Histology: A Guide for Medical Studies

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In medical school, histology lectures are accompanied by a microscopy course, which allows for practical consolidation of theoretical knowledge. After completing the course, each student should be able to recognize organs based on their histological specimens. This guide helps you understand the extensive discipline of histology and to master it with flying colors.

Definition: What is Histology?

Histology as part of microscopic anatomy

Histology (Greek: histos = tissue and logos = teaching) is the study of tissue and belongs to the field of microscopic anatomy. It deals with the arrangement and structure of cells and their organization as a cellular unit in various tissue types.

Histology lectures and a microscopy course are offered in the first and second semesters of preclinical studies. This is especially relevant for the following clinical phase, as it equips one with the skills for future diagnosis from tissue samples.
General Histology

The first step for identifying the specimen is looking at the section directly, i.e. without a microscope. One should consider the following questions at this point: ‘How many edges do I see?’ and ‘Does the section have a lumen?’.

Then the specimen is viewed in the lowest magnification, in order to gain a general overview and to eventually develop an initial hypothesis. It is best to work your way to larger magnifications in this manner, in order to capture details and to confirm or disprove the hypothesis with the assistance of this.

For orientation purposes, in order to not get lost in the section, it is advisable to always return to the lowest magnification and zoom in on the parts of interest once again. However, for success in the histology course, you need to not only recognize the section; you also need to have the background theoretical knowledge at hand.

Tissues

1. Epithelial tissue
Epithelium represents a group of cells that line various organs. There are three principal shapes:

- squamous
- cuboidal
- columnar

The presence of epithelium is an important clue for the diagnosis of the section. The epithelium type further assists one in establishing a rough guess with respect to the section.

In addition to the systematic structure, it is important for every doctor to know the distribution and function of all epithelial types in order to apply basic knowledge to the understanding of pathology.

2. Bone tissue
Bone is also tissue and can be sliced into a section. How is bone structured? Which cells are within bone? And how many bones does man really have? For physicians, it is important to understand the structure and the structure of a bone in the exam.

3. Muscle tissue

Muscles decisively define the body; its function is extremely important. Movement is the result of alternating contraction and relaxation (relaxation) of muscles, which account for about 30-40% of total body weight. The conversion of chemical energy into mechanical energy, in order to perform work, is the primary function of the muscle.

The muscles of the body can be classified into 3 different histological types:

<table>
<thead>
<tr>
<th>Type</th>
<th>Image</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smooth muscles as visceral muscles (muscles of internal hollow organs)</td>
<td><img src="image" alt="Smooth muscles" /></td>
</tr>
<tr>
<td>Cardiac muscle or myocardium</td>
<td><img src="image" alt="Cardiac muscle" /></td>
</tr>
<tr>
<td>Striated or skeletal muscle as a component of the active musculoskeletal system</td>
<td><img src="image" alt="Skeletal muscle" /></td>
</tr>
</tbody>
</table>

A concise overview of the different types of muscle, their structure, how to derive their
movement from their origin and insertion points, and the auxiliaries they use is essential for any physician.

Cells

The cell is the functional unit of a living organism. Organisms such as bacteria and algae are unicellular while complex organisms such as human beings are multicellular. In addition to this, complex organisms have an extracellular matrix and a complex organization of intracellular structures.

The cell is the basic building block of all life; it is only a few microns in size, yet it accomplishes incredible feats as a biological unit. With their numerous organelles, the cytoskeleton, and cell-cell junctions, they make for a popular examination topic in biology, biochemistry, and histology.

Special Histology

Down to business: which organs contain which tissue types in which composition, and how do these cell groups function as a whole?

Blood
Blood (Latin: sanguis, Greek: haima) is a suspension of various cells in a protein-containing saline solution. It accounts for 6-8% of body weight and has a pH value of 7.4. Blood performs numerous vital functions and is the linchpin of the entire organism.

