Practical classes 4_ Endocrine system

SUPRARENAL GLAND

The adrenal (suprarenal) glands are located retroperitoneally at the upper pole of the kidneys. The parenchyma of the adrenal glands is divided into cortex and medulla. The **cortex** is larger and occupies 4/5 of the parenchyma. The cortex is composed of trabeculae of epithelial cells surrounded by a small amount of reticular connective tissue with blood sinusoids. The cortex can be divided into three zones according to the shape of the trabeculae. Just under the capsule there is the **zona glomerulosa**, whose arcuate trabecules resemble glomeruli. The endocrine cells of this layer produce mineralocorticoids, including aldosterone. The most striking and widest is the **zona fasciculata**; its cords run parallel like 'fascicles'. The fascicles are composed of large, pale, polyhedral cells with a centrally located nucleus. Because their cytoplasm contains numerous lipid droplets, these cells are referred to as spongiocytes. Spongiocytes produce and release glucocorticoids. The **zona reticularis** is the deepest layer of the cortex, whose anastomosing trabeculae run in different directions and resemble an intricate network (Lat. *rete*, network). The epithelial cells of this zone have a darker cytoplasm containing lipofuscin. The cells produce androgens, especially dehydroepiandrosterone. All of the above hormones are examples of steroid hormones. Therefore, the ultrastructure of the endocrine cells of the adrenal cortex also corresponds to that of steroid-synthesizing cells.

The **adrenal medulla** has a different structure. It contains **chromaffin cells**, which are formed by the transformation of sympathetic neurons. The chromaffin cells are polyhedral in shape and their body is without projections. Transmission electron microscopy detects secretory granules and rough endoplasmic reticulum in the body of these cells. Two subpopulations of chromaffin cells produce catecholamines: one produces epinephrine (adrenaline) and the other norepinephrine (noradrenaline). A more detailed description of the adrenal glands and their hormones is provided in the e-course Endocrine System II.

The different histological structure of the cortex and marrow is explained by a different origin of both parts. The cortex is derived from the coelomic epithelium (i.e. it is of mesodermal origin), whereas the medulla develops from the neuroectoderm of the neural crest. During embryonic development, the two parts converge and the cortex subsequently surrounds the medulla.

