Jan Balko, Zbyněk Tonar,
Ivan Varga et al.

1st edition

MEMORIX HISTOLOGY

Managing editor: Radovan Hudák

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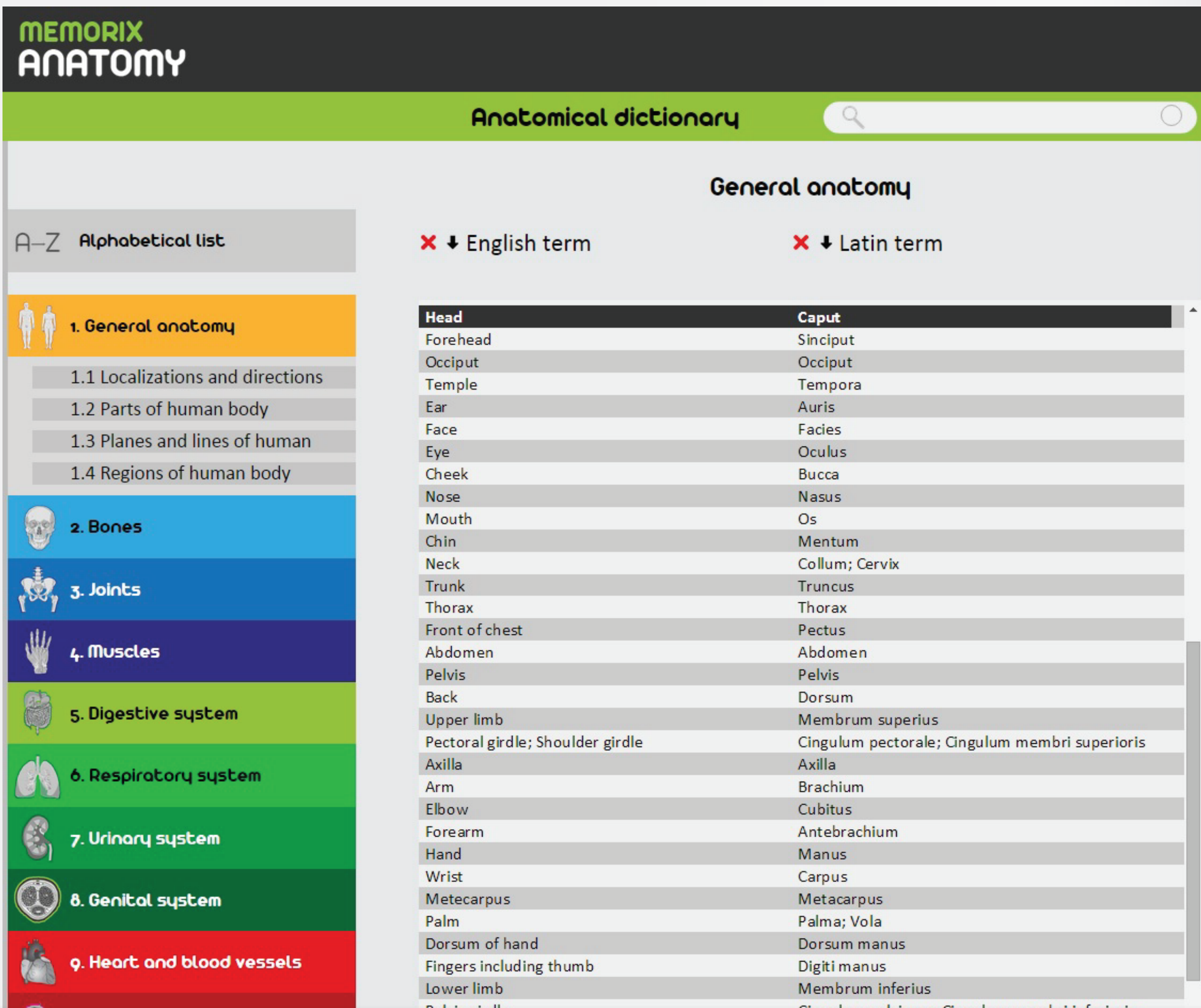