<table>
<thead>
<tr>
<th>Blood components in %</th>
<th>Blood subcomponents in %</th>
<th>Type in % (if need be)</th>
<th>Production site</th>
<th>Main functions</th>
</tr>
</thead>
</table>

**Image:** “Hematopoietic System of Bone Marrow” by Phil Schatz. License: [CC BY 4.0](https://creativecommons.org/licenses/by/4.0/).
<table>
<thead>
<tr>
<th>Plasma</th>
<th>Water 92 %</th>
<th>Liquid</th>
<th>Absorbed through the intestinal tract or produced during metabolism</th>
<th>Transport medium</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Albumin 54-60 %</td>
<td>Liver</td>
<td>Maintains the osmotic concentration, transports lipid molecules</td>
<td></td>
</tr>
<tr>
<td>Plasma proteins 7 %</td>
<td>Globulin 35-38 %</td>
<td>Alpha globulin - Liver</td>
<td>Transport, maintains the osmotic concentration</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Beta globulin - Liver</td>
<td>Transport, maintains the osmotic concentration</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Gamma globulin (Immunoglobulin) - Plasma cells</td>
<td>Immune response</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fibrinogen 4-7 %</td>
<td>Liver</td>
<td>Coagulation during hemostasis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Regulatory proteins &lt;1 %</td>
<td>Hormones and enzymes</td>
<td>Various sites</td>
<td>Regulates various bodily functions</td>
</tr>
<tr>
<td></td>
<td>Other solutes 1 %</td>
<td>Nutrients, gases, and waste products</td>
<td>Absorbed by intestines, gas exchange in the respiratory tract or produced by cells</td>
<td>Several different functions</td>
</tr>
<tr>
<td>Erythrocytes 99 %</td>
<td>Erythrocytes</td>
<td>Redbone marrow</td>
<td>Transports gases, primarily oxygen and some carbon dioxide</td>
<td></td>
</tr>
<tr>
<td>Main components 37-54 %</td>
<td>Granulocytes: neutrophils, eosinophils, and basophils</td>
<td>Redbone marrow</td>
<td>Innate immunity</td>
<td></td>
</tr>
<tr>
<td>Leucocytes &lt;1 %, thrombocytes &lt;1 %</td>
<td>Lymphocytes: bone marrow and lymphatic tissue</td>
<td></td>
<td>Lymphocytes: adaptive immunity</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Agranular leukocytes: lymphocytes, monocytes</td>
<td></td>
<td>Monocytes: innate immunity</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Monocytes: red bone marrow</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Thrombocytes &lt;1 %</td>
<td>Megakaryocytes: red bone marrow</td>
<td>Coagulation</td>
<td></td>
</tr>
</tbody>
</table>

Blood vessels: The wall structure of arteries and veins

Blood vessels move in and out of a histological section. They should be recognized as such, and one should be able to differentiate arteries from veins. The main difference lies in the wall structure.
Circulatory system

The human circulatory system is the convective transport of respiratory gases, nutrients, hormones, and heat. The medium for this is blood, which is pumped from the heart through the blood vessels and is returned to the heart.
The blood circulation is a rapidly modifiable system which is indispensable for the maintenance of bodily functions. High blood pressure (arterial hypertension) is one of the most common diseases in society. It is therefore important for physicians to know and understand the circulatory system.

Respiratory system

Along with the intestines and the skin, the lung is another organ with direct contact with the outside world. Its purpose is the basis of our existence: gas exchange by diffusion. In order to perform this feat every second, a transport system for waste gases and fresh air is required.

Equally important is a space in which the walls are thin enough for gas diffusion, and a transport service for the gases in a chemically bound form. Histologists must closely
inspect how these tasks are handled by the individual structures.

The integumentary system

The skin, subcutaneous fat, hair, and nails protect us from external influences and keep us intact. For this, they must be sealed so that our body fluids aren’t simply emptied. The skin is the largest organ and has a weight of 3-10 kg. In an individual who is 170 cm tall, it’s surface area equals 1.8 m². The skin is also the site of vitamin D synthesis.