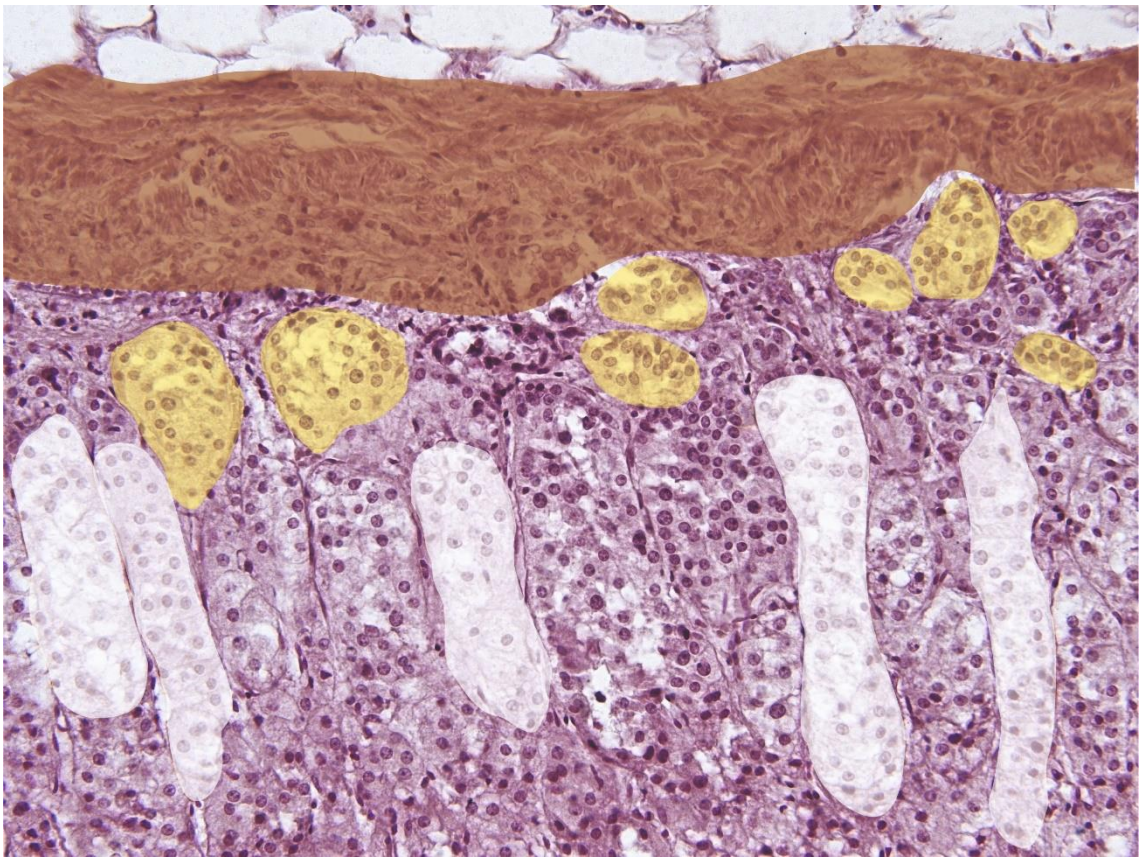
ORIENTATION IN THE SLIDE

This slide of adrenal (suprarenal) gland has a characteristic triangular shape. The entire organ is seen here, which is externally covered by a dense connective tissue **capsule** surrounded by **adipose tissue**. These structures are located retroperitoneally. The tissue beneath the capsule forms the **cortex** of the adrenal gland. At this magnification, a broad belt of light epithelial cells (spongiocytes) corresponding to the zona fasciculata

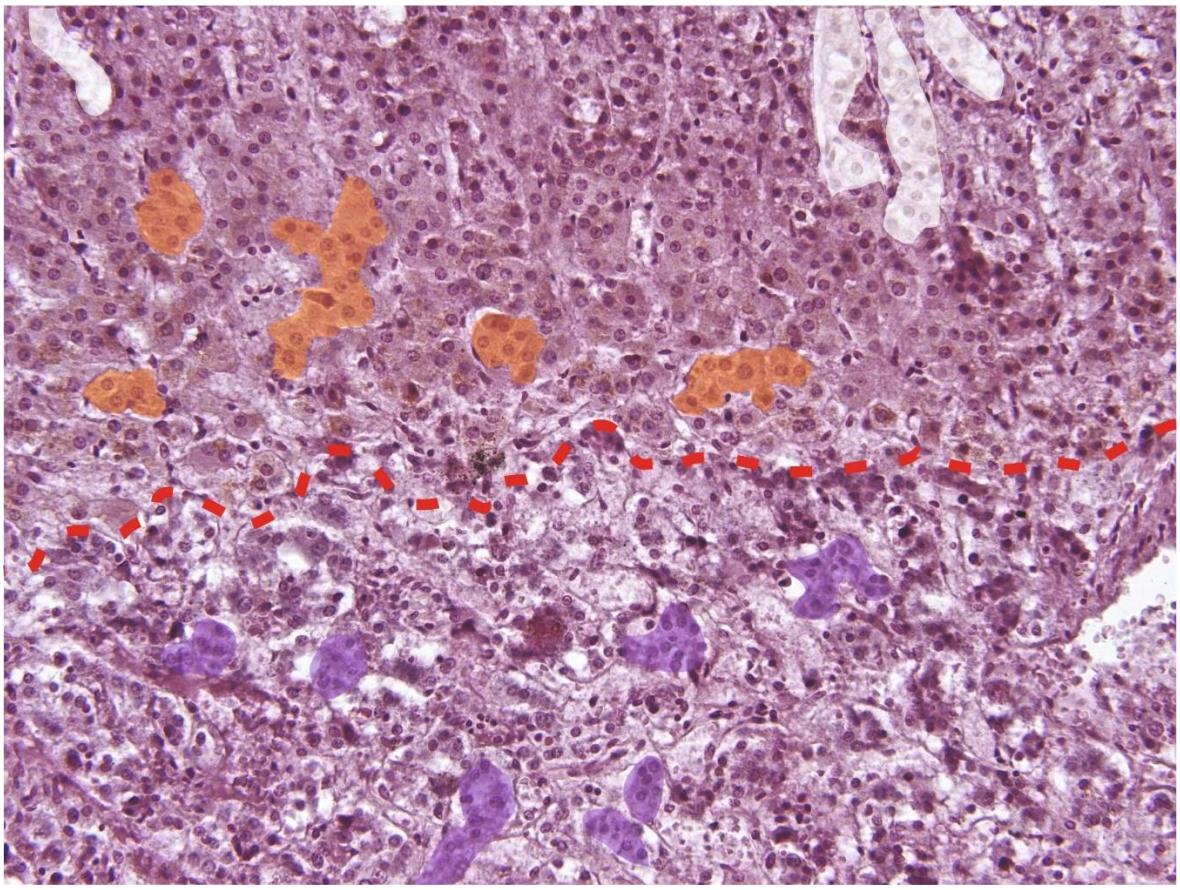
can be seen. On the ohter hand the **medulla** is darker and can be seen in the middle of the wide (i.e. right) part of the organ in an image.