Head	Caput
Forehead	Sinciput
Occiput	Occiput
Temple	Tempora
Ear	Auris
Face	Facies
Eye	Oculus
Cheek	Bucca
Nose	Nasus
Mouth	Os
Chin	Mentum
Neck	Collum; Cervix
Trunk	Truncus
Thorax	Thorax
Front of chest	Pectus
Abdomen	Abdomen
Pelvis	Pelvis
Back	Dorsum
Upper limb	Membrum superius
Pectoral girdle; Shoulder girdle	Cingulum pectorale; Cingulum membri superioris
Axilla	Axilla
Arm	Brachium
Elbow	Cubitus
Forearm	Antebrachium
Hand	Manus
Wrist	Carpus
Metecarpus	Metacarpus
Palm	Palma; Vola
Dorsum of hand	Dorsum manus
Fingers including thumb	Digiti manus
Lower limb	Membrum inferius
Pelvic girdle	Cingulum pelvicum; Cingulum membri inferioris

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Dedicated to everyone who is a Histologist by eye
and can light up for the smallest things.

Jan Balko
Zbyněk Tonar
Ivan Varga
et al.

MEMORIX HISTOLOGY

1st edition

MEMORIX

Jan Balko, Zbyněk Tonar, Ivan Varga et al.
MEMORIX HISTOLOGY

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We live in times with easy access to information, **its quantity being so vast that it is almost impossible to cover it**. New information channels that have emerged in recent decades, **such as televisions and mobile phones** and especially the Internet, constantly provide new knowledge**. Even traditional forms of information transfer, such as** books recently experienced an unprecedented boom**.** Almost every theoretical institute at medical schools published a book or translated one of successful foreign titles**. The result is that we are slowly getting lost in this sea of information**. The more choices we have, the harder it is to choose **which teacher to believe, which books are worthy investing the time, what should be the basis of decisions in the exam and clinical practice** etc. This fact has resulted in the so–called **decision paralysis.** In medicine, it means that we are not able to decide what to learn, so in the worst case we do not learn from anything.

Book full of compromises

At the primary and secondary schools, we are used to the situation where **the vast majority of information provided during lessons or written in books** was the same. We could be confident that **if we acquire the knowledge, we will know everything** correctly. It's different at the college. In every field there is much basal **information**, presented by every teacher or doctor in the same way, but then, there is much of information **under discussion for many reasons**. Most often it has never been 100% verified or there have been some scientific discoveries. **In histology, the subjective opinion of histologists plays a big role,** they can see various shapes of cells in the microscope. Students who are used to learn dogmas **get lost in the mixture of information, lose their energy to study new things and worry that they will never have a chance to learn it**. The students will then get even more confused when the **professor lectures the lessons learned from his/her experience and the latest scientific articles**, **assistants teach according to the recommended literature and** student lecturers **recommended the** notes**prepared from students of higher grades.**

This **information gap** motivated us to try to **create study materials that meet the requirements of all the parties involved**. We invited **younger and more experienced histology specialists, pathologists, clinicians, of course, but also many students**. We tried to make a book that would contain **histological information both from available literature, the latest scientific papers, as well as from renowned histology specialists**. Pathologists and clinicians **gave emphasis on the quality of clinical correlations**, reflecting their importance for the medical practice. **Young doctors and students were trying to make the text readable and interesting**. Because only a **comprehensive, correct and graphically friendly textbooks can truly motivate students** to spent much of their youth with it, and older doctors to come back to it with love.

Memorix Histology is a textbook of huge compromises. If we put in all the information suggested by the authors and reviewers, it **would contain approximately 2,000 pages**. If we put in little information, it would not be respected in the academic sphere. **We believe that Memorix Histology will become a successful and popular textbook** and bring joy to all interested in this colorful morphological study.

