretes as an exocrine gland all kinds of enzymes, necessary for the food digestion, and at the same time the pancreas secretes as an endocrine gland \textbf{insulin} and \textbf{glucagon} into the blood stream to control the concentration of glucose in the blood.
• The liver is an accessory gland of the gastro-intestinal tract but it has a remarkable diversity of other functions unrelated to alimentation. The liver is the largest gland in the body, weighing about 1.5 kg in the adult. It is situated in the right upper quadrant of the abdominal cavity with its rounded upper surface conforming to the dome of the diaphragm. Its thin investment of connective tissue, Glisson’s capsule, is covered over most of its surface by peritoneal mesothelium. On its under side, blood vessels enter, and the right and left hepatic ducts leave the organ at its hilus, the porta hepatis.

• The liver has an indispensable role in the metabolism of absorbed nutrients that depends on its unique relationship to the two major subdivisions of the vascular system. It has a dual blood supply, receiving well-oxygenated blood from the general circulation via hepatic artery (25%) and a larger volume of poorly oxygenated blood coming from the intestinal tract via portal vein (75%). Blood from these two sources mingles in the hepatic sinusoids, where the dissolved substances in the blood have direct access to the hepatic cells. The blood leaving the organ is carried via hepatic veins to the inferior vena cava. Thus, interposed between the intestinal tract and the general circulation, the liver receives absorbed nutrients and stores or degrades them to smaller molecules that are released into the systemic circulation for distribution to the other tissues and organs of the body.

• The liver continuously produces bile, a fluid that is ultimately secreted into the duodenum via the common bile duct. As much as 1 liter is produced daily, but the greater portion is diverted to the gall bladder where it is concentrated up to 10-fold and stored until released in response to the ingestion of food. The bile facilitates digestion by emulsifying dietary fats and reducing them to micelles that are more readily absorbed by the intestinal epithelium. In
addition to its exocrine function, the liver synthesizes plasma proteins and delivers them directly into the blood. It also exercises considerable control over the general metabolism of the body through its ability to store carbohydrate in the form of glycogen and release glucose as needed to maintain the normal concentration of this important energy source in the blood. The liver also takes up drugs and other potentially harmful substances absorbed by the intestines and degrades them by oxidation or forms harmless conjugates that are excreted back into the intestines in the bile.

- The organization of the liver is quite different from that of the majority of the exocrine glands. The epithelial cells constituting the liver present a remarkably uniform appearance throughout the organ and structural subunits are not easy to identify. The liver consists of innumerable roughly hexagonal cylinders, about 0.7 mm in diameter and 2 mm in height, called the hepatic lobules, that are enveloped by a thin coat of connective tissue fibers. In the hepatic lobules the parenchymal (hepatic) cells form two-cell-thick cell-cords, that branch and anastomose one another repeatedly and are arranged radially around the central vein and form fenestrated plates. These plates are piled up on top of one another at one-cell-thick intervals, and arranged perpendicular to the longitudinal axis of the lobule. The hepatic cell cords constituting these plates anastomose freely with those of the neighboring plates, so that the hepatic cells constitute three dimensional complex meshwork. The meshes are filled by thin-walled blood vessels, hepatic sinusoids.