MICROSCOPIC STRUCTURE

Under middle magnification epithelial cells arranged in cords can be found in the cortex. Immediately under the broad capsule sheath of dense connective tissue (brown) are the cords arranged like a glomeruli - the **zona glomerulosa** (shown in yellow in interactive Fig. 2). The width of this layer is relatively small (about one tenth of the cortex thickness). The underlying cords run in parallel (the most prominent "fasciculi" are marked in white) and perpendicular to the surface. Due to their length, this area - the **zona fasciculata** - occupies the largest part of the cortex. This is also where the largest and most striking epithelial cells can be found. Due to the large content of fat droplets, their cytoplasm has a spongy appearance, and therefore these endocrine cells are referred to as **spongiocytes**. Sinusoidal capillaries can be found in the connective tissue between the trabeculae.



Next image shows the boundary between cortex and medulla at the same magnification. In the interactive microphotograph, the course of the boundary is indicated by the red dashed line. Above this line can be seen the trabeculae of epithelial cells without a regular arrangement that form the **zona reticularis**. These cells often contain ageing pigment (lipofuscin) and are therefore brownish in colour. In general, the cells of this zone are darker and the cords of cells with a conspicuous lipofuscin content are shown in orange. Above this zone, parallel arranged trabeculae of zona fasciculata (white) containing light spongiocytes can be seen in some places.



The adrenal **medulla** contains smaller polyhedral endocrine elements called **chromaffin cells**. The clustering of small cells into groups and rays contributes to the medulla appearing darker than the overlying cortex. The most prominent groups of chromaffin cells are shown in purple in the interactive microphotograph. In the spaces between the cells, sinusoidal capillaries can be seen within the reticular connective tissue. Isolated larger cells with light chromatin and a prominent nucleus represent ganglion cells; one or more satellite cells can often be seen at the surface of ganglion perikarya.

THYROID GLAND

The parenchyma of the thyroid gland (*glandula thyroidea*) has an unmistakable microscopic structure, as it consists of follicles filled with colloid. The spherical enclosed follicles reach a diameter of 50-200 µm, so that they are clearly visible in the microscope at low magnification. The colloid appears as an amorphous substance which is PAS reactive. The surface of the thyroid gland is covered by a capsule of irregular dense connective tissue from which the septa emanate and divide the parenchyma into lobules.

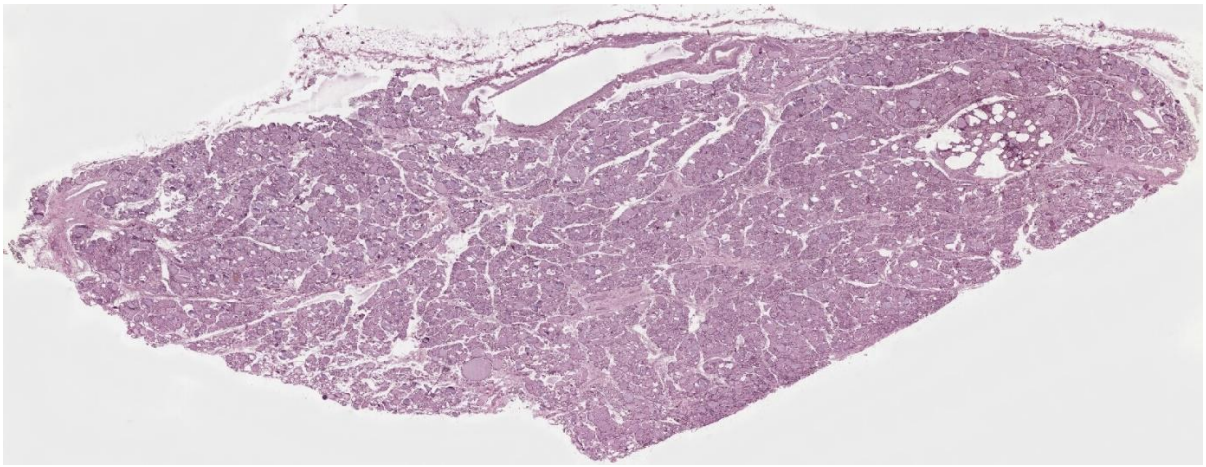
The follicle wall is composed of a single layer of follicular cells that sit on the basement membrane. The height of the follicular cells reflects their functional state; cuboidal cells are most commonly found, but with increased function the cells elongate into columnar cells, while a hypofunctional gland is characterized by flattened **follicular cells**. With the change in the height of the glandular epithelium, the amount of colloid changes (hyperfunction is characterized by small follicles that contain less colloid, whereas