MEMORIX
REVOLUTIONARY MEDICAL EDUCATION

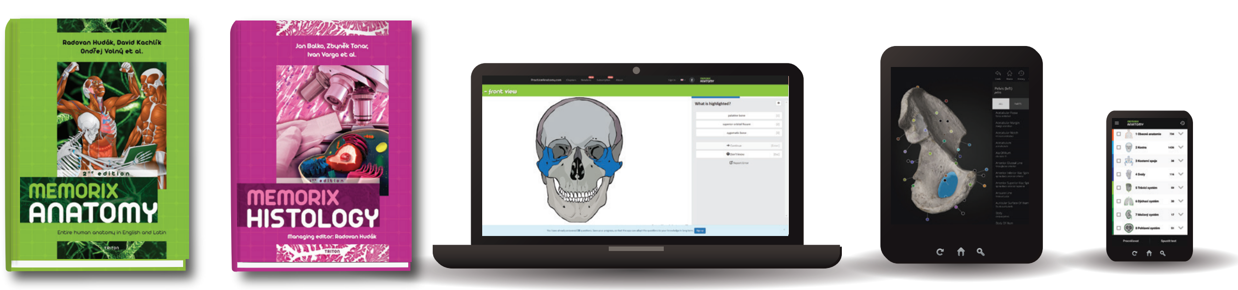
The idea of the Memorix

It's been 5 years since we completed the first edition of Memorix Anatomy. Since then, we have managed to prepare the **improved fourth edition of the Czech** and **the second English edition**, which got to various countries after a short time. There is already a Polish and Italian Memorix Anatomy and soon, the Hungarian version will be released. In addition, we embarked on the development of the **anatomical online dictionary (www.anatomicalterm.com),** which will be expanded by **many terms in various languages over the next years**, **but by the descriptions and images of anatomical structures**. Furthermore, **together with the group Adaptive Learning,** consisting of IT enthusiasts, we prepared a **web application www.practiceanatomy.com**, where you can revise the anatomy at your computer. Our newest and largest projects include **Memorix Anatomy QUIZ** mobile application, which will make anatomy revision more pleasant, anywhere, on Android and iOS and **Anatomyka**, the interactive 3D human anatomy atlas, allow you explore and interact with human anatomy in all its breathtaking complexity!

We do not want to brag with the list of our problems. Of course, we are proud **about them, but above all, we want to show that the** idea of Memorix does not lie only in publishing books. **Our aim is to** motivate all the students and teachers **to lose their fears and cooperate on the development of** study materials**. The list of options is virtually infinite (books, applications, videos, audio etc.) and it is impossible to fully appreciate the contribution. And lastly, we have a question: Why to be afraid to be successful and develop successful projects?** Success is not a coincidence. It is a choice everyone can make.

Look at our website **www.memorixanatomy.com**

Radovan Hudák
Prague 11. 6. 2018



Dear colleagues. **You are holding the first edition of the Memorix Histology**. **Never before, the people interested in the study of this specialization had a wider choice of high–quality printed and electronic study materials than today.** Despite that, or rather due to that, **a group of authors and graphic designers stemming from new graduates, students and teachers decided to contribute to histology education** in a way tested in the previous versions of Memorix Anatomy. **Do you want to know more about your body than you can see with the naked eye?** If so, read on. **Histology is interesting, and it deserves this attention.** This book has been written to help histology get your attention. In return, it will bring you the **knowledge of what is hidden under the microscope**.

Why are we studying and teaching histology?

Histological approach to knowledge of the human body is the link between the macroscopic **anatomy, developmental biology (embryology), cell biology, physiology, biochemistry and other areas** of the study of medicine and science. This makes it extremely useful and many generations of students can confirm that **efforts devoted to the study pay off many times in subsequent and related fields**. Only part of physicians actively use their knowledge and skills in cytology, tissue science, and microscopic anatomy in their diagnostic and therapeutic practice. But all those who seek understanding of anatomy during their education **find a logical explanation of relationships and mechanisms between cell organelles, cells, extracellular matrix and tissues. At a level hidden to an unarmed human eye, a microscope can explain much of what is observed during the development of the embryo and fetus, with anatomical autopsy, study of chemical reactions or homeostasis feedback loops. Histology, thanks to its explanatory capabilities,** not only satisfies the age–old human curiosity and desire for knowledge of hidden things, but it has structured the thinking of doctors for several centuries**. Like anatomy, histology teaches us to watch,** note, recognize and describe what they see**. It makes us observers and motivates us to think about how the observed structure of tissues and organs is related to their function. This helps us** remember a relatively large amount of subject thanks to logic, built on a solid foundation**. At the same time, it teaches us to think about the causes and consequences from the microscopic level to the level of the whole organism, which is the** key in shaping the thinking of future physicians, regardless of their specialization**. Learning to think and solve complex problems necessarily implies not to be tied up with the practice of a single specialization, but rather to learn how to use the study of acquired knowledge and skills according to the situation.** Only their combination provides the doctors and scientists the ability to think independently and critically **and to move the boundaries of knowledge. We provide this contemplation to our students as a response to the frequent and legitimate question "**where they will use histology **". Another explanation is available on the next page in the article on "The use of histology in pathology and clinical fields"**.