- At the corners of these hexagonal areas there is a small triangular area of connective tissue, interlobular connective tissue, enclosing a small bile duct, a branch of the hepatic artery, and a branch of the portal vein. This complex is called the portal triad or portal area. Lateral branches of these vessels, occurring at short intervals along their length, confluent with hepatic sinusoids and drain into the central vein. The fenestrated plates of hepatic cells are, thus, exposed to a large volume of blood flowing centripetally in the labyrinthine system into a meshwork of sinusoids. Bile is continuously secreted into a meshwork of intercellular bile canaliculi within the cell plates and flows outward to bile ductules in the portal areas at the periphery.
• This is to show the three-dimensional structure of a hepatic lobule. The red line divides the lower transverse (horizontal) section and the upper longitudinal (vertical) section. In the horizontal section, at each corner there is the portal triad, interlobular bile duct, interlobular artery and interlobular vein; the interlobular artery and interlobular vein flow into the hepatic sinusoids which drain into the central vein. The intercellular bile canaliculi running centrifugally throughout the axial portion of the hepatic cell cords empty into the interlobular bile ducts at the periphery of the hepatic lobule. These interrelationship is also recognized in the vertical section. The central vein becomes sublobular vein after leaving the lobule.
• This is a general view of human liver; hepatic cells are stained uniformly deep red. At center of this figure one central vein, and at lower right and lower left interlobular connective tissues, portal areas, are seen. In human, interlobular connective tissues are poorly developed so that hexagonal contour of the hepatic tubules is difficult to perceive.
• The upper edge is the connective tissue of the hepatic capsule, beneath it is the parenchyma of the liver consisting of uniformly red stained hepatic cell cords. The meshes of the meshwork of the hepatic cell cords are filled by hepatic sinusoids. They appear as rents between the cell cords. In this figure, no hepatic lobule is identified.
• In the pig liver, as the interlobular connective tissue is very well developed, the boundary of each lobule is conspicuously recognized. In this figure the boundary of the hepatic lobules is distinct. The large lobule locating at center right is sectioned oblique longitudinally. At the right edge of this lobule the portal triad is conspicuous.
• Masson-Goldner (M-G) stain stains the connective tissue fibers deep green. Therefore in this specimen the boundary of each hepatic lobule is evident.
This figure shows one hepatic lobule, distinctly enclosed by the interlobular connective tissue. At center opens a central vein. The hepatic sinusoids appear as rents among the hepatic cell cords. The red stained small substances are erythrocytes in the sinusoids.
At lower left opens a central vein (Vc), from which radiate the hepatic cell cords and hepatic sinusoids. At the right edge is the portal area, containing an interlobular vein (Vi) and interlobular bile ducts. The interlobular artery is not perceived in this magnification. The radial arrangement of hepatic cell cords as well as sinusoids is distinctly seen.
At center opens a central vein, around which the radial arrangement of the hepatic cell cords and sinusoids is evident. Interlobular connective tissues at the right, upper left and lower left indicate the boundary of this lobule.
In this figure, the central vein (Vc) and sublobular vein (Vs) are shown. Into the Vc open the sinusoids whereas Vs has a connective tissue covering and no direct connection with sinusoids.
• Higher magnification of 12-02. At center traverses a central vein (Vc), opening at its right end into a sublobular vein (Vs). At the left end of this central vein open several sinusoids. The hepatic cell cords stains homogeneously deep red.
At upper right and upper left the interlobular connective tissues containing the interlobular vein (Vi) limit the lobule. At lower right is a central vein opening into the sublobular vein (Vs).

Higher magnification of this vein is shown in 12-12.
• Higher magnification of 12-11.
• At center a short central vein (Vc) traverses and opens into the sublobular vein (Vs) at the right end. Into this central vein flow several hepatic sinusoids at the left end. The meshwork of the hepatic cell cords are clearly recognized.

- At center is a transverse section of the central vein (Vc), into which opens a hepatic sinusoid (arrow). The relationship of the hepatic cell cords and hepatic sinusoids is clearly recognized. In the sinusoids erythrocytes are scattered.
In the middle of this figure is a triangular interlobular connective tissue, staining light pink, in which a large and a slender interlobular veins (Vi 1 and Vi 2) are seen. Above Vi 1 there are two interlobular arteries, appearing as deep red circles, and two lymphatics (arrows) are recognized. Right to the artery is an interlobular bile duct. The hepatic cells surrounding the interlobular connective tissue are smaller and deeper red stained than the other hepatic cells.
• Higher magnification of an interlobular connective tissue. In the middle a Y formed interlobular vein (Vi) is evident; right to this there are an interlobular artery (A), a lymphatic (L) and a thick (long arrow) and several thin (short arrows) interlobular bile ducts. The thin ducts may be the canals of Hering. The hepatic cells surrounding this connective tissue are smaller and deeper red stained than the other hepatic cells.
• This is to show the smallest interlobular connective tissue, containing only a small interlobular vein and a small interlobular bile duct. Among the hepatic cells there are cells of two nuclei and also cells of tetraploid nuclei (arrows).
As in this specimen collagen fibers stain green, the interlobular connective tissue and sinusoids, encircled by reticular fibers, are easily discerned. In the interlobular connective tissue an interlobular vein (Vi), an interlobular artery (arrow) and several interlobular bile ducts are seen.
In this specimen hepatic cells stain red, reticular fibers encircling the sinusoids, green and erythrocytes in the sinusoids, deep reddish orange. The relationship of hepatic cell cord and the sinusoids is very clear. The cell boundary of the hepatic cells is indicated by the bile canaliculi.
As this specimen was freshly fixed, the space of Disse is not widened. The reticular fibers encircling the sinusoids attach to the hepatic cell cords. In the sinusoids there are numerous Kupffer cells containing carbon particles.
• In the middle one central vein traverses throughout the field. Into this vein flow numerous sinusoids from upper and lower sides.