hypofunction is reflected by a high amount of colloid and larger follicles). The cytoplasm of follicular cells has a richly developed rough endoplasmic reticulum and therefore appears basophilic. The Golgi apparatus, mitochondria, lysosomes and numerous vesicles can also be found in the cytoplasm. The basolateral plasmalemma of follicular cells contains a membrane protein, called pendrin, which functions as an ion carrier and allows the uptake of iodine anions (iodides). On the apical surface, these secretory cells produce the glycoprotein thyroglobulin, which is stored inside of the follicle. The follicular cells also resorb the thyreoglobulin through the apical surface to convert it into the active thyroid hormones, triiodothyronine and tetraiodothyronine (thyroxine), which they transport into the blood on the basal surface into the adjacent network of fenestrated blood capillaries that surround each follicle externally. The synthesis of thyroglobulin, thyroid hormones and their function is described in detail in the electronic course for the lecture Endocrine System II.

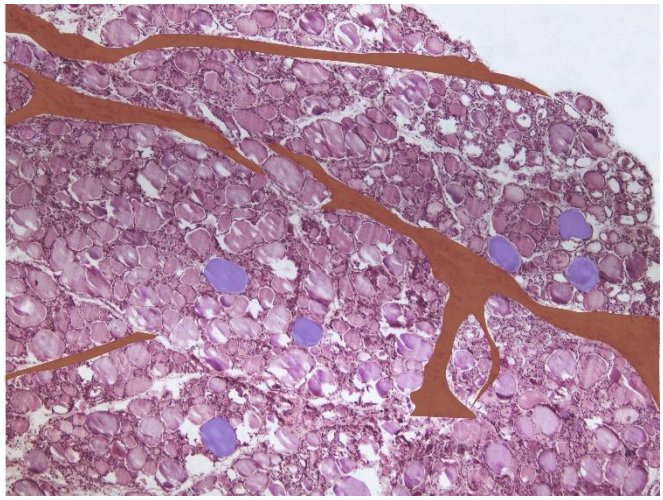
The second population of epithelial cells found in the thyroid gland are the **parafollicular cells** (C cells). These cells are not part of the follicles but are most often found in clusters between them; when included in the follicles, they never reach its lumen. These cells are larger than follicular cells and their cytoplasm is lighter due to the lower content of rough endoplasmic reticulum. Electronmicroscopically, the cisterns of the Golgi apparatus and numerous secretory vesicles can be detected here. These cells also show endocrine activity, as they produce and release the polypeptide hormone calcitonin, which is important for the regulation of calcium and phosphorus metabolism. The function is explained in more detail in the e-course Endocrine System II. Both cell populations of the glandular epithelium have different origins. Follicular cells are of endodermal origin while parafollicular cells are derived from the neural crest.

ORIENTATION IN THE SLIDE

Under small magnification a histological section reveals a structure of a parenchymal organ. The microphotograph captures a larger part of the organ with the **capsule** covering most of the surface (capsule is missing in the lower left part). Adipous connective tissue and large blood vessels can be seen in the capsule at the upper edge. Small **septa** extend from the capsule, dividing the parenchyma of the gland into small **lobules**. The parenchyma itself is relatively compact. However, on close inspection, larger **follicles** filled with colloid can be recognised, which are the most typical microscopic feature of the thyroid gland. The follicles are better seen at higher magnification.