The histological approach to discovering the human body is a link between macroscopic anatomy, developmental biology (embryology), cellular biology, physiology, biochemistry and other areas of study of medicine and the natural sciences.

What to put into the histology textbook?

From its beginnings, **histology is a field of research into the structure, function and development of cells, tissues and organs**. It borders on many disciplines, but **the knowledge in each of them is constantly growing and overlapping**. Some faculties in our countries and abroad teach two different subjects – **the field of tissue science (general histology)**, and **separately, most commonly within anatomy, the microscopic organ structure (special histology)**. In other countries, both are included in one exam, often with embryology. Whether histology is taught and tested as a separate subject or integrated into multidisciplinary learning blocks, its role of explaining and interconnecting remains the same.

The selection of the knowledge we finally decided to include in the book was based on the mapping of the penetration between the matter taught at the medical faculties in the Czech Republic and Slovakia. Our goal was not to remove **any medically significant knowledge from our own histology in the narrower sense of the word** – as it belongs to its tradition and as it is included in the internationally recognized classification of terms – **Terminologia Histologica**. **Where the interpretation of histology already bordered on the following subjects** (e.g. with biochemistry or physiology), **we did not go too far beyond the histology, and** we remained only within the morphological foundations of the matter in a simplified form so that the students could extend the knowledge acquired in histology in these further subjects, so that the acquired knowledge would not need changes and corrections in the future.

The book would not come without the support of our reviewers from many sites in both republics. Thanks to their feedback, we have **removed some errors, refined and supplemented the interpretation or clarified confusing areas**. A number of ideas for **extending the chapters, which we did not included into the final version**. Often these were the same expanding remarks that the authors of the chapters themselves had originally included, but they did not go through the narrower selection for the final editions of the chapters, so that the section of the book remained readable and faithful to the overall concept of the textbook. **Embryology notes** are not a permanent and standardized part of all chapters, **but are only mentioned in selected cases** (e.g. tissue division according to the origin, in the nerve or reproductive system, etc.). **Without the knowledge of the development, it is impossible to understand the structure and functions of the human body.** However, we could not include and explain the development and ontogenetic associations in all the discussed organs and we refer to relevant embryology books. **If we used all the remarks of the reviewers, the extent of chapter would be disproportionately increased, diminishing the legibility and clarity**. There are many other references in the references recommended at the end of the chapters. On the other hand, we have received a number of proposals for the exclusion of certain areas. We are aware of the variety of teaching styles, the choice of test specimens and the test questions at individual faculties. We therefore encourage students to follow the recommendations of their teachers in these areas.

Texts, diagrams, atlas and microscopy

Effective study of histology requires the combination of several types of study materials with practical activities. The text books, scripts or lectures are used as the source of terms, their definitions and explanations of their relationships. **This reading and listening part cannot be skipped** as **even the most talented student cannot describe a preparation without the relevant terms**. The text part of our book **uses the internationally accepted terminology (Terminologia Histologica), while trying to respect both the common and newer forms of the Czech terminology**. All the terms are explained and staged so that the student does not lose the overview of the level. **The decision algorithms** included in several chapters are not the only possible ones, they do not include all the organs and are not intended for memorizing, but as **an inspiration for the questions, which are suitable for distinguishing preparations from different organs**.