12-20. V. centralis, longitudinal section 1. Human, MG stain, x 40.
Higher magnification of 12-20. Confluences of sinusoids into the central vein (arrows) are clearly recognized.
• At middle right a sublobular vein (Vs) traverses rightward, whose wall consists of collagen fibers without any discontinuation. Into its left end flows a central vein lower right wards. Around these the meshwork of the hepatic cell cords and sinusoids are clearly recognized.
• This is a longitudinal section of a sublobular vein (Vs), whose lumen is bordered by endothelium and underlying collagen fibers. No sinusoid flows directly into the sublobular vein.
• This is to show the fine structures of the hepatic cell cords and sinusoids, based on the electron microscopic findings.

• Hepatic cells constitute the two-cell-thick cell cords. A bile canaliculus is a minute channel, 0.5 ~ 1.5μm in diameter, located midway along the interface between adjoining hepatic cells. This starts at the central portion of the hepatic lobule and runs to its periphery where it drains into the interlobular bile duct, via a thin short ductile, called the canal of Hering. As the hepatic cell cords form three-dimensional meshwork, these canaliculi also form a meshwork within the plates of hepatic cells. Owing to the branchings and anastomosing of the cell plates the meshwork of the canaliculi is continuous throughout the lobule.

• The basal surface of the hepatic cells facing the sinusoids is provided with numerous microvilli. The hepatic sinusoids are wider than capillaries and their walls conform to the surface of the plates of hepatic cells on either side but are separated from them by a narrow space, called space of Disse.

• The endothelium of the sinusoids is extremely thin and perforated by innumerable minute pores of various size and underlay with reticular fibers.

• The blood coming into the sinusoids from interlobular veins and from interlobular arteries flows centripetal and drains into the central vein and during the flow the exchange of substances between blood and hepatic cells
takes place.

- Within the sinusoids there are Kupffer cells, that show the active phagocytosis. They are situated on the surface of the endothelial cells but without desmosomes or other specializations for cell-to-cell attachment. One more type of cells is found in the perisinusoidal space, namely, space of Disse. These cells show no phagocytosis but store lipid droplets in the cytoplasm. They are called “fat-storing cells of Ito” or vitamin A-storing cells.
In the middle traverses one hepatic cell cord and at its axial portion the minute bile canaliculus runs longitudinally (arrow). In this specimen the space of Disse is widened as post mortem artifact (double arrows).
In this figure hepatic cell cords form a meshwork. Transverse sections of bile canaliculi are evidently recognizable (arrows).
• In this specimen bile canaliculi are visualized by Golgi’s silver impregnation. The zig-zag course of the bile canaliculi and their branchings and anastomosings are evident.
• At lower center a canal of Hering (arrow) attaches to the hepatic cell cord where the lumen of the canal continues with bile canaliculus. At lower left corner one more canal of Hering is seen.
• At center the lumen of the canal of Hering (arrow) continues with a bile canaliculus of the hepatic cell cord. At lower right corner a longitudinally sectioned canal of Hering is seen.
• In this specimen reticular fibers are visualized by Suzuki’s silver impregnation method and thereafter counter-stained with Kernechtrot. As the reticular fibers underlie the endothelium of sinusoids, the relationship between the hepatic cell cords and sinusoids is clearly understood. The radial arrangement of hepatic cell cords and sinusoids around the central vein is evident.
Higher magnification of 12-30. At lower center is the central vein (Vc), into which four sinusoids open. As this monkey was freshly fixed, the space of Disse is not recognized.
• When an animal is infused tripan blue suspended in saline into the vein, cells of phagocytosis function incorporate the tripan blue and thereby they are visualized. This method is called “vital stain”. In the liver the Kupffer cells are visualized by this method. In upper left, lower left and middle right areas of this figure large cells containing the substance of dark blue color are seen in the sinusoids; they are the Kupffer cells.
Higher magnification of 12-32. The large cells containing the substance of dark blue color in the sinusoids are the Kupffer cells.
• In this specimen vital stain was performed with India ink. The Kupffer cells incorporate particles of India ink are more conspicuous than in 12-32 and 12-33.
In this specimen, because of thinness of the section, about 0.5μm thick, relation between hepatic cell cords and sinusoids is clear.
Higher magnification of 12-35. In this figure bile canaliculi are indicated with arrows. The endothelium of sinusoid is extremely thin and the narrow space of Disse is clearly recognized. In the sinusoid there is a Kupffer cell containing phagosomes (double arrows).
Hepatic cells densely contain the glycogen granules but in usual specimens they are dissolved and disappeared. This specimen was fixed with 100% alcohol so that they are well preserved and deep red stained by Best’s carmine stain.
• In embryo the liver is a hemopoietic organ rather than an alimentary organ. The space between the hepatic cells and sinusoids, later space of Disse, is filled by mesenchymal cells, which proliferate actively and produce all kinds of blood cells.