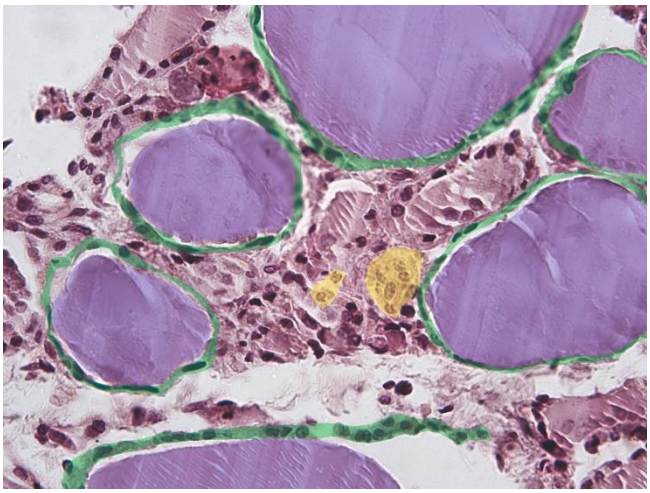


MICROSCOPIC STRUCTURE



The medium magnification allows to clearly identify the thyroid gland, as its parenchyma consists mainly of **follicles** filled with amorphous colloid (marked in blue). The follicles are spherical or oval and their size varies slightly. Their wall is lined by a single layer of cells - but this is better visible at higher magnification. The parenchyma is divided by the course of the septa into small lobules. The **septa** are formed by irregular dense connective tissue and their course is marked in brown. As it is a purely endocrine gland, the septum contains no ducts.

The largest magnification reveals **follicular cells** lining in a single layer the follicle wall. The follicular cells are indicated in green in the interactive image for the largest follicles. In this microphotograph, the follicular cells appear squamous to cuboidal, indicating their lower endocrine activity. The interior of the follicles is filled with **amorphous colloid** (marked in blue). A small slit that appears in the slide between the colloid and the epithelial lining is arteficial (due to tissue shrinkage during histological processing of the tissue). A second population of endocrine cells can be found between follicles - these cells are larger than follicular cells and differ in their chromatin; because of their characteristic location, these cells are referred to as **parafollicular cells** (indicated in yellow).



PARATHYROID GLANDS

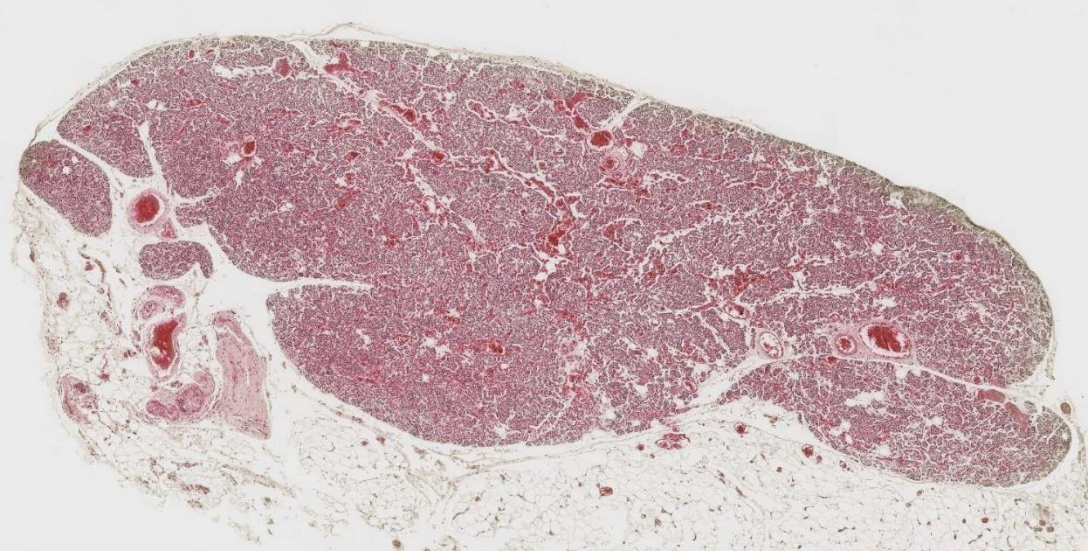
The four parathyroid glands (*glandulae parathyroideae*) are located in the capsule of a dorsal part of the thyroid gland. Each gland is encapsulated; tiny connective tissue septa divide the parenchyma of the gland into tiny lobules. The parenchyma itself consists of epithelial cells arranged in cords or groups. The predominant cells are referred to as chief (principal) cells. The **chief cells** measure approximately 8 µm, have a spherical nucleus and a light cytoplasm (containing glycogen). They produce parathormone, which they deliver from their secretory granules to adjacent fenestrated capillaries. Parathormone acts as a calcitonin antagonist, so that it raises blood calcium levels. The second population of epithelial cells are **oxyphilic cells**. As their name suggests, their characteristic feature is eosinophilia cused by the multiplication of mitochondria in the cytoplasm. Oxyphilic cells

are larger than the chief cells. These cells do not appear until about 10 years of age. They have no secretory granules and therefore show no endocrine activity.