Kidney and excretory organs

The kidney is a vital excretory organ and controls the water and electrolyte balance in our body. Their exact mechanism of action can only be understood at the microscopic level. Each renal tissue type is purpose-built and the sophisticated function of the kidney reveals itself in its histology.

Endocrine organs and hormonal system

Without our hormonal system, our bodies would not function as a whole. Endocrine organs ensure communication between individual specialized systems. All of these can only coordinate adequate responses to our environment in this manner.

The control of bodily functions through the messengers (hormones) of the endocrine system is the subject of anatomy, physiology, and biochemistry; for clinical practice, too, a thorough understanding of the hormones and their functions is essential. Pituitary, thyroid, parathyroid, adrenal, and pineal glands belong to the group of endocrine organs, in the strictest sense of the term. As a result of their characteristic structures, they are not difficult to identify in a histological section, but there are some things that you should consider.

Study table: Endocrine glands and their main hormones

<table>
<thead>
<tr>
<th>Endocrine gland</th>
<th>Associated hormones</th>
<th>Chemical class</th>
<th>Effect</th>
</tr>
</thead>
</table>

*Image: “Layers of Skin” by Phil Schatz. License: CC BY 4.0*
The immune system
The **lymphoid organs**, which include the thymus, spleen (milt), lymph nodes and tonsils, are exciting points of interest, and important parts of the study of medicine. The lymphatic system is involved in numerous processes and exerts its effects throughout the body. Its function is defense, and it is complex. Understanding this system is crucial for the diagnosis of several disease processes.

**Nervous system**
The nervous system 'only' weighs 2 kg, which amounts to app. 3 % of total body weight. It is a small and complex body system because it consists of a complex network of nerve cells, neurons and an even greater number of neuroglia. For all physicians, it is important to know how the nervous system works and how it is structured.

**Sensory system**

The sensory organs allow us to interact with our environment and to perceive things outside of our body. Their functions are as fascinating as they are complex, substantial topics in the study of medicine.

Despite the great diversity of the sense organs, however, they all follow basic principles in their structure and function. Starting from the basics, it is only a small step to the level of detailed knowledge required about the different senses.

**The digestive system and gastrointestinal tract**
The digestive system gives many doctors headaches. It is important to clarify the subtle differences between each component of it.

The breakdown of nutrients and the subsequent supply of these to the organism can be understood through digestion. Nutrients are then transported into individual cells of the body via the bloodstream.

The pancreas
The pancreas is both an exocrine and an endocrine organ. It is essential for digestion and the metabolism of carbohydrates, which is why a loss of function leads to severe diseases.

Female Reproductive System – follicular, mucous and breast tissue

The female sex organs undergo periodically recurring changes in structure. This should be recognized and understood.

In the female sex organs, a number of processes run under hormonal influence. Folliculogenesis in the uterus, the structure of the mammary gland tissue, and lactation are processes that are required knowledge among medical students.

The male reproductive system

The understanding of the male reproductive system requires a lot of biological knowledge. The male reproductive organs with testis and vas deferens are divided into different sections.

Staining of Histological Preparations

Staining is an additional process of microscopy that serves to enhance the contrast of the microbiological image. They help to highlight tissues in focus. To do better in the microscopy course, it is worthwhile having a look at the different histological stains and to understand which dye stains which structure:

H&E stain
H&E abbreviates the two dyes used: hematoxylin and eosin. In this stain, the nucleus appears blue and the cytoplasm appears pale red. Collagen fibers are stained a strong red, as are muscle and bone. Elastic fibers are a brighter red. Erythrocytes are orange-to-red under with H&E stain. Hyaline cartilage is stained blue.

Azan stain

The Azan staining uses three dyes: azocarmine, orange G and aniline blue. In the presence of this dye, the nucleus is bright red and the cytoplasm is pale pink. Collagen fibers appear blue, as does hyaline cartilage. Elastic fibers, muscle tissue, and bone are all stained red. Erythrocytes are dyed orange to red, just as they are with H&E stain.

