Lip and salivary glands

The lip consist of cutaneous part, red part and mucous part.

## Cutenous part

Epidermis is the stratified squamous keratinized epithelium. Langerhan cells and melanocytes are found in the epidermis. Langerhan cells will take up antigens during skin infection and become antigenpresenting cells.

* stratum corneum
* stratum lucidum
* stratum granulosum
* stratum polygonale
* stratum basale

Dermis is dense irregular connective tissue. We find the hair follicles in the dermis, and the sebacious glands always open into the hair follicles. NB: around lip, genitalia and nipple sebaceous glands can occur alone. Sebaceous are holocrine.

* Stratum papillare send papilla into the epithelium. We find Meissner corpuscule in this layer
* Stratum reticulare contain network of arteries and veins. The lowest part contain the sweat glands which usually have double layer of cuboidal epithelium.

Subcutis contains fat and maybe skeletal muscle

## Red part

This part is less keratinized and does not contain hair follicles, sebaceous glands or sweat glands. The connection from the epidermis to dermis is rich in connective tissue papilla with capillary loops inside them. Numerous meissner corpuscules are seen in the papillaries in the lip.

## Mucous part

Stratified squamous non keratinized epithelium. There are salivary glands in the submucosa.

# Salivary glands

All the 3 major salivary glands contain a dense connective tissue capsule that penetrate into the glands as connective tissue septa, which divide the glands into lobes and lobules. This connective tissue septa contain the vessels and excretory ducts supplying the glands. There are myoepithelial cells between the cell membrane and basal lamine of the glands to push out the fluid. Salivary glands are merocrine.

The glands functions are

* lubrication of mucosa
* moist food
* aid in taste stimulation
* providing a buffer inside the oral cavity due to high bicarbonate levels
* cleave starch
* kill bacterias

## Serous glands

They produce amylase, therefore they have a lot of rER so they stain basophilic with HE stain. They produce a non viscous fluid functioning in hydrolysis of starch and killing bacterias. The cells are pyramidal in shape with a central nuclei. Relative to mucous acinus they have a small lumen.

## Mucous glands

More vicous fluid and funtion more as lubrication of the mucosa. They secrete mucin which is rich in glycoproteins. They are stained pale by HE. It has wider lumen then serous glands and the nuclei are located in the basal part of the cell.

## Duct system

The intercalated ducts are the first ducts and are found inside the lobules. They have cuboidal epithelium. Next ducts are the interlobular ducts. They have striated parts which are collections of mitochondria sitting in folds in the basal part of the cells. They indicate lots of ion transport in and out of the cells making the saliva hypoosmotic, and secrete immunoglobulins. The interlobular ducts can have cuboid or columnar epithelium. They drain into interlobar ducts which have columnar of pseudostratified epithelium.

## Parotid gland

Biggest of the salivary glands and does only contain serous acinus. Amount of fat are seen, and the amount increases with age. Facial nerve may be seen in the slide since it crosses medially to it. Secrete the fluid in the oral vestbule on the oppsite side of the upper 2nd molar tooth in the bucca. Compound tuboalveolar.

## Sublingual

Located below and lateral to the tongue. Have ducts to submandibular duct and directly into the oral cavity. Compound tuboalveolar glands. About 2/3 is mucous. Demilunes are seen which are serous cells wedged between the mucous glands. The duct system is simpler in the sublingual than the two other. PAS-H staining is often used for sublingual because it stains mucous, glycogen and reticular fibers. This will stain the mucous glands and the lumen disappear because of the mucous inside.

## Submandibular

The glands here are mostly serous (75%). It is a compound tuboalveolar gland

Demilunes are also seen here. It drains into the oral cavity next the frenulum of the tongue. The intercalated ducts are shorter, and the interlobular are longer relative to the parotid duct. Submandibular is the largest producer of saliva 75%. Parotid next biggest.

The teeth and the development of teeth

Corona/crown – the part we can see that protrudes out of the gum. Consist of the enamel and the dentinum.

Root – the part that penetrates the gum. Consists of dentinum and cementum

Neck – the junction between crown and root where the cement and crown meets.

The teeth can be divided in soft and hard tissue. The hard tissue is the enamel, dentinum and cementum. The soft part is the pulp chamber and odontoblast layer. The teeth are located on the alveolar process on the mandible or maxilla. The grooves are called dental alveoli, and they are bordered by interalveolar septa.

## Dentinum

The dentin is one of the mayor parts of the tooth. Covered by enamel, and cementum, and surrounds the pulp chamber. Composed of 70% inorganic material, mostly hydroxyapatite. Inside the dentinum there are dentinal tubulues extending from the pulp to the dentinocemental junction or dentinoenamel junction. Inside the tubulues are the odontoblast processes. Tubulues connect via canalicular system. The inside of the dentimun are covered by odontoblasts. The odontoblast never stop creating dentin, so the pulp become smaller by age. This new dentin also help in reparations and is called secondary dentin.

Granulated layer of Tomes are spaces created when the specimen dries and shrinks. Interglobular spaced in the dentin are usually near the enamel and are black areas less mineralized than the surrounding dentin.

## Cementum

Covers the roots of the teeth, and connects to the interalveolar septa through the periodental ligaments which are collagenous and elastic. The interalveolar septa is the part of the mandible and maxilla that act as the anchor for the teeth. The sockets are called dental alveoli. Produced by cementocytes which are similar to osteocytes and are located on the external surface. Lower part is called cellular because it have cementocytes, upper parts i acellular.

## Pulp

The dentinal pulp consist of the odontoblast layer and connective tissue. They cover the neurovascular system of the tooth which goes down the root canals and out of the apical foramen. There may be other canals going out the the tooth.

## Enamel

The basic structure is enamel rod. They are the whole length of the enamel. 98 % inorganic substanses. Catabolized by acids. The enamel will have lines of Retzius which are 45 degrees lines, and Hunter-Schreger lines which are perpendicular to the dentinoenamel junction.

# Development

The first thing that happens is the apparence of the dental lamina which gives rise to the dental buds (bud stage). These buds are invaginations from the ectodermal epithelium into the ectomesechyme (neural crest derived). This is the cap stage of the tooth. The epithelium will give rise to the inner (columnar) and outer enamel cells (cuboid) and also the stellate reticulum. The dental papilla is the bell shaped organ inside the dental follicle. It consist of ectomesechyme and will develop into the pulp and give rise to the columnar odontoblasts. The dental follicle has an important role in forming the cementum and peridontium. The border between the inner and outer enamel cells are called the cervical loop and will form the Hertwigs root sheat which is essential for the development of the roots. Adamantoblasts are formed from the inner enamel cell layer. These are also columnar cells. The entire organ is called enamel organ!

The bell will grow and eventually penetrate through the outer enamel cell layer. The odontoblasts derived from the ectomesenchyme will produce predentin which transition into dentin. The next layer is the enamel because the adamantoblasts are located on the external side of the enamel.

Ectoderm epithelium --> inner and outer enamel cell layers and stellate reticulum.

Inner enamel cells --> adamantoblasts

Ectomesenchyme --> odontoblasts and pulp

Dental follicle --> cementum and peridontium

Tongue

## General

The tounge is a skeletal muscular organ covered by a mucous membrame. Mucous membrane consists of epithelium mucousa and an underlying lamina propria. The epithelium is stratified squamous non keratinized.

## Innervation

**Papillary part**

General sensory – lingual nerve, mandiular branch of trigeminal nerve

Taste – chorda tympani, facial nerve

Motoric – hypoglossal nerve

**Follicular part**

Sensory – glossopharyngeal nerve

Motoric – hypoglossal

* There are glands on the tounge as well, but mostly serous, and few mucous glands.
* The taste buds (caliculi gustatori) dont make connections to the lamina propia. Sweet, sour, salt and bitter. They are built up by gustatory cells and supportive cells. Gustatory cells are receptor cells.
* There are muscles in three directions. They can be seen as two longitudinal and one transversely cut.
* There can be seen lymphatic follicles (groups of lymphocytes) in the tongue (other than in the lingual tonsil)
* Detritus are dead organic material, often encapsuled in the human body.

On the tongue we can find many projections called papillae. There are 4 kinds:

Filiform papillae

Taller and more numerous. They give the white color of the tongue. They are keratinized, but not keratinized in babies. Responsible for sensation by thermoreceptors, mechoreceptors and nocireceptors. No taste buds.

Fungiform papillae

Shorter and wider and can be seen as red dots on the tongue. They are mushroom shaped and may have caliculi gustatori (taste buds) on the sides. Connective tissue papillae: are invaginations from the lamina propria into the epithelium layer. They are to give greater surface area between lamina propria and the epithelium to easier transfer nutrition to the epithelium layer.

## Papilla circumvallate

The papillae circumvallate can be found on the border of the root and body of the tongue (sulcus terminalis) and are dome shaped. They are 9-11 in a V-shape. In the trench around the papilla, can find taste buds. The trenches are cleaned by serous glands (Ebners glands) that open into them so that new taste can be sensed quickly.

## Folate papilla

On the postolateral side of the tongue. They send 3 parallel rigdes of lamina propria into the epithelium. They contain taste buds.