A more detailed description of the parathyroid glands is available in the e-course Endocrine System II. The parathyroid glands are derived from the endoderm of the pharyngeal pouches. The lower pair, the *glandulae parathyroideae inferiores*, derive from the dorsal part of the 3rd pharyngeal endodermal pouches. The upper pair, superior parathyroid glands, is derived from the dorsal portions of the 4th pharyngeal endodermal pouches.

ORIENTATION IN THE SLIDE

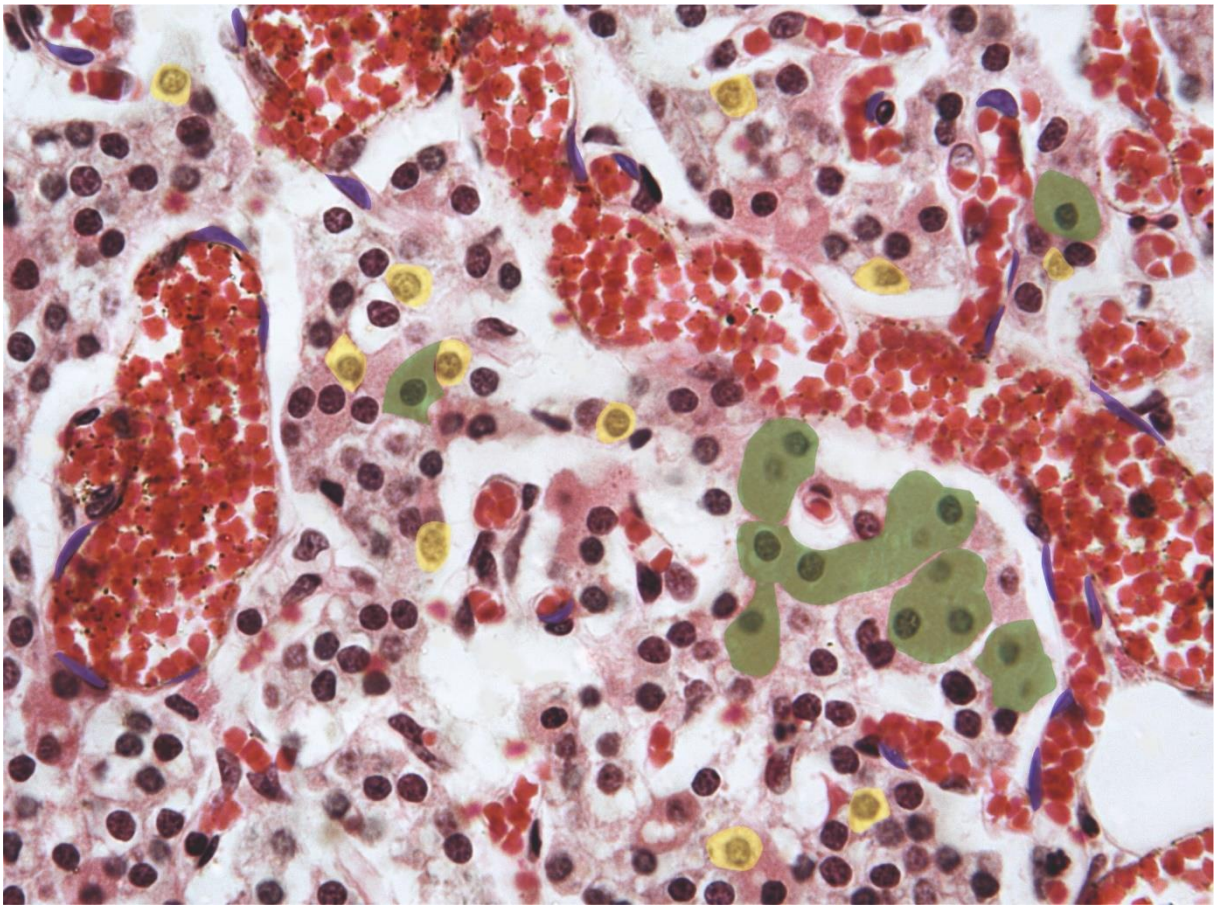
Under small magnification, no typical structures can be found on the slide. The surface is covered by a connective tissue **capsule**, which separates the gland from the parenchyma of the thyroid gland (which may be present in some slides). The capsule projects into relatively thin **septa** which divide the gland into small lobules. The parenchyma itself shows a compact arrangement. Numerous **blood vessels** can be found in septa and parenchyma. In the lower part of the specimen, white adipous connective tissue is observed. In addition to the separate parathyroid gland preparation, this gland can also be found in the slide with the structures of mediastinum or in the slide of the thyroid gland.