• This figure shows a part of the hemopoietic liver. At lower middle is the central vein (Vc), from which hepatic cell cords, deep red stained, and sinusoids radiate. The hepatic cell cords are relatively slender whereas the sinusoids are wide. Around the hepatic cell cords crowd small round nuclei, darkly blue stained; they are the hemopoietic cells.
Higher magnification of 12-38. Around the hepatic cell cords, stained deep red, crowd the hemopoietic cells of various sizes and stainabilities. Mainly they are in the space of Disse, but some are in the sinuoids. The erythrocytes generate here also.
The gallbladder is a pear-shaped, hollow sack closely attached to the posterior surface of the liver. It consists of a blindly ending fundus, a body, and a neck, which continues into the cystic duct. It measures approximately 10 by 4 cm in adult man. The upper surface attaches to the liver with connective tissue whereas the lower surface faces to the abdominal cavity and covered by peritoneum.

- The wall consists of a mucous layer consisting of a surface epithelium and a lamina propria, a layer of smooth muscles and a perimuscular connective tissue. The mucous layer is thrown into frequent folds.
- As this animal was treated by perfusion fixation, structures of the gallbladder is well preserved. Numerous folds of the mucous membrane thrown into the cavity are evident.
The epithelium consists of a single layer of tall columnar cells, showing no specialization on the free surface. They have oval nuclei located toward the base of the cells, and are underlain by a distinct basement membrane. The lamina propria consists of a very loose connective tissue.

The pancreas consists of an exocrine gland and an endocrine gland; the former elaborates about 1200 ml of digestive juice a day, containing all kinds of digestive enzymes, and the latter secretes hormones which control the carbohydrate metabolism of the body.

The exocrine pancreas is a compound acinar gland whose lobules are bound together by loose connective tissue, through which run blood vessels, nerves, lymphatics, and excretory ducts. The pancreatic acini consist of a single row of pyramidal epithelial cells enclosing a central lumen and resting upon a basal lamina supported by delicate reticular fibers. The acinar cells show striking differences in the various stages of secretion. In usual sections stained with H-E stain, the basal parts of the acinar cells stain dark blue-violet, while the secretory granules, zymogen granules, in the apical part of the cells appear bright orange-red. After releasing the secretory granules, after taking meal, secretory granules disappear and the area staining dark violet widens to the apical part of the cells and nuclei locate more centrally.

The duct system of the pancreas consists of the intercalated ducts and the simple ducts. The lumen of each acinus is continuous with the lumen of small duct bounded by the centroacinar cells. They are easily distinguished by their pale staining in histological sections. Proximally they drain into the thin duct, called intercalated duct, consisting of simple cuboidal or flat cuboidal epithelial cells with pale blue staining cytoplasm. They are turned into the
interlobular duct consisting of simple cuboidal epithelial cells. They repeatedly join one another and become thicker and finally as the ductus pancreaticus, confluents with the ductus hepaticus forming the ductus choledocus and drains into the duodenum.
• This is to show the general structural feature of the pancreas. The pancreas is as a whole enveloped by a thin layer of loose connective tissue which enters into the organ dividing the parenchyma numerous lobes and lobules. These connective tissues are called interlobar and interlobular connective tissue, through which run blood vessels, nerves, lymphatics and excretory ducts. The pancreatic parenchyma stains dark blue-violet uniformly and at such low power magnification the endocrine units are not perceived.
• At this magnification the endocrine units, pancreatic islets, are recognized. Among the exocrine acini three islets are scattered.
• At center locates one pancreatic islet, surrounded by a number of exocrine acini. The epithelial cells of the islets are small polyhedral in shape and constitute cell cords branching and anastomosing one another to form three dimensional meshwork. Their cytoplasm stains usually faint pink.