## Lignual tonsil

The lingual tonsil can be found on the posterior part of the tongue - the follicular part. A tonsil is an accumulation of lymphocytes. The lingual tonsil differs from other lymphatic structes by their surface epithelium being stratified squamous non-keratinized, their lack of krypts (if crypts present they are small) and salivary glands to wash out bacterias making them very resistant to infections. The lymphatic follicles are in the reticular connctive tissue of the lamina propria.

Respiratory tract

Respiratory tract is the nasal cavity, larynx, trachea, bronchus and bronchioles. The epithelium is pseudostratified columnar epithelium with kinocilia. Below the epithelium is a basal layer of cells which function as reserve cells for the epithelium. The basic skeleton of respiratory tract is hyalin cartilage. Due to the high amount of elastic fibers in the respiratory tract, there is a lot of fibroblasts in the connective tissue. Elastic fibers are stained eosinophilic by HE, and are specially stained by Orcein.

The layers:

1. pseudostratified columnar epithelium with kinocilia
2. basal cells
3. basement membrane of dense connective tissue, high amount of collagen
4. lamina propria, loose connective tissue
5. elastic fibers
6. submucosa

Hyalin cartilge can be recognized by the nearly homegenous matrix, with lacunae in the matrix. The lacunae contains the chondrocytes, but the lacunae are artifacts. The chondrocytes take up the entire lacunae, but shrinks during staining.

## Larynx

Glands can only be seen below pseudostratified epithelium, so there is not glands below the vocal fold where the epithelium is stratified squamous. In the vocal fold we can find the vocalis muscle and also the vocal ligament and the connecting conus elasticus. These two structures are elastic connective tissue.

The mucous membrane of larynx contain goblet cells, and we may find taste buds. The lamina propria is filled with mixed salivary glands, and lymphatic follicles may be seen.

The vestibular fold contain the quadrangular membrane, and the muscle fibers seen are most likely thyroarytenoid muscle. The vocalis muscle is internal to the thryoarytenoid muscle.

Thyroid cartilage is seen, with the perichondrium surrounding it. Perichondrium is dense irregular connective tissue and function to decrease healing time of cartilage and give blood supply to the cartilage. Muscles outside the cartilage are most likely the cricoarytenoid muscle.

Thyroid gland may also be seen.

As we grow old, cartilage begin to ossify, so if the slide is from an old person, you will se bone formation and also bone marrow.

## Trachea

Respiratory epithelium with goblet cells. Kinocilia with their basal bodies are seen. The supporting lamina propria is made of loose connective tissue and contain small vessels and lots of elastic fibers. Deeper to the lamina propria is the submucosa which contains mixed salivary glands and fat cells. This is not similiar to the larynx where we find the salivary glands in the lamina propria. Often there is an elastic membrane dividing lamina propria and the underlying submucosa.

MALT (mucous associated lymphoid tissue) are found in the lamina propria of the trachea.

Trachea consist mainly of C-chaped hylian cartilage rings and the smooth muscle trachealis muscle connecting to the two ends of the cartilage. Again covered by perichondrium. Below the epithelium is of course lamina propria, and submucosa with mixed salivary glands. Cartilaginous part og membranous part.

The outer layer is adventitia which is composed of loose connective tissue. The adventitia hold the organ in place and bind it to adjacent structures.

So the layers of the trachea is a following:

1. pseudostratified ciliated columnar epithelium
2. basement membrane
3. lamina propria
4. elastic membrane
5. submucosa (mixed salivary glands, fat, vessels)
6. cartilage or muscle
7. adventitia

## Lung

1. trachea
2. main bronchi
3. lobar bronchi
4. segmental bronchi
5. bronchi (dichotomous divisions)
6. terminal bronchi
7. bronchiole (< 1 mm)
8. terminal bronchiole
9. respratory bronchiole
10. alveolar duct
11. alveoli

The cartilage disappear when terminal bronchi turns to bronchiole, and the wall becomes only smooth muscle. This can be seen as decreased lumen caused by curved walls caused by the drying of the specimen which contract the muscles around.

The bronchus contain mixed salivary glands in the submucosa, but the glands disappear in terminal bronchiolus. The lamina propria is rich in lymphocytes, especially macrophages are abundant due to particles inhaled. The amount of goblet cells decrease, and are not found in the bronchioles.

Bronchiolus – pseudostratified ciliated columnar

Terminal bronchiolus – simple ciliated columnar, then loose cilia

Respiratory bronchiolus – cuboidal, then squamous

The alveoli are lined with pneumocyte 1 and 2. 1 is sqamous and cover 90% of the alveoli , while 2 is cuboidal and produce surfactant. Sufactant is mostly phospholipid, but also protein and cholesterole. There are approximately 300 million alveoli in the lungs, and they cover an area of 150 m2.

Other cells found in the mucosa worth to mention is clara cells, neuroendodrine cells, brush cells, mast cells and MALT.

Alveoli can open into respiratory bronchioli, but most are found in the end of alveolar ducts.

Bronchopulmonary segment is the supplied by 1 segmental bronchus. Is it bounded by connective tissue septa. The pulmonary artery runs along the bronchial tree, while the veins runs i the periphery.

Pulmonary lobule is the territory that belongs to 1 bronchiolus.

The lungs are supplied by both blood circulations, the bronchial arteries from the systemic circulation and the pulmonary arteries from the pulmonary ciculation.

Orsein stain show elastic fiber, which is abundant in the lungs.

Air-blood barrier is 0.5-2 micrometer

* pneumocytes
* basal membrane of pneumocyte

the basement membranes may fuse together

* capillary basal membrane
* endothelium

Esophagus and stomach

## General

**Tunica mucousa**

* epithelium mucousa --> stratified squamous non keratinized
* lamina propria --> loose connective tissue, with lots of connective tissue papilla rich in capillaries
* lamina musculare mucousa --> longitudinal smooth muscle

The function of the mucosa is to protect against the harsh enviroment caused by low pH in stomach and by the food entering. The lamina propria contains fenestrated vessels specialized for absorption of nutrients.

**Tunica submucousa**

* loose connective tissue (but denser)
* meisner plexus/submucosal plexus
* glands
* vessels
* lymphatic follicles

meissner plexus innervate the epithelial cells and muscularis mucosa, and has some sensory innervation as well. It has only parasympathetic fibers.

**Tunica muscularis**

* inner circular layer
* auerbachs plexus/myenteric plexus
* outer longitudinal layer

By looking at the two muscular layer you can determine if the cut is longitudinal or cross section. Auerbachs plexus has both sympathetic and parasympathetic fibers and innervate the tunica muscularis.

**Tunica adventita/tunica subserosa + serousa**

* adventitia is loose connective tissue (retroperitoneal)
* subserosa is a thin layer of connective tissue and serousa is mesothelium (intraperitoneal)

## Esophagus

The esophagus has a well developed muscularis mucosa. The upper tunica muscularis is skeletal, while the lower become smooth. There are mucous glands in the lamina propria, but just in the upper an lower regions. The submucosa has both serous and mucous glands. The fluid secreted is to aid the food going down the esophagus. Tunica adventita.

## Cardia

Cardia is the border between the esophagus and the stomach. Here we can see the transition from stratified squamous non keratinized to simple columnar. Glands in the lamina propria of this area are cardiac glands. But these glands may penetrate through the muscularis mucosa into the submucosa, even though glands in the submucosa of stomach is not typical. They are tubular, branched and coiled. They produce mucous which have the effect of protecting the esophagus from gastric reflux. They also produce some of the gastric juices. They stain well with PAS-H. It will be covered by subserosa and serosa. The transition from stratified squamous to simple columnar is the cardioesophageal junction.

## Stomach

The optimal pH is 2, but there needs to be a fine equilibrium between protecting factors and pH. Overproduction of HCl can lead to gastric ulcers. Mucous is the main protection against the harsh environment of the stomach and low production also leed to diseases. Mucin are glykoproteins with high affinito to water. There are 3 muscles layers in the stomach, inner oblique, middle circular and outer longitudinal.

## Fundus/corpus

The gastric pits reach 1/3 in the lamina propria. They surface are always covered by the epithelium layer, also in the pits. Gastric glands (simple tubular) open into the pits. They cover the last 2/3 of the lamina propria. Below the lamina propria is the lamina muscularis mucousa.

The glands can be divided into an upper isthmus and lower fundus

**Isthmus**: large eosinophilic cells (parietal cells). They produce hydrocloric acid and intrinsic factor which helps in the absorption of B12-vitamin. Parietal cells can be seen in the fundus as well, but are more abundant in the isthmus. Parietal cells have tubovesicular system which means that it can create deep infoldnings of the membrane to increase the surface of secretion if needed with the H/K-ATPase and K/Cl symport.

**Fundus**: chief cells which produce pepsinogen (protein digesting enzyme). HCl will activate pepsin from the inactive form pepsinogen.