MICROSCOPIC STRUCTURE

At the highest magnification, epithelial cells arranged in cords or clusters can be seen in the parenchyma of the parathyroid glands. The space between the cells is filled with a relatively small amount of reticular connective tissue, dominated by numerous blood vessels. **Blood vessels** have a thin wall composed of a single layer of endothelial cells; in the interactive image, the flattened bodies with the nuclei of some endothelial cells are marked in purple. The lumen of the blood vessels is filled with numerous erythrocytes - their characteristic colour and morphology facilitates their identification. Among the epithelial cells of the gland, small polygonal cells with light cytoplasm predominate (some are shown in yellow). Because these cells predominate in the tissue, they are referred to as **chief** (principal) **cells**; these are cells with endocrine activity. Stainability of the cytoplasm varies according to the amount of secretory granules; however, most cells normally show minimal secretory activity due to normal

calcium levels and look like cuboidal cells. The cell nucleus is spherical and chromatin staining, which reflects cell activity, is lighter to darker. These cells are present in the gland from birth. From puberty onwards, **oxyphilic cells** also begin to appear among them. These are larger, their cytoplasm is distinctly eosinophilic and the nucleus is darker (these are not cells with active hormone production). The oxyphilic cells are again arranged in cords or groups (which increase in size with age). In the interactive microphotograph, some typical oxyphil cells are labelled in light green.



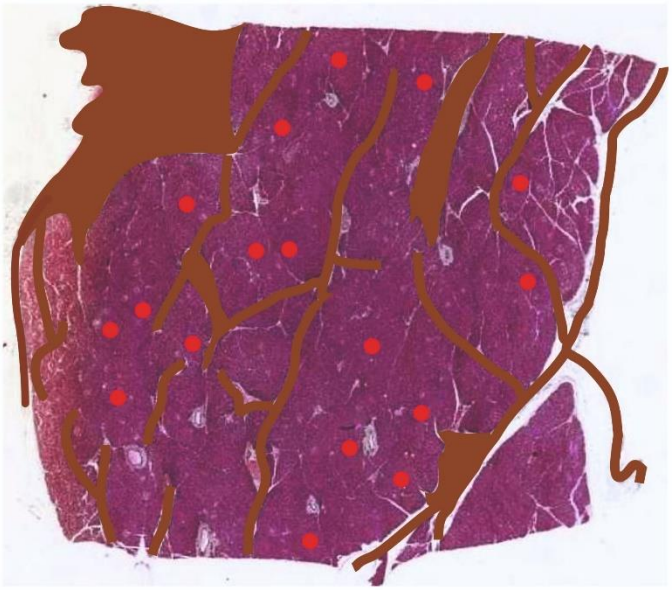
ISLETS OF LANGERHANS

The pancreas is a mixed gland: the endocrine part of the pancreas consists of more than a million spherical **islets of Langerhans**. They can be easily seen in the pancreatic parenchyma at the lowest magnification, as they measure about 100-200 µm, are lighter than the serous acini (which represent the exocrine component of the gland), from which they are separated by a fine connective tissue sheath. The islets themselves consist of polygonal epithelial cells arranged in cords; the space between the cords is filled by a small amount of reticular connective tissue containing a network of sinusoidal capillaries. Transmission electron microscopy of the glandular cells of the islets of Langerhans confirms the characteristic of polypeptide-producing cells: their cytoplasm contains numerous cisterns of rough endoplasmic reticulum and secretory granules accumulating in the cytoplasm attached to the sinusoids. According to the nature of the secretory granules, different cell types with different endocrine activity can be distinguished. The most numerous (60-80%) are **B cells**, which are mainly found in the central parts of the

islets. These cells produce insulin, which increases the transfer of glucose into the cells and therefore lowers blood sugar levels. **A cells** representing nearly 20% of insular cells are found mainly in the peripheral parts of the islets. They are slightly larger than B cells and produce glucagon, which acts as an insulin antagonist, i.e. it raises blood glucose levels. **D cells** represent about 5% of insular cells; their product is somatostatin, which inhibits the release of other hormones from the islets of Langerhans and also reduces exocrine pancreatic secretion. D cells are mainly scattered in the superficial parts of the islets. **F cells** (PP cells) are found at the ventral areas of the islets and produce pancreatic polypeptide, which inhibits the secretion of pancreatic juice and bile. The least numerous endocrine cells (less than 1% of all cells) are D1 cells, which produce vasoactive intestinal peptide, EC cells (releasing substance P and serotonin), and G1 cells, which perinatally produce gastrin. The function and structure are explained in more detail in the e-course Endocrine System II.