• The exocrine acini surrounding the islet show typical features of staining, basal portion of the acinar cells stains deep blue-violet and apical portion brilliant pink-red; this is because of a lot of zymogen granules.
Stained with basic dye, toluidine blue, the basal cytoplasm of the acinar cells stains intensely dark blue, owing to the presence of highly developed rER in this part of the cell. The nuclei locate near the basement membrane and supranuclear cytoplasm is densely filled by the coarse secretory granules stained deep red with eosin. At center, in the middle of several acini there are several long elliptic nuclei stained faint blue; they are called the centroacinar cells (arrow).
In this specimen zymogen granules are all released so that the structure of acini are well observed. At center two large acini are penetrated by one intercalated duct, which is thin and consists of simple low cuboidal or flat epithelial cells with faintly staining cytoplasm. In the middle of this figure an intercalated duct enters the acinus and opens into the acinar lumen (arrow), then goes further leftward and penetrates the second acinus. The epithelial cells of intercalated duct are turned into the centroacinar cells enclosing the lumen. The basal portion of each acinar cell stains deep violet and contains a round nucleus, whereas the supranuclear portion stains faint violet and cell boundary is distinct because of the absence of the zymogen granules. At upper right corner a transverse section of an intercalated duct is seen.
In this specimen the supranuclear portion of the acinar cells is densely filled by zymogen granules staining deep red. At center is one large acinus with centroacinar cells. To its left side attaches one thin intercalated duct (arrow) consisting of flat cuboidal epithelial cells.
• An intercalated duct traverses from right to left and enters into a large complex of acini, locating at center. During the penetrating, epithelial cells are turned into the centroacinar cells and at its left end it divides into two and ends as the centroacinar cells at the acinar lumen. As this specimen is about 5μm thick such microscopic features are well recognized. Compare with 12-49.
• An intercalated duct runs transversely from right to left and end in an acinus as centroacinar cells. As this specimen is about 30μm thick, microscopic features are not so well observed as in 12-48. But the intensely basophilic basal cytoplasm and zymogen granules filling the supranuclear cytoplasm and staining deep red are conspicuous.
• The pancreatic islets, also called islets of Langerhans, contain three principal types of cells, each secreting a different hormone: α-cells (A-cells) secreting glucagons; β-cells (B-cells) secreting insulin; and δ-cells (D-cells) secreting somatostatin. These cannot be distinguished in routine H-E stained preparations. Methods have been devised for selective staining for these cell types. The α-cells contain acidophil granules; the β-cells, basophil granules; and D-cells, granules demonstrated by Hellman’s silver impregnation method. Because the granules in the β-cells are glycoprotein and water soluble, their preservation is not easy using the routine fixatives. Specimens from 12-53 to 12-61 were fixed with Bouin’s fluid, which is effective for the fixation of glycoprotein.

• In this figure an islet is shown at center. The islet cells are arranged in irregular cords forming a meshwork, intermingled with capillary meshwork, and are stained paler than surrounding excretory acini. No secretion granules in the islet cells can be seen in this routine H-E preparations. The islets are more or less completely demarcated from the surrounding acini by a thin layer of reticular fibers.
• This specimen was freshly taken and fixed with Bouin’ fluid, so that the microscopic features are well preserved; however the identification of the islet cells is not possible.
• In this section α-cells stain selectively red and connective tissue fibers appear green.

- In this specimen β-cells are selectively dark blue stained.
• In this specimen β-cells are stained selectively dark blue with Victoria blue and α-cells, red with phloxin. An arrow indicates the colorless cells; they are D-cells.
• Higher magnification of 12-54. Arrows indicate three cells with colorless cytoplasm, that are D-cells. As in the previous specimen, α-cells stain red with phloxin and β-cells, dark blue with Victoria blue.
• This section was stained first with Victoria blue and phloxin and thereafter with light green to visualize the connective tissue fibers. Higher magnification of the small portion at top center is shown in 12-57 and 12-58.
At this magnification, $\alpha$-cells and $\beta$-cells are well distinguished. An arrow indicates a cell with colorless cytoplasm.

- Higher magnification of 12-57. An arrow indicates a cell with colorless cytoplasm. The identification between the $\alpha$-cells and the $\beta$-cells is clear.
In this section two islets of Langerhans are shown. The neighboring section with this was treated with Hellman’s silver impregnation method, which visualizes the D-cells selectively. Compare these two sections.
• In this specimen D-cells are all blackened. The distribution of the D-cells in each islet varies largely. Higher magnification of the left islet is shown in 12-61.
• Higher magnification of 12-60. The cytoplasm of the D-cells are filled with coarse granules, blackened by this method. Distribution of D-cells is quite random.
In this preparation α-cell are demonstrated by antiglucagon reaction after Nakane.

This specimen was made by Dr. S. Fujii.
• In this specimen D-cells are demonstrated by antisomstostatin reaction after Nakane.
• This specimen was made by Dr. S. Fujii.