Mucous neck cells are small mucous producing cells near the parietal cells, but they can not be seen in the slides. They will give the middle third of the mucosa a lighter color. This area is called the neck. (upper part of gastric pits)

Undifferentiated cells and enteroendocrine cells are not supposed to be identified, but they are smalls cells secreting serotonin, VIP, gastrin, substance P, somatostatin and bombesin

## Pyloric part

The gastric pits reach at least half of the lamina propria. The glands below are more crosscut because they are coiled glands. There are no chief cells or parietal cells here. Most of the cells are mucous cells to protects the duodenum against the gastric acid. Enteroendocrine cells here as well which produce serotonin and somatostatin. Serotonin makes the food travel faster in the gut, and is secreted by enterochromaffine cells. Somatostatin inhibit the parietal cells to produce HCl.

Intestines

Common for the entire gut except last part of rectum

* simple columnar epithelium with thight junctions, brush border and goblet cells
* simple tubular crypts of Lieberkuhn in the lamina propria
* folds made by submucosa

# Small intestines

They have villi made by the lamina propria. The epithelial cells are enterocytes which function in digestion and absorption. The villi contain arteriole and venule, and a central lacteal which aids in the fat absorption. Bile salts emulsify the fat, colipase and lipase break them down, and they are absorbed into the enterocytes. There they are rearranged as trigylcerides and secreted out into the central lacteal as chylomicrons (lipoprotein). The folds made by the submucosa are called folds of Kerkring and they are permanent folds. The longer down in the intestinal system, the amount of goblet cells increase. Microvilli increase the surface the most with about 30x. Tight junctions between the epithelial cells.

Enterocytes are the most abundant cell in the epithelium of the intestines. It function in the absorption and digestion. It has a glycocalyx layer on the surface that contains digestive enzymes. The cells also have a secretory role by secreting immunoglobulins. They absorb carbohydrates, fat, peptide and aminoacids, vitamine B12 and reabsorb bile salts.

Between the villi, are the Lieberkuhn glands. They are simple tubular glands. At the base of these glands are the mucosa muscularis. These crypts consist of columnar cells, Paneth cells with eosinophilic zymogen granules that containt antibacterial lysosim enzyme, goblet cells, reserve cells and enteroendocrine cells. Paneth cells can only be seen in newer slides. These cells secrete somatostatin, VIP, substance P, glucagon, gastrin, serotonin etc.

## Duodenum

The connective tissue of submucosa containts vessels and Brunner´s glands which are compund tubular glands. They function to neutralize the low pH coming from the stomach, lubricate the intestine and create a good environment for the enzymes to work. They secrete a mucous rich alkaline secretion, rich in bicarbonate.

The plexus submucosus lies here as well.

Tunica muscularis contains inner circular and outer longitudinal layer. Between these two layers are the myenteric plexus

Something around nothing: crypts

Nothing around something: villi

## Jejunum

What separated the jejunum from the duodenum is the lack of Brunners glands. The rest is basically the same. Since all of the jejunum is inside the peritoneum, we will always see serosa and subserosa on the surface. There can be seen many goblet cells in the epithelial layer.

## Ileum

Because ileum is close to the large intestine where most of the gut bacteria are located, it is importan to protect the small intestine from these bacterias. Therefore the submucosa of ileum contains many lymphatic follicles called Payers patches. These are most often located on the antimesenterial edge. They can often penetrate into the lamina propria and function with the M-cells. M-cells have mucosal fold instead of microvilli and they bring antigens from the intestinal lumen to the lymphocytes. The Payers patches are a part of GALT (gut associated lymphoid tissue). They turn the connective tissue into reticular connective tissue.

## Large intestine

The main difference between large and small intestine are the lack of villi in large intestine. But there are crypts of Lieberkuhn and the mucous membrane is covered in microvilli. The epithelial cells is the same as in the small intestine except their lack of Paneth cells. Epithelial cells are often called colonocytes. There are also very few enteroendocrine cells in the large intestine. The main function is absorption of water and salts. The folds made by subucosa are called semilunar/semicircular folds, and they are temporary folds. The outer longitudinal muscle thickens at 3 places along the large intestine called tenias. Tenias are not seen in the appendix, rectum or anal canal. Epoploic appendixes are numerous on the large intestine and are mostly made of fat. Goblet cells are also numerous. Depending on where the slide is, the outer layer can be either serosa/subserosa or adventita.

## Appendix

Always shown in crosscut, and can be recognized by the abundance of big lymphatic follicles as part of the GALT. The follicles may penetrate into the mucosa. The tenias do not cover the appendix, so the tunica muscularis should be smooth. Appendix is intraperitoneal so serosa/subserosa on the surface.

## Rectum

Has an upper intestinal part that is identical to the large intestine. Below that is the anal canal, where we can see epithelium transition. This zone is divided in 3.

**Columnar zone**: the anal columns are covered by stratified squamous non keratinized. Between the columns are the anal sinuses where we find simple stratified columnar epithelium with microvilli. But since most of the slides are from babies, the anal colums may also have stratified columnar epithelium .

**Hemorrhoidal zone**: covered by stratified squamous non keratinizing. In adults we can se wide veins, but not in fetus slides. Hemorrhoids can be caused by sitting, holding in stool or smoking.

**Cutaneous zone**: covered by stratified squamous keratizing epithelium. At the anus this continues into the external skin that contains hair follicles, sebaceous glands, sweat glands.

The internal and external anal sphincter can be seen in the submucosa. External lies laterally to the internal. The internal is smooth muscle and is the continuation of tunica musculari. The external transition from smooth to skeletal early in life. The not matured muscle cells of the baby will be paler than the matured muscle cells.

## Myenteric plexus

The enzyme NADPH diaphorase is an enzyme which utilize NADPH as substrate. During staining, NADPH transfer an electron to the nitroblue tetrazolium which gives a blue end product. Since NADPH diaphorase is produced by nerve cells, nerve are stained well by this procedure. There are vegetative ganglion cells at the junctions.

Liver, gall bladder and pancreas

# Liver

## Functions

* Metabolism of fat, carbohydrates and amino acids
* glycogen storage (produce and catabolise too)
* produce serum proteins (albumin, globulin, blood clotting factors, hormones. During embryonic development it produce red blood cells(hemopoesis))
* produce bile (bile breaks down bigger fat drops --> increase surface of fat for intestines to work on)
* vitamine storage
* detoxification of metabolites. If it cant break down it makes is hydrofilic so kidneys can secrete out of body

## Anatomy

The functional part of the liver is the lobules which are hexagonal in shape. 1mm wide and 2 mm long. There are NOT connective tissue in the borders of the lobules (CT in some animals)

The middle of the lobules has the central vein

Portal triade can be found in about every second corner of lobules. Contain:

* interlobular vein (not round in shape)
* interlobular artery
* bile duct (cuboidal epithelium)

## Blood supply

* proper hepatic artery (25% of total blood, oxygenated)
* portal vein (75% of total blood, deoxygenated, nutritious)

1. lobar artery and vein
2. interlobar artery and vein
3. Interlobular artery and vein
4. Circumlobular/perilobular artery and vein
5. Hepatic sinusoids
6. Central vein
7. Sublobular vein
8. Hepatic veins
9. Inverior vena cava

## Cell cords

From the borders of the lobules, the cell cords begin, and they fill up almost everything inside the lobules. They make channels where blood from circumlobular vein and artery mix (oxygenated + nutritious). These channels are called hepatic sinusoids. They are bordered by the hepatocyte cells. The hepatocytes are the cell which does the work of the liver.

The sinusoids are covered by endothelium. The space between the endothelium and hepatocytes is called the space of Disse. In the space of Disse, are the stellate cells. They produce reticular fibers, but this is not connective tissue because the stellate cells are not connective tissue cells. Stellate cells also store vitamine A and fat. Space of Disse or stellar cells can not be seen. The liver cells are supported and held together by retular fibers, but this is not the same as reticular connective tissue

Inside the sinusoid are the Kupfer cells. They are the macrophages of the liver and can be seen.

Between the hepatocytes are where the bile is produced. The flow though the bile capillaries/ductus biliferus. Bile capillaries are not epithelum covered vessels, but are "false" vessel created by hepatocytes with thight junctions between.

## Other classifications of lobules

**Portal lobule** mostly used in scientific papers.

1. take 3 lobules which are connected together
2. draw a line between the central veins of these 3 lobules

The space inside is the portal lobule. The center of this space must contain a portal triade.

**Hepatic acinus** mostly used in pathology

1. take 2 lobules fused on one of the sides (will look like an 8)
2. draw a line from both central vein to the two shared corners

The space will be a square (two triangles connected on the shared border)

Both of the 2 triangles can be divided in 3 parts, the 1st closest to the shared border, and the 3rd close to the central vein.

Poison will kill most cells in order 1>2>3

Hypoxia will kill most cells in order 3>2>1

Indian ink is a stain where ink is injected into the portal vein. This stains the veins totally black, but not the arteries. Look at the portal triade

Gogli stain (silver) will show the bile capillaries. The hepatocytes will be yellow, with a darker color in the bile capillaries.

# Gall bladder

Left and right hepatic duct go out from liver and fuse to make the common hepatic duct. This fuse with the cystic duct from the gladdbladder and continue as common bile duct until it fused with major pancreatic duct. Bile flows in 2 directions in the cystic duct.