Elastica stain

The Elastic fibers in mammary glands coulered by Weigert’s elastic stain. Elastic fibers are blue.” by R.Denzer. License: CC BY-SA 3.0
Elastic fibers and membranes are selectively presented with resorcinol-fuchsin or orcein. These appear as pale violet (resorcinol-fuchsin) or reddish-brown (orcein) in histological sections.

Van Gieson’s stain

Van Gieson’s stain is a mixture of iron hematoxylin, picric acid, and acid fuchsin. It dyes the nucleus black-brown and the cytoplasm yellowish. Collagen fibers appear red. Elastic fibers, hyaline cartilage, muscle tissue, bone, and red blood cells are all yellowish with this dye.

Crossmon stain

The Crossmon stain consists of iron hematoxylin, orange G and light green SF. Through this, the nucleus is also colored black-brown, while the cytoplasm appears reddish. Collagen fibers take on a green hue. Elastic fibers and bones are light-red. Erythrocytes are stained orange with Crossmon.

Special stains

Furthermore, there are a number of special stains, in which histochemical stains play the biggest role. They enable one to get a glimpse of the dynamic cellular events; for instance, carbohydrate components such as glycoproteins or glycogen (PAS reaction), negatively charged components such as glycosaminoglycans or hyaluronic acid (Alcian blue stain), or lipids (fatty dyes such as Sudan III) represent the site of their natural occurrence within cells and tissues.

Finally, take immunohistochemical methods into account. Here, specific proteins or peptides may be detected using an antigen-antibody reaction.

If you want to display specific DNA or RNA sequences, in-situ hybridization is the method of choice. Radioactively or non-radioactively labeled samples are applied to the histological section and can be localized accordingly.

Study Table: Commonly used stains

<table>
<thead>
<tr>
<th>Stain</th>
<th>General application</th>
<th>Nucleus</th>
<th>Cytoplasm</th>
<th>Red blood cells</th>
<th>Collagen fibers</th>
<th>Special stains</th>
</tr>
</thead>
</table>

Image: “Colored bronchi of ostrich, after Van Gieson” by Lycaon.cl. License: CC BY-SA 4.0
<table>
<thead>
<tr>
<th>Stain/Method</th>
<th>Application</th>
<th>Stain Colors</th>
<th>Additional Stains</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Haematoxylin</strong></td>
<td>Commonly used staining, often paired with eosin</td>
<td>Orange, cyan, blue or green</td>
<td>Blue/brown/black</td>
</tr>
<tr>
<td><strong>Eosin</strong></td>
<td>Commonly used staining, often paired with haematoxylin</td>
<td>N/A</td>
<td>Pink</td>
</tr>
<tr>
<td><strong>Toluidine blue</strong></td>
<td>Commonly used staining</td>
<td>Blue</td>
<td>Blue</td>
</tr>
<tr>
<td><strong>Masson’s trichrome stain</strong></td>
<td>Connective tissue</td>
<td>Black</td>
<td>Red/Pink</td>
</tr>
<tr>
<td><strong>Mallory´s trichrome stain</strong></td>
<td>Connective tissue</td>
<td>Red</td>
<td>Pale red</td>
</tr>
<tr>
<td><strong>Elastica stain</strong></td>
<td>Elastica fibers</td>
<td>Blue/black</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Azan stain</strong></td>
<td>Separates cells from extracellular components</td>
<td>Red/purple</td>
<td>Pink</td>
</tr>
<tr>
<td><strong>Silver stain</strong></td>
<td>Reticular fibers, nerve fibers, fungi</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Wright stain</strong></td>
<td>Blood cells</td>
<td>Bluish/purple</td>
<td>Bluish/purple</td>
</tr>
<tr>
<td><strong>Orcein stain</strong></td>
<td>Elastic fibers</td>
<td>Dark blue</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>PAS reaction</strong></td>
<td>Basal membrane, localization of carbohydrates</td>
<td>Blue</td>
<td>N/A</td>
</tr>
</tbody>
</table>

Table: “Common laboratory stains” by Wikipedia.