The pancreas, including its exocrine and endocrine portions, is of endodermal origin (arises from fusion of the dorsal and ventral buds of the embryonic duodenum).

ORIENTATION IN THE SLIDE

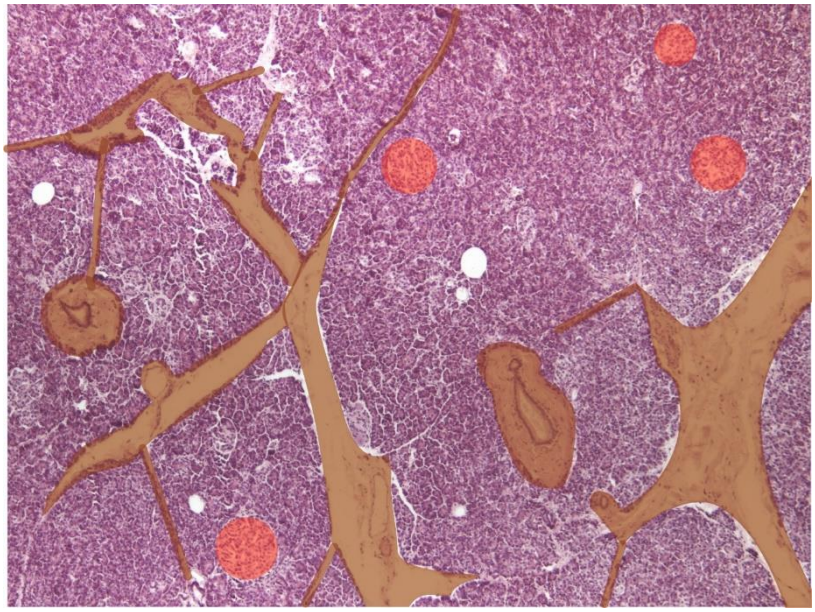


Under small magnification, a typical parenchymatous organ can be recognized. It is a large organ because the **capsule** covers only part of the surface - the upper and lower surfaces are cut off (these margins are smooth and not covered by the capsule). In the capsule at the upper left edge we can see large blood vessels (artery and vein). Numerous **septa** emanate from the capsule and vary in thickness; some are thin while others are wider because they involve other structures (blood vessels, nerves, and ducts). The septa divide parenchyma into lobes and **lobules**. The septum and capsule are labelled in brown. The parenchyma itself shows a relatively compact arrangement. More abundant is the exocrine tissue, the secretory cells of which are basophilic. With careful observation, scattered small, light, spherical islets of endocrine tissue (some marked in red) can already be seen in the exocrine pancreas under small magnification; they have been named **islets of Langerhans** after their discoverer, Paul Langerhans.

MICROSCOPIC STRUCTURE

Middle magnification reveals no other structures. Most of the microscopic field is occupied by the exocrine part of the pancreas, consisting of basophilic cells. **Septa** parcelate the exocrine pancreas into small lobules. The septa are formed by iregular dense connective tissue and their course is marked in brown. In two septa (round and oval in shape to the left and right of the centre), the interlobular **ducts** (draining a product of the exocrine

pancreas) are seen in a transverse section. In addition, the **islets of Langerhans** can be seen in the exocrine part of the pancreas. Three prominent islets are labelled in red. They can be distinguished from the exocrine tissue according to their light colour and spherical shape.



A detail view of the **islet of Langerhans** reveals that its epithelial cells show a different arrangement than those of the exocrine pancreas. The insular cells are arranged in **cords**, between which there is a small amount of reticular connective tissue and **sinusoid** capillaries (red). The density of blood capillaries inside the islet is higher than in the exocrine tissue. The microphotograph clearly shows an arrangement of endocrine cells in cords in the middle of the islet between two adjacent capillaries. The cells of the islet are polygonal and have a pale cytoplasm. The nucleus of the cells is round or oval with a prominent nucleolus; the light chromatin indicates activity in transcription of genetic information. The surface of the islet is covered by a thin capsule (dotted red line) that separates the endocrine tissue from the exocrine tissue. The flattened nuclei with dark chromatin inside this capsule likely belong to Schwann cells, which enter with innervation of the islets. The septum in the exocrine pancreas is shown in brown.