Gall bladder only store bile, and concentrate it by active transport of NaCl into the interceullular space creating an osmotic gradient and pulling in the water.

* epithelium mucosa (simple columnar with microvilli)
* lamina propria (loose connective tissue, this creates the fold on the surface)
* NOT muscularis mucosa or submucosa
* muscular layer (not important to know in what directions because it is not as visible as in intestines)
* subserosa + serosa or adventita (adventitia where gall bladder connect to liver)

NB! Gall bladder look very like seminal vesicle.

**Luschka channels** are channels from the lumen of gall bladder to the liver. These may be seen externally to the muscle layer.

**Rokitansky-Aschoff channels** are deep pouches in the wall of the gall bladder. These are NOT lumens, but continuations of surface.

# Pancreas

Lobulated organ separated by connective tissue septa (typical for lobulated organs).

The paler parts of the lobules are the endocrine parts (islets of Langerhans). They are built up of cell cords and sinusoid capillaries between them.

Alfa cells – glucagon (20%)

Beta cells – insulin (75%)

Delta cells – somatostatin and VIP

The rest is the exocrine part and are called pancreatic acinus. These acinus are basophilic in the base, and eosinophilic in the center. In the center of the acinus we can see centroacinar cells. These cells are not actually located in the middle, but are parts of the intercalated ducts which are pressed a little bit into the acinus. So the cut might show the beggining on the ducts inside the acisnus.

The secretion of enzymes is merocrine. The enzymes are endo- and exopeptidases, amylase, lipase, nucleotic enzymes, trypsinogen and more. Trypsinogen is activated by enzymes on the glycocalyx on the intestinal villi. Trypsin will then activate the other proenzymes, and enhance the activation of trypsinogen (positive feedback). Pancreas is very similar to parotid gland, but the differences are presence of fat in parotid, langerhans islets, centroacinar cells, and stronger capillarisation.

Kidney, ureter and bladder

# Kidney

**Parts of the nephron**

* malpighian corpuscule: glomerulus + bowmans capsule
* thick proximal convoluted tubule
* thick descending straight part of loop of henle
* thin descending and ascending part of loop og henle
* thick ascending part of loop of henle
* distal convoluted tubule

There are two types of nephrons

Juxtaglomerular – renal corpuscule is located in the outer cortex. The loop of henle only touch the upper part of the medulla.

Cortical – renal corpuscule lower down in the cortex, so the loop of henle go deep in the medulla. Most of the nephrons are cortical.

## Blood supply

1. abdominal aorta
2. renal artery
3. segmental artery
4. interlobar
5. arcuate artery
6. interlobular
7. afferent
8. glomerulus
9. efferent
10. peritubular capillary plexus to cortex or medulla
11. vasa recta for the medullary capillary plexus
12. interlobular vein
13. arcuate vein
14. interlobar vein
15. renal vein
16. inferior vena cava

the vasa recta will wrap around the loop of henle and by countercurrent reabsorb much of the filtrate.

The afteries can be found in the specimen by looking for squamous cells.

## Cortex

Consist of the malpighian corpuscule and the medullary rays. The area between the medullary rays is the cortical labyrinth. Since the medullary rays do not reach the capsule of the kidney, there is a space in the cortex without it – this is called cortex corticis. In the middle of the medullary rays would be the interlobular arteries. Cortical lobules are bordered by the interlobular arteries – therefore they have a medullary ray in the middle surrounded by the cortical labyrinth. Medullary ray is parts of the straight parts of the loop of henle.

Most of the cross section in the cortex are from the proximal convoluted tubule. They are narrower than distal convoluted tubulue, both both of them have cuboidal epithelium.

## Bowmans capsule

The capsule have a basement membrane and have squamous parietal cells. Inside the capsule are the capillaries made by endothelium cells. On the endothelium cells inside the capsule are podocytes covering them. The podocytes have pedicles which cover most of the endothelium. The parietal part of the Bowmans capsule are not covered by podocytes, but simple squamous epithelium.

Mesangial cells make up much of the cells in the malpighian corpuscule. There are intraglomerular mesangial cells which are found between the capillaries, and extraglomerular mesangial cells found between the afferent and efferent arteriole. The function of the mesangial cells are

* formation of the capillary loops during development
* contraction regulating capillary flow
* phagocytosis of macromolecules – cleaning the glomerular filter
* structural support of podocytes

Granular/juxtaglomerular cells are found between the cells of the distal convoluted tubule and the afferent arteriole. The cells of the distal convoluted tubule are the macula densa cells. These two cell types make up the juxtaglomerular apparatus. They will release renin if they sense low blood pressure. Renin will turn angiotensinogen to angiotensin 1, which will turn to angiotensin 2 by angiotensin converting enzyme (ACE) in the lungs. Angiotensin 2 will lead to aldosterone and ADH secretion, more H2O reabsorption in the collecting duct, vasoconstriction and tubular Na+ and Cl- reabsorption. All of this will increase blood pressure.

Vascular pole: where the afferent and efferent arteriole enter and leave the corpuscule.

Urinary pole: where the urin go into the proximal convoluted tubule

The filtration process involve 3 layers:

* fenestrated capillaries
* basement membrane of the endothelial cells and podocytes
* podocyes with pedicles

## Tubulues

The distal and proximal convoluted tubule are lined with cuboidal epithelium. But because the proximal convoluted tubules are lined with microvilli, the lumen look smaller than in the distal convoluted tubule which does not contain microvilli. The thin part of loop of henle are lined with squamous epithelium.

There are plicae in the proximal convoluted tubule which allows for distension if fluid volume increase. Thin descending loop are permeable to water, but not much for solutes. The opposite for the thin ascending loop.

The collecting ducts have usually more distinct cell borders, and the cytoplasm is relativly clear.

## Calyx

The calyxes of the kidney are lined with transitional epithelium. The renal papilla/area cribrosa has columnar epithelial cells.

# Ureter

The epithelium of the urether is transitional. The next layer is the lamina propria and the connective tissue of it is not easily separated from the inner longitudinal muscle layer. The outer muscle layer is circular. Further down there may be an outermost longitudinal layer again. Since the ureters are retroperitoneal organs, they do not have serous membrane covering it, but instead have loose connective tissue adventitia. There are no submucosa.

# Bladder

Also the bladder has transitional epithelium. There is both lamina propria and submucosa, but hard to differentiate them. There are 3 layers of muscle. Inner longitudinal, middle circular and outer longitudinal. Depending on where the cut is taken, there can be serosa/subserosa or adventitia

1. Translation of alpha and beta chains (preprocollagen)
2. When finished they are released in to lumen og rER
3. Signal peptides are cleaved – now they are known as pro alpha chains
4. Hydroxylation of lysine and proline residues – need vitamin C
5. Glycosylation of specific hydroxylysine residues
6. Tripple helix are formed inside rER by 2 alpha-1 and 1 alpha-2 chain
7. Procollagen sent to golgi apparatus for exocytosis
8. Outside the cell they are cleaved to tropocollagen
9. Moltiple tropocollagen forms fibrils
10. Many fibrils form collagen fibers

Male genitalia

# Testis

The testis are surrounded by a dense connective tissue capsule called tunica albuginea made mostly by collagen fibers. The testis are divided into many lobes, bordered by testicular septa. There are about 200-300 lobes in each testicle. The lobes contain the seminiferous tubules which are very coiled. These tubules are lined with a very special stratified epitelium called seminal epithelium, which is basically the developing sperms during spermatogenesis. The seminiferous tubules become the rete testis, which drain their content into the epididymus via the efferent ducts of testis.

The tubes are lined on the basal membrane by sertoli cells and are regonized by their prominent nucleolus. They make up the blood-testis barrier and protect and feed the sperm cells. Sertoli cell are connected by thight junctions and communicate through gap junctions. External to the basal membrane are contractile myoepithelial cells which makes the tubes move the sperm out. Beneath the barrier made by the sartoli cells, but above basal membrane are the spermatogonia. Since these cells are 46 2n the blood will not kill them. Above the barrier we find in order from inner to outer the primary spermatocytes, secondary spermatocytes and spermatids. Very few secondary spermatocytes. On the sartoli cell membrane we find the spermatozoa.

Leydig cells are found between the tubulues. They are large, often in groups and produce testosterone. Pituitary gland produce LH and FSH. LH stimulate Leydig to produce testosterone. Testosterone inhibit pituitary gland secreting. Testosterone and FSH stimulate sartoli cells which stimulate the spermatogenesis.

## Development of sperm

The development can be divided into spermatocytogenesis and spermiogenesis. The spermacytogenesis begins with the spermatogonia (46, 2n) which contain fine chromatine granules. They do mitosis (A type) and meiosis (B type). The spermatogonia will become primary spermatocyte (46, 4n) and then secondary spermatocyte (23, 2n). Primary has a rough chromatin structure. Secondary spermatocytes only stay 8-9 hours, so there will be very few on the slide. The last step of the spermatocytogenesis is the formation of the spermatids (23, n). These are always in groups. Meiosis 1 happens in the primary spermatocyte, while meiosis 2 happens in secondary spermatocyte. The finish of the meiosis 1 and 2 mark the transition to secondary spermatocyte or spermatids.