Advice for Final Exams

Histology is a very extensive subject. It’s reasonable to wonder whether or not the effort is worthwhile, considering the number of questions asked about it. A clear ‘yes’ should be the answer to this question, because histology is a subject central to medicine and covers areas of anatomy, biology, physiology, even through to biochemistry. A basic...
understanding of histology facilitates the learning of other essential subjects and makes it possible to view pre-clinical knowledge not only in individualized compartments but as a connected unit, allowing you to see the big picture.

To make this easier for, here are a few **histology mnemonics**:

- **Titin** sounds like **Titan** and is the **largest** protein in the body.
- **T**-cells come from the **thymus**.
- **B**-cells come from **bone**.
- **Plexus submucosus** (Meissner) is responsible for the **mucosa**, lies centrally.
- **Plexus myentericus** (Auerbach) innervates muscles, lies externally.
- **Osteoclasts** chew up bone.
- **Osteoblasts** build up bone.
- **C**-cells make **calcitonin** which reduces Ca\(^{2+}\)-levels in plasma.
- **Parathyroid hormone** provides the body with Ca\(^{2+}\) (in blood).

### 20 Popular Exam Questions on Histology

The answers are below the last question.

1. **Which of these statements regarding epithelial tissue is false?**
   1. Epithelial tissue is embryologically derived from all three germ layers.
   2. Epithelial tissue has no appreciable intercellular elements.
   3. Epithelial tissue is located at the skin surface or on the inside of hollow organs.
   4. Epithelial tissue is supported in the intercellular space and by blood vessels.
   5. The cells of epithelial tissue have an apical and a basal pole.

2. **Which of the following items are not part of the basal lamina of basement membranes?**
   1. Lamina rara externa
   2. Lamina densa
   3. Lamina propria
   4. Lamina fibroreticularis
   5. Lamina rara interna

3. **Which relationship does not fit?**
   1. Osteoblasts build up bone.
   2. Osteocytes maintain the tissue structure.
   3. Osteoclasts break down bone.
   4. Osteons are small units of bone.
   5. Canaliculi are narrow gaps.

4. **Which statement about ossification is true?**
   1. The process of bone loss is called ossification.
   2. Chondral ossification is part of intramembranous ossification.
   3. Perichondral ossification is one of the steps of chondral ossification.
   4. Intramembranous ossification turns cartilage into bone.
   5. Chondral ossification is described as the direct pathway of ossification.

5. **Blood plasma refers to:**
   1. The fluid that remains after the coagulation of blood
2. The ionized components of blood
3. An isotonic saline solution for blood
4. The supernatant fluid after centrifugation of blood
5. The cellular portion of blood

6. Iron deficiency anemia is most commonly caused by:
   1. Chronic blood loss
   2. Vitamin B12 deficiency
   3. Increased iron excretion as a result of renal failure
   4. Increased consumption of alcohol
   5. Damage to the blood-forming bone marrow

7. Which statement concerning the construction of a blood vessel is true?
   1. Tunica interna consists only of simple squamous epithelium.
   2. Elastic type arteries, the subendothelial stratum is next to non-existent.
   3. Tight junctions are found in non-fenestrated capillaries.
   4. The musculature of venule walls can regulate the flow rate of the blood, which is why venules are also called resistance vessels.

8. Which statement about the capillary exchange system is false?
   1. The flow rate in arteries is 1000x higher than that of capillaries.
   2. Due to the small cross-sectional area of capillaries, erythrocytes can pass through by changing shape.
   3. The vessel wall of all capillaries consists of an endothelial layer, as well as from pericytes and a basement membrane.
   4. Fenestrated capillaries are found in places with large blood flow.