The spermiogenesis is the morphological development of the spermatids to spermatozoa. The spermatozoa forms a tail by growing microtubules. The middle part thickens and are filled with mitochondria. The DNA is tightly packed and is surounded by the golgi apparatus becomming the acrosome. Most of the cytoplasm and unnecessary organelles is removed. The excess cytoplasm is called residual bodies and is absorbed by sertoli cells.

## Meiosis – mitosis

Normal cell: 46 chromosomes/chromatids 2n

Meiosis 1: 46 chromosomes 92 chromatids 4n

Meiosis 2 profase and metafase: 23 chromosomes 46 chromatids 2n

Meiosis 2 anafase and telofase: 46 chromosomes 46 chromatids 2n

After meiosis 2: 23 chromosomes/chromatids 1n

Difference in the mitosis and meiosis 1 is that during anaphase in meiosis, the 2 homologous pairs are pulled each way, but in mitosis, the homologous pair is broken in 2 and pulled each way.

# Epididymis

Has pseudostratified columnar epithelium with stereocilia which are cytoplasm protrusions similar to microvilli. Stereocilia are only found here, in vas deference and sensory (hair) cells in inner ear. The epididymis is connected to the testis via the efferent ducts of testis which have simple cuboid epithelium. Epididymis containt 2 kinds of ducts; efferent duct of the testis and ductus epididymidis.

Efferent ducts of the testis have an irregular looking lumen due to the epithelium being uneven – cuboid, columnar, with cilia, without cilia. Around we find myoid cells.

Ductus epididymidis is lined with pseduostratified columnar epithelium with stereocilia. Around the duct in the head of epididymis we find myoid cells, but this is distally replaced by smooth muscle. Basal cells in the duct.

# Spermatic cord

The spermatic cord is a cord like structure in male formed by vas deference and surounding tissue that runs in the inguinal canal to each testicle. Tunica vaginalis covers it and are derived from peritoneum. There are 3 layers around it

* external spermatic fascia
* cremaster muscle and fascia
* internal spermatic fascia

The content of the spermatic cord is

* vas deference
* artery of vas deference
* testicular artery
* pampiniform plexus (later turn into testicular vein)
* cremaster artery and vein
* cremaster muscle
* ilioinguinal nerve
* genital branch of genitofemoral nerve

Pampiniform plexus is a temperature changing system that is needed to cool down the arterial blood going to the testicles due to favorable temperature less than body temperature. The veins of spermatic cord usually contain more smooth muscle, but remember that arteries does not have smooth muscle in their adventitia.

Vas deference is covered by 3 layers of muscle. Inner and outer longitudinal and middle circular.

# Prostate

The prostate is composed of fibromuscular tissue with lots of glands. It is covered by a vascular fibroelastic capsule. There are 3 main types of glands.

* mucous glands are glands opening directly into the seminal collicle. They is simple tuboalveolar glands
* inner submucosal glands are the next layers of glands and drain into excretory ducts before they drains into the seminal collicle. They are compound tuboalveolar glands
* outer submucosal are the exact same as inner, but are just located outside of the inner ones. They can not be distinguished from the inner

All of the prostatic glands are lined with different epithelium (height, pseduostratified, simple columnar) and they are apocrine. They produce 30% of the non cellular elements of the sperm. Important substances they produce are prostaglandins and proteolytic enzymes. Prostatic specific antigen (PSA) is a proteolytic enzyme which will increase in amount by prostatic cancer.

In some slided the male vagina/prostatic utricle and ejaculatory ducts are seen. And the glands may sometimes contain deposits called prostatic concretions. They look like blood.

The parenchyma of the prostate is divided into 3 zones

* transitional zone: contains the mucosal glands and tumors here can compress the urethra.
* central zone: containts 25% of the glandular tissue and resistant to inflammation and carcinomas.
* peripheral zone: contains 70% of the glandular tissue, and tumors here are palpable through the anus and rectum.

**Uretheral epithelium**

Bladder to seminal collicle – urothelium / transitional

Seminal collicle to navicular fossa – stratified columnar

Navicular fossa to external uretheral orifice – stratified squamous non-keratinize

# Seminal vesicle

The seminal vesicle is a long and very torteous tube lined with pseudostratified epithelium. Can have simple columnar epithelium too. It is a secretory epithelium. The mucosa is extremely folded by the underlying lamina propria. The crypts may be cut is cross section, so they look like closed spaced in the mucoa. There are always more than 1 cross section of the tube. There is an inner circular muscle layer and outer longitudinal. They are hard to distinguish from another. It may look like the gall bladder, but differs in the epithelium, number of cross sections of the tube and that the gall bladder has striated border. The seminal vesicle produce 70% of the non cellular element of sperm. It contains vitamin C, fructose, prostaglandin and amino acids.

# Penis glans

The glans penis cut are covered by the prepuce. The prepuce will be covered both inside and outside by stratified squamous keratinizing epithelium. There is a space between the prepuce and the glans in adults, but is not perfect in babies. This is because the prepuce is formed by resorption of the middle cells. Often there are malformations of this resorption called cellular adhesion. This makes the prepuce hard to withdraw. Phimosis is the condition where the prepuce can not be withdrawn due to tight opening of the prepuce. The prepuce is connected to the glans by the frenulum.

The glans is made of corpus spongiosum. It is pigmented and without hair follicles just like inner surface of the prepuce. There may contain modified sebaceous glands. The corpus spongiosum contains lots of elastic fibers. The tunica albuginea around it is also very rich in elastic fibers. This makes the spongiosum not so hard and will allow the urethera to remain open during erection. The spaces that are filled with blood are called cavernosal spaces. These spaces are lined by endothelium. Trabecula of connective tissue and smooth muscle separates the lacunae into apartments.

# Penis corpus part

This cut can be from anywhere of the penis. We may see a Y-shaped tunica albuginea that separated the two corpus cavernosum and the corpus spongiosum. We see 2 kinds of glands. Endoepithelial and Littre glands. These glands secrete glycoaminoglycans that function to protect the urethra against the urine.

The penis is covered in this order

* superficial fascia
* superficial dorsal penile vein
* deep fascia
* deep dorsal penile vein and dorsal penile artery
* tunica albuginea

Lymphatic organs

The lymphatic system is the bodys defense mechanism against pathogens such as viruses, parasites and bacterias, foreign bodies such as splinters, and tumor cells. The interstitial fluid (lymph) is drained by lymphatic vessels to primary lymph nodes. The lymph in then sent to secondary and tertiary lymph nodes, before they are transferred through the big lymph vessels to the greater veins of the body. Lymph vessels are more permeable than blood vessels. This allows pathogens to more easily enter the lymphatic system. White blood cells are abundant, but there are no red blood cells.

**Capsulated lymphatic tissue**

* spleen
* lymph nodes
* thymus

**Non-capsulated lymphatic tissue**

* loose lymphatic tissue (for example tonsils)
* bone marrow
* GALT
* MALT

**Lymphatic follicle** – group of lymphocytes, does not necessary have a germinal center. Inactive without germinative center are called primary lymphatic follicles.

**Tonsil** – group of lymphatic follicles covered by a mucous membrane.

**Lymph node** – a group of regulary arranged lymphatic follicles covered by a capsule with lymphatic vessels and blood vessels.

Lymphatic tissue appear basophilic with HE stain because of heterochromatine DNA.

## Primary and secondary lymph organs

Primary – bone marrow develop all the cellular elements of the blood, and lymphatic cell precursors. The thymus differentiate T-lymphycytes into mature functionally T-lymphocyte groups

Secondary – other lymphatic organs storing the matured lymphocytes, such as spleen, lymph nodes, tonsils and lymphatic follicles.

## Immunity – innate and acquired

Cells of the innate immunesystem consists of granulocytes, monocytes, macrophages, dentritic cells and natural killer cells.

**Granulocytes** – eosinophilic, basiphilic and neutrophilic. They produce toxins to kill bacterias, and often gå to the place of a wound quickly.

**Monocytes and macrophages** – they digest pathogens by phagocytosis, produce cytokines and present antigens of the pathogen to other cells such as T-lymphocytes.

**Dendrittic cells** – present antigens, produce cytokines and phagocytosis of pathogens

**Natural killer cells** – release cytotoxins to kill infected cells og tumor cells.

Cells of the adaptive immun system consist of B- and T-lymphocytes

**B-lymphocytes** – can be found in secondary lymphatic follicles and in the blood. They differentiate into plasma cells that creates antibodies for that spesific antigen.

**T-helper cell** - activates other cells, such as macrophage and differentiation of B-cells to plasma cells. Also called CD4 cell

**T-killer cell** – also called cytotoxic T-lymphocyte or CD8 cell eliminate virus infected cell or tumor cells.

Proerythroblast --> erythrocyte

Monoblast --> monocyte

Myeloblast --> neutrophil, basophil, eosinophil

Lymphoblast --> lymphocyte

Megacaryoblast --> megacaryocyte

Lymphocytes --> B-cell, T-cell and natural killer cell

# Thymus

Thymus is an encapsulated lymphatic organ. The thymus differentiate bone marrow produced T-lymphocytes to mature cells. It consist of lobes and lobules divided by connective tissue septa called trabecula. These contain blood vessels and just efferent lymph vessel. The thymus is divided into an outer cortex and inner medulla which can be shared by several lobes. The framework is made by epithelial reticular cells. These are cells with processes covered by basal lamina. These cells produce thymosine which is needed during the maturation of the the T-cells.

Since thymus just mature T-cells, you will not find any B-cells. Its three phases are epithelial, lymphatic and adipose. In the thymus the T-cells are confronted with both foreign and selv antigens – positive and negative selection. As they mature they move from the cortex to the medulla. It is important that no antigens invade the thymus because it interfere with the development. Therefore there is a a blood-thymus barrier which consist of 5 layers:

* endothelium of vessel
* basal membrane
* connective tissue with macrophages which phagocyteose any antigen that might slip through
* basal membrane
* epithelioreticular cell

In the cortex there are only capillaries and postcapillary venules. The matured T-cells may only exit the parenchyme through the postcapillary venules. The medulla contain also macrophages and dendrittic cells. This is becuase 90% of T-cells die during their maturation. Hassals bodies are also found in the medulla and are formed by epitheloid cells and contain keratohyalin.

# Palatine tonsil

Tonsils are diffuse lymphatic tissue masses surrounded by mucosa. The palatine tonsil are covered by stratified squamous non keratinizing epithelium. The palatine tonsil is a part of several tonsils in the mouth/nose area called Waldyers ring. Lingual tonsil is also covered by stratified squamous, but the key difference between these two is that palatine tonsil have deep crypts, while lingual may have small. In the lingual, 3 directions of muscle can be seen due to the tongue. Muscles in palatine tonsil are the two palatine arches. The deep crypts mean that it makes good living conditions for bacterias to grow. Due to this palatine tonsil are often inflammed.

The tonsil are built up of reticular connective tissue which acts as a soft skeleton. The lymphatic tissue are in groups called lymphatic follicles. These can be either primary or secondary by their precense or lack of germinal centers. The germial center will hold the differentiating, active lymphocytes, while the corona will hold the resting lymphocytes. Only B-cell are found in the lymphatic follicles. T-cells can also be found, but they are located between the lymphatic follicles. The germinal follicle are paler due to the DNA being less condensed because they are more active. Reticular connective tissue are rich in carbohydrates so PAS-H is a good staining method. High endothelial veins may be seen in the connective tissue. The epithelium of HEV are special and easily allows lymphocytes to cross it into the tonsil. There are two more tonsil, the tubarian and pharyngeal. These have respiratory epithelium, but only the tubarian have cartilage in it from the auditory tube. ALL the tonsils may containt salivary glands. You may therefore also see excretory ducts.

# Lymph node

The lymph node is an encapsulated organ and contains all phagocytic cells (macrophages, monocytes, neutrophile, dendrittic, mast) and lymphocytes. As most of the lymphoid tissue of the body, it has a reticular connective tissue skeleton. Reticular connetive tissue is always built up of collagen type 3.

The afferent lymph vessels enter in the capsule, the concave area of the lymph node. The efferent lymph vessels and arteries and veins enter in the hilus of the node. Below the capsule, are the cortex containting follicles with mostly B-lymphocytes. The next layer is the paracortex with mostly T-lymphocytes. The innermost layer is the medulla. Medulla contains medullary cords (mostly basophilic and B-lymphocytes) and medullary sinuses (lighter stained areas) and blood vessels. Medullary cords are cords of lymphatic tissue containing B-cells, makrophages and plasma cells. Medullary sinus are vessel like structures separating the cords. There are lymph in the medullary sinuses.

Route of the lymph flow:

1. afferent lymph vessel
2. subcapsular sinus / marginal sinus
3. trabecular sinus / cortical sinus
4. paracortical sinus
5. medullary sinus
6. effent lymp vessel

Lymphocytes can enter the node though high endothelial venules, or afferent lymph vessel, but most enter through HEV. Here the T-cells leave the vessel to meet up with antigen presenting cells, most often dendrittic cells.

# Spleen

The spleen has an immunological filtering function and also remove old blood cells. It is surrounded by a dense connective tissue capsule that gives of trabecula inside. The capsule also contain som myofibroblasts. It contains much of the thrombocytes found in the body. During fetal development it has hemotopoietic functions until the 7th month.

The hilum is where the splenic artery, splenic vein, nerves and ONLY efferent (like the thymus) lymph vessels leave and enter. The vessels go to the white pulp of the spleen. The white pulp are basophilic in color and are composed of mostly lymphocytes. Inside this white pulp runs the central artery which comes from the trabecular artery from the splenic artery. The central artery send branches to the white pulp, or through the marginal sinus which are located on the periphery of the white pulp near the red pulp. Lymphocytes aggregates around the central artery forming what is called PALS – periarterial lymphatic sheat. The PALS looks like a lymphatic follicle, but is recognizable due to the presence of the central artery. The lymphatic cells close around the artery are T-lymphocytes. The outer cells are B-lymphocytes and these areas are given branches from the central artery. These areas with B-cells are lymphatic follicles, and can therefore have a germinal center. These lymphatic follicles can be very big, and are called splenic nodules. BUT remember that all of this is still the white pulp.

The central artery may also continue into the red pulp of the spleen. Here it will give of penicillar arterioles, which will give of the ellipsoid arteries. They are sheated capillaries. This sheat is built up of macrophages, plasma cells, reticular cells and reticular fibers. This has a role in detecting antigens. At this point, the blood can go two directions. The first is freely into the red pulp, by non continuous capillaries. This space is called splenic cords and is filled with marcophages, lymphocytes, dendrittic cells, plasma cells and granulocytes. The blood is screened by macrophages which remove old blood cells. The blood then returns to splenic sinusoids. These sinusoids are very fenestrated. The other direction for the blood is directly into these splenic sinusoids. The blood then leaves in the venules, veins, trabecular veins and splenic vein.

Female genitalia

# Development

Primordial germ cells arive in the gonad during the embryonic development. Here they will rapidly proliferate by mitosis. They will then be called oogonium. Some of these will arrest in prophase 1. These are now 46 4n and are called primary oocytes. The number of oogonium will reach 7 million at 5th intrauterine month and then start to die. At birth there are 1-2 million left. All the surviving oogonium will have become primary oocytes. These will be a part of the primordial follicle.

Not until puberty, will the primary oocytes continue their development. Around 40 000 left at this point. The ovarian follicle will continue to develop around the oocyte. Every month 20-30 primordial follicle will enter further development. And late in the stage of development, the primary oocyte will finish meiosis 1, and begin meiosis 2. It stops in metaphase 2, 3 hours before ovulation. Meiosis 2 is not finished before fertilization happens. This means that most of the follicles of the different stages contain a primary oocyte. At the late preovulatory stage, the primary become secondary. I guess this happens in the antral follicle.

1. Primordial germ cell
2. Mitosis
3. Oogonium (46, 2n)
4. Incomplete meiosis which stops in prophase
5. Primary oocyte (46, 4n)
6. Puberty
7. Some finish meiosis 1
8. Secondary oocyte (23, 2n)
9. Ovulation
10. Begin meiosis 2 and stop in metaphase
11. Fertiliztion
12. Ovum (23, 1n)

# Ovaries

Cuboidal epithelium, with dense connective tissue below. This connective tissue is called tunica albuginea. The ovaria have cortex with the follicles at different stages and medulla with blood, lymph vessels and nerves. The cell rich connective tissue of the ovary is called stroma.

Close to the surface are the small primordial follicles containing the primary oocyte. They have a single squamous layer of pregranulosa cells. These cells are separated from the surrounding connective tissue by basement membrane. The primordial follicles are 30 micrometers. When the pregranulosa cells become cuboidal, the follicle becomes primary follicle. Between the granulosa layer and the oocyte the zona pellucida will develop

The next stage is the secondary / preantral follicle. The connective tissue next to the basement membrane creates the theca interna and theca externa. The secondary follicle are 120 micrometers and it takes approximately 120-150 days to reach that size.

The granulosa layers will grow more, and will get a cavity inside called the antrum. The follicle is now called antral or tertiary follice. We divide the antral follicle in early and late by the size. There will still be granulosa cells attached to the oocyte, which will be called cumulus oophorus. Open spaces below the cumulus oophorus will be a sign of a degenerating follicle.

There will be granulosa cells on the oocyte as well, and these will become the corona radiata.

Many follicles will reach this stage, but only 1 will become the graafian follicle that will later ovulate. It takes 60 days to go from 120 micrometers to 1 millimeter. 20 days later, the follicle will ovulate.

During the degeneration of the follicle, the granulosa cells will fall into the antrum which will be filled with connective tissue. The basal membrane thickens and turns to membrana vitrea, and will be surrounded by densely packed cells from the theca cells.

If there can be seen granulosa cells in the antrum, it means that the follicle is degenerating.

## Corpus lutem and albicans

Aftet the ovulation, the follicle will become corpus luteum. Corpus luteum will have lutein cells derived from granulosa og theca interna cells. Theca lutein cells will produce androgens and progesterone, while granulosa lutein cells will produce progesterone, estrogen and inhibin A. Granulosa lutein will be paler than the theca lutein cells. They look pale because they contain steroid hormones. The antrum will first be invaded by fibrin and then fibrocytes. The theca externa will form a capsule around the corpus luteum.