9. Which relationship is true?
   1. Zona glomerulosa of the adrenal medulla – glucocorticoids
   2. Zona fasciculata – aldosterone
   3. Zona reticularis – testosterone
   4. C cells of the thyroid – parathyroid hormone
   5. Epiphysis – melatonin

10. The hormones T3 and T4...
    1. ...are cholesterol derivatives.
    2. ...reduce the basal metabolic rate.
    3. ...are formed in the C cells of the thyroid gland.
    4. ...are stored extracellularly.
    5. ...are delivered directly into the blood.

11. Red pulp...
    1. ...stores lymphocytes.
    2. ...produces lymphocytes.
    3. ...breaks down leukocytes.
    4. ...gives off blood platelets.
    5. ... is located outside the spleen.

12. The thymus...
    1. ...is vital in youth and in old age.
    2. ... doubles its weight through fat deposits.
3. ... should be formed only in newborns.
4. ... keeps glandular tissue throughout life.
5. ... is important in children for the development of the immune system.

13. Which salivary gland defends the oral cavity from germs?
   1. Glandula parotidea (parotid gland)
   2. Glandula submandibularis (submandibular gland)
   3. Glandula sublingualis (sublingual gland)
   4. Glandulae buccales in the buccal mucosa
   5. Glandulae palatinae in the mucous membrane of the palate

14. What three special features does the mucosa of the small intestine have for the absorption of nutrients?
   1. Villi, microvilli and Brunner’s glands
   2. Microvilli, Brunner’s glands, and haustra
   3. Kerckring folds, villi and microvilli
   4. Kerckring folds, villi and haustra
   5. Adventitia, Brunner’s glands, and haustra

15. Which statement about the exocrine pancreas is true?
   1. The exocrine pancreas is a serous, tubuloalveolar gland.
   2. The secretory cells part with their secretion along with part of the cell membrane and the cytoplasm.
   3. The gland cells have one excretory duct at most, but with multiple terminal branches.
   4. A typical microscopic image of the exocrine pancreas is a tree-like branched duct system with striated and intercalated ducts.
   5. The histological appearance shows so-called centroacinar cells as parts of intercalated ducts.

16. Which statement is not true for the Langerhans islets?
   1. Langerhans islets consist of about 1 million cell aggregates that are like islets between the exocrine pancreas parts.
   2. B-cells of the Langerhans islets secrete the peptide hormone insulin, which lowers blood sugar levels.
   3. Somatostatin, which is in D-cells of the entire intestinal tract, inhibits the secretion of pancreatic secretion.
   4. Approximately 70% of islet cells contain the peptide hormone insulin in the β-granules.
   5. Glucagon activates glycogenesis.

17. Which statement is true?
   1. Graafian follicle is another word for tertiary follicles.
   2. Theca interna and externa are cellular waste products.
   3. FSH is also known as follitropin.
   4. Theca interna produces no hormones.
   5. Tertiary follicles have a size of about 0.5 cm.

18. Which statement is true?
   1. The endometrium is glandular tissue.
   2. The endometrium contains uterine glands.
3. The endometrium consists of connective tissue.
4. The endometrium is constantly regenerated.
5. The endometrium contains spiral muscles.

19. Tubuli seminiferi are...
1. ... excretory ducts of the testes.
2. ... Cowper’s glands.
3. ... another word for the inguinal canal.
4. ... seminiferous tubules.
5. ... supplying vessels of the germinal epithelium.

20. Flow in the testis:
1. The acrosome covers the head of the sperm partially.
2. Cowper’s glands cleanse the urethra before ejaculation.
3. Testosterone does not act on the accessory glands.
4. Sperm cells pass from the epididymis into the vas deferens.
5. Androgen produced in the interstitial cells of Leydig.

Correct answers: 1D, 2C, 3B, 4C, 5D, 6A, 7C, 8D, 9E, 10D, 11D, 12E, 13A, 14C, 15E, 16E, 17C, 18B, 19D, 20C

References


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