Blood and lymph vessels from the theca interna grows into the granulosa layer, and it become highy vascularized. The corpus luteum remains active for 14 days. If fertilization does not occur/hCG (human chorionic gonadotropin) is not secreted (by syncytiotrophoblast), the secreting of estrogens and progesterone decrease and after 9 days it become corpus luteum of menstruation / menstruatatis. It will later become the corpus albicans. Corpus albicans will slowly disappear over a few months.

# Uterine tube

The epithelium is ciliated simple columnar, and there are also PEG secretory cells. PEG cells number varies in the cycle, mainly by the precense of progesterone. The lamina propria is very vascularized. There are two muscular layers, inner circular and outer longitudinal, and the surface is covered by peritoneum.

There a many projection into the lumen of the uterine tube called mucosa folds made by the lamina propria. The ovum is in the uterine tube for about 3 days until it enters the uterus.

# Uterus

The uterus consist of 3 layers, perimetrium, myometrium and endometrium. And the endometrium has 2 main layers. Stratum basale which is a constant layer which thickness i not affected by the cycles and the deepest of the two. The upper layer is the stratum functionale which is affected by the cycles. It can further be divided into stratum compactum and stratum spongiosum.

Endometrium = stratum basale + stratum functionale

Stratum functionale = upper stratum compactum + lower stratum spongiosum

The myometrium muscle cells seems randomly organized in the slide. During pregnancy the muscle cells undergo hypertrophy and their diameter increase 10x.

Since there are no progesterone/estrogen receptors in stratum basale – nothing happen to that layer during the cycles.

The perimetrium is subserosa (loose connective tissue) and serosa (mesothelium)

## Proliferative phase

The inner uterine surface is lined with simple columnar epithelium, some can have kinocilia. They are short so they may look like cuboidal epithelium. There can be see uterine glands in the stratum basale with simple columnar, latering turning to pseudostratified columnar. Between the glands are the stroma. There is no submucosa in the uterus. The stroma is supplied by spiral arteries, and the wall on the endometrium is about 3 mm at the end of proliferative phase.

Stratum compactum is just below the uterine epithelium and look red-ish (on some slides).

The phase is initated by estrogen, and at this point there is only stratum basale at 1mm. Growth of the endometrium will occur which will be the stratum functionale. The spiral arteries lengthen but does not reach the upper third of the endometrium.

The phase end about one day ofter ovulation and is then 3mm

The glands in stratum basale is more linear, while the glands of the stratum functionale is more coiled.

Stratum basale function as a place for the functional layer to grow. Estrogen will growth of everything in the layer: stroma, glands, spiral arteries. Progesterone will pseudodecidualize the compact layer. Progesterone will make the glands very coiled and look cork screw like. They will produce glycogen rich mucous for the developing embryo.

## Secretory/luteal phase

Is initiated by progesterone about 1-2 days after ovulation. The mucous (lamina propria) thickens and the glands dilate and become tortuous. Glycogen accumulate in the base of the gland epithelium and glycoproteins are found in the glandular lumen.

Due to higher levels of progesterone in the stratum compactum, the stroma cells will enlarge and become epithelium like. This is called decidualization and the cells are called pseudodecidual cells.

## Menstrual phase

When the corpus luteum stop secreting progesterone, the vessles in the stratum functionale contract and stratum functionale becomes ischemic. Disruption of surface epithelium and blood vessels happen. Spiral arteries cut off. Uterine glands stop production.

## Pregnant uterus

Parietal decidua is what covers the wall of the uterus but not the embryo during development. These cells are located under the epithelium and is derived from the stratum compactum by the presence of progesterone. Remember that these cells are pale because they contain glycogen. After some time, the space between the perietal decidua and capsular decidua will disappear and be filled with fibrin. Therefore the layers of a slide from this area will have these structures:

* Amnion (simple cuboidal)
* chorionic mesoderm
* capsular decidua and cellular trophoblast layer
* fibrin
* parietal decidua
* myometrium

The area where the embryo connects to the uterus will be the basal decidua. Marginal deciduia is found as a ring aorung the chorionic plate/basal decidua.

# Ovarian and uterine cycle

## Ovarian

Hypothalamus will release GnRH (gonadotropin releasing hormone), which will stimulate the secretion of FSH which stimulate the growth of the primordial follicle. Later a spike in the amount of LH will stumulate the olvulation of the Graafian follicle. This marks the end of the follicular phase of the ovarian cycle, and the beginning of the luteal phase, and happens around day 14.

## Uterine

The beginning of the cycle is the menstrual phase, and happens at the same time as the follic. So during the follicular phase of the ovarian cycle, the menstrual phase happens and also the proliferating phase. At ovulation, the uterine wall is getting thick. Around a week later, the uterine wall are optimal for implantation. The reason it keeps growing is the corpus luteum which release progesterone. If the implantation does not happen --> HCG is not secreted --> corpus luteum degenerate --> progesterone secretion stops --> menstrual phase begin.

Hypothalamus secrete GnRH. This will cause secretion of FSH. FSH saves 15-20 developing preantral follicles from atresion. As these develop, the theca interna and granulsa cell will begin to produce estrogen. Increase in estrogen levels will eventually cause the hypothalamus to secrete LH. Low amount of estrogen inhibits . LH is what cause the Graafian follicle to finish meiosis 1, being meiosis 2 and trigger ovulation.

# Cervix

The cervix is divided in vaginal and supravaginal parts. The supravaginal parts epithelium is called endocervix and is mucin producing columnar epithelium. The exocervix is covered by stratified squamous non keratinizing epithelium. The junction between these two epithelium is squamocolumnar junction. The place of this junction varies through the life. At pregnancy is it lower, and at menopause it is higher. During puberty it go more distally.

The mucous produced in the endocervix has protective properties against infections and during ovulation it changes to allow sperm cells to pass. It also lubricates the vagina normally.

Is stay closed until birth and give protection against infections

During pregnancy the stroma of the cervix change drastically to allow for dilation during delivery.

# Vagina

1. stratified squamous non keratinized epithelium. This looks pale beacuse the presence of much glycogen
2. no muscularis mucosa, submucosa or glands
3. can see lymph follicles
4. inner circular and outer longitudinal muscle, but these are not very visible/destinguishable
5. elastic fibers rich lamina propria
6. adventitia

The glycogen is fermentated by bacterias to form lactic acid which makes the pH acidic in the vagina. This together with the lymphatic follicles protect the inside from the outside.

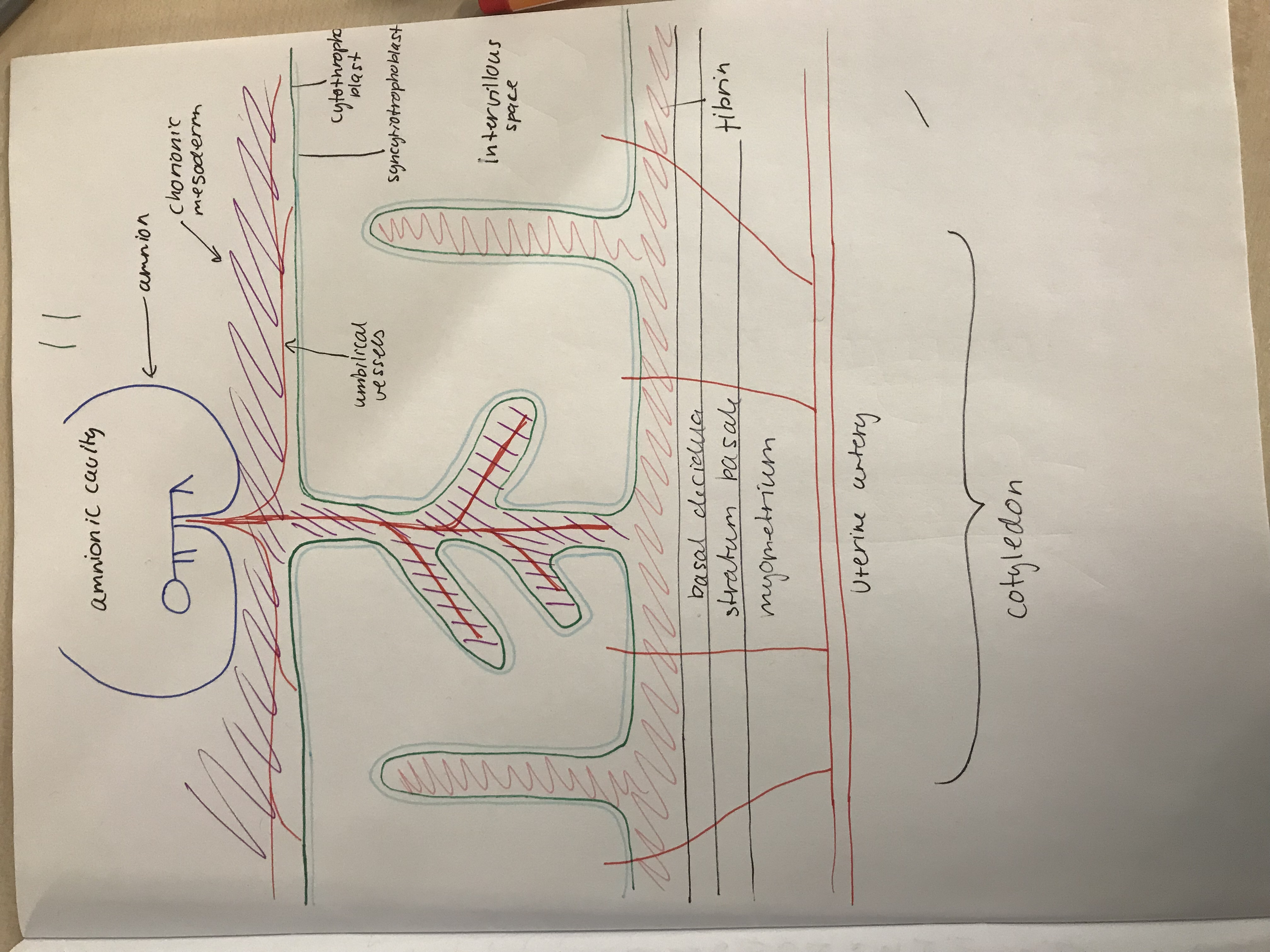
Since there are no glands in the vagina, other functions lubricate it

* when glycogen is broken down the colloid pressure increase and water is absorbed into the lumen
* cervical glands
* bartholins glands in the labia majora which only work during sexual arousal.

Remember fibromuscular tissue

# Mammary gland

The lobules are embedded in a fiber rich stroma which contains various amounts of fat. The connective tissue is cell-rich. These lobules are located near the terminal duct and consist of acinus and connective tissue. A group of lobules make up the lobes.

The duct system is made up of 2 layers of epithelium, an inner cuboidal and outer myoepithelial layer. The acinus drain into the terminal duct --> lactiferous duct --> lactiferous sinus. Lactiferous sinus are dilations in the lactiferous ducts which holds milk. The duct system before puberty in girls, and always in men are rudimentary and ends blindly

There are progenitor cells in the connective tissue in the intralobular space near the terminal duct, which proliferate during pregnancy. These cells are often the ones responsible for cancer.

The nipple has different structures. The protruding part is the mammary papilla and areola is the skin around. Both of them are highly pigmented. Areolar glands can be seen in the areola lubricating and protecting the nipple.

## During lactation

The mammary glands are compound tuboalveolar apocrine glands. During pregnancy the amount of fat and connective tissue decreases. Cells proliferate by mitotic division. Estrogen induce the proliferation of ducts, while progesterone induce the growth of the alveoli. There will be myoepithelial cells below the epithelium of the ducts, which can be either cuboidal or columnar. There will be connective tissue between the lobes.

The epithelium of the glands is of variable hights and secrete fat (apocrine) and protein (merocrine). Immun systemt structures are found which aids in the secretion of antibodies for the child.

# Placenta

The synsytiotrophoblast grow into the maternal tissue and creates lacunea which are then filled up with maternal blood. This is the establishment of the primitive uteroplacental circulation at day 11-13. Then primary chorionic villi will grow into these lacunae. These primary chorinic villi will be filled with chorionic mesoderm and then be called secondary chorionic villi at day 16. At the end of the third week the secondary chorionic villi will be vascularized and then called tertiary chorionic villi. Cytotrophoblast will totally capsulate the syncytiotrophoblast which holds the maternal blood. The trophoblast shell are penetrated some places by uterine artery branches called spiral arteries.

Growing villi happens all over the amnion, but only on the decidua basalis they will continue to grow. On the decidua capsularis they will begin to degenerate.

Placenta ceptum grow into the intervillous space but does not fuse with the chorionic plate. They create the cotyledons. Anchoring villi go all the way from the chorionic plate to the the trophoblast on the maternal side.

Later the cytotrophoblast will disappear, and the vessels moves to the wall of the villi. This will make the barrier from maternal to fetal blood shorter. From endothelium, basal membrame, chorionic mesoderm, basal membrane, cytotrophoblast, syncytiotrophoblast, maternal blood --> endothelium, basal membrane, basal membrane, syncytiotrophoblast.

The placenta produce many hormones such as hCG, hCS, IGF1 and IGF2, Relactin, Leptin. Syncytial knots can be seen as aggregates of syncityotrophoblast nuclei.

# Umbilical cord

The umbilical cord consist of 2 umbilical arteries, 1 umbilical vein, whartons jelly and amnion eptihelium. The wharton jelly contains glycosamioglycans and hyaluronic acid. It has a very high water content to cushion the vessels, and to evaporate quickly after birth. The epithelium is simple cuboidal, but can look flat.

The two arteries has smooth muscle in in tunica media but not tunica adventita. The vein has smooth muscles in both tunica media and adventitia. The umbilical cord may have a structure in the middle which is the remnant of the allantois.

Heart

## Types of muscle

**Skeletal muscle**

* consist of many muscle fibers called myofibrills
* each myofibrill consist of multiple sarcomere
* 1 sarcomere is about 2 micrometer long
* single mononucleated myoblast fuse to form multinucleated muscle fibers
* the nuclei is in the periphery/edge of the fiber

**Smooth muscle**

* they are made up of multiple cells with gap junctions, but only have 1 central nucleus
* these cells lack the striated apparence because the actin and myosin are randomly arranged
* myoepithelial cells are very abundant in the body around tubes

**Cardiac muscle**

* these are striated just like the skeletal because the regular arrangment of actin en myosin, but they are not voluntary
* the cell usually have just one central nucleus
* they are often branched
* intercalated discs are the meeting point between the cardiac muscle cells. These are tightly connected specialised junctions. This disc contain gap junctions, adhering junctions and desmosomes. The gap junctions allow the cells to be electrically connected.

## Cardiac layers

**Endocardium**

This layers lines the inner surface and consist of an endothelial layer and subendothelial layer. The subendothelial layer differ in thickness and contain the purkinje fibers. They may contain sensory fibers.

**Myocardium**

This is most of the thickness of the wall. There is a connective tissue between the muscle cell and this also connect to subendothelial layer and subepicardial layer. The wall is very richly vascularized, almost every muscle cell has a capillary next to it.

**Epicardium**

Also called visceral pericardium. This consist of an outer mesothelial layer, a serous layer. Between this and the myocardium we find the subepicardial layer. The subepicardial layer consist of connective tissue and fat cells. Large vessel of the heart and their nerves are embedded in the subepicardial layer.

**Parietal pericardium**

Is the outermost layer of the heart and consist of an innen mesothelial layer and outer fibrous layer. The mesothelial layer come in contact with the mesothelial layer of the epicardium, and between are some serous fluid to minimize friction. The fibrous layer is made of dense connective tissue.

Histo 1

# Intramembranous ossification

Mesenchymal tissue with mesenchymal cells. The cells undergo differentiation to osteblasts. They will produce osteoid with is collagen type 1 and ground substance. This ground substance is later mineralized by the adding of calcium salts. When the cells are covered by the osteoid they become ostecytes. Spiculas are processes from this substance and can connect many together. They can also grow around vessels to increase nutrition and waste exchange. The outer layer of this now formed bone can be modified to osteons. The bone have an outer layer called periosteum, and the inner layer of this contain osteoblasts which can create more bone in a process called appositional growth.

This process give rise to spongy bone.

# Endochondral ossification

Mesenchymal stem cells will give rise to a hyalin cartilage. Primary ossification center start to form in the middle of the cartilage. An outer layer of osteoblasts will covers the shaft of the hyalin cartilage and begin secreting osteoid, as in intramembranous ossification. Chondrocytes inside will begin to die because the bony collar around the shaft will interferie with the nutrition diffusion. Vessels break into the center and bring with osteclasts and osteoblasts. Osteoclasts break up the inside to create the bone marrow cavity. They are on the surface of the trabecula.

Secondary ossification center happens in the epiphyses and it ossifies. There is cartilage plate between the diaphyses and epiphyses which will be the center for growing and elongation of the bone.

# Aorta

Tunica intima is a single layer endothelial cells supported by an elastic memebrane below.

Vasa vasorum o the tunica adventitia

## More

If the slide is from an old person, lipofuscin pigment can be seen. These are residues from lysosomal digestion. Can for example contain carbohydrates, lipids, membrane fragment or metallic ions. It is often a sign of an old cell. And since cardiac cells live for a very long time, they can often be seen in the heart.

FeH staining is very good to show the intercalated discs and striations. Remember that the striations does not cross over the intercalated discs.

The surface of the valves are continous with the endocardial surface. Inside they have a spongy and fibrous layer. The fibrous layer is continous with the annulus fribrosus / the cardiac skeleton. The spongy layer contains fibroblast, macrophages, hyaluronic acid, proteoglycans and some fibers. No blood vessels in the valves.

The atria can release ANP (atrial natriuretic peptide) and released due to high blood pressure. Has multiple effect on the organs of the body. The ventricle secrete a similar hormone called brain natriuretic hormone.