The knowledge is illustrated using schemes to capture the shapes, proportions and typical staining of histological structures, which is often a useful lead reflecting their chemical composition. There are at least three reasons to create these schemes. **Schemes help us understand what to expect in the actual preparations** and increase the likelihood of finding the relevant structures in the preparation. **Schemes serve as a guide and inspiration for drawing of the actually observed cells and tissues**. Finally, **drawing of diagrams increases our attention to detail when using the microscope**. A well–drawn scheme can summarize the knowledge gained from observing many real–world specimens. In addition to the hundreds of schemes included in the book, you can also find recommendations on how to draw your own schemes and note your observations. **Schemes in the book are not quite photorealistic, and in selected cases, they depict the structures, which** would require replacing the lens in the microscope, disproportionately at various scales. Rather than memorizing, they are intended to inspire readers for their own observations. The advantage of schemes is the possibility to **depict the knowledge gained by observing a large amount of preparations,** which is one of the differences from photography, showing always only one particular segment of the cut.

Effective study of histology requires the combination of several types of study materials with practical activities.

Whether we watch **histological specimens through a microscope, or study their digitized, scanned virtual form**, we will encounter the restrictions associated with cartoon schemes. **Actual preparations appear to be less clear**; it is often difficult to find the boundaries between cells **and we need to acquire and not to lose the orientation when using different lenses**. Good tool are **the photomicrographs at the end of chapter**. For readers, we **carefully selected the preparations and images magnifications with regard to their readability,** so that they can serve as a start line for practical lessons. However, with the current range of the book, the images do not form a coherent atlas, and there is no need to include images of all the specimens and all magnifications showing the objects of interest. That is why we recommend using other printed or electronic histological atlases for practical microscopy. For microscope control and effective description of the preparations, we offer the readers the guidance in the chapter **Microscopy techniques**.

Microscope – window into the micro–world

Until microscopes were invented, improved and became a part of the education of physicians and naturalists, **the concepts of the internal structure of the body, its functioning, the causes and mechanisms of most diseases were cloudy or vice versa boldly speculative**. Microscopes are devices that have fundamentally shifted and are still moving the limits of human knowledge. **We cannot even imagine how the medicine would look without microscopes today**. The way microscopes expand our horizons, forces us to face tasks beyond our routine and everyday experience, especially in the introduction to histology (and other disciplines such as microbiology and physiology). We do not have direct contact with objects as small as cells or fibers and extracellular matter molecules. **Initially, we lack the idea of the dimensions and patterns**, which, unlike our macrocosm, **control the processes at the cellular and even smaller level**. We lack the terms for the descriptions of units generated by processing and staining of sections, **we have to distinguish a number of artificially induced changes in the preparations (artifacts)**. During its existence, histology nurtured **a rather effective terminology**, which has a similar role like. the small multiplication table in math – only its mastering opens more horizons where we can work and move. **The rate of use of microscopy at secondary schools is very diverse** , approach to teaching the basics of classical languages (Latin and Greek) in secondary schools and medical faculties are different and histology is included into different semesters of the curriculum of medical faculties. **Since we consider the knowledge of the key terms essential** (without the terms, one cannot create a meaningful sentence and without the original sentence, no response at the test, let alone during a discussion with the teacher)**, we followed the following principles when writing Memorix**: **All terms are explained as clearly as possible in place of the first occurrence, and only then they are placed in context**. **Simpler terms are preceded by more complicated ones**. Where it is absolutely necessary to explain the concept and there is no stable Czech term**, we provide the original Latin or English terms in the text**. Because the required level of Latin in histological terminology may vary at various faculties, at the end of the book, there is a Latin–Czech Cytological dictionary **of less frequently used terms**.

We were very pleased with the favorable reactions to the first edition and a number of suggestions for further improvements, which we happily incorporated into the second edition of the Memorix. Based on the experience of students and teachers, we have made **hundreds of both smaller and larger amendments and clarification of the text, we have added 56 new microphotographies, added some schemes** and took into account the comments of the main clinical reviewer in the areas that help use information from histology in other fields of medicine study.

We therefore present this book to you, our readers. Our goal is to make your life more enjoyable and to encourage you to study deeper. Your suggestions for improvements or additions are welcome at the web site **www.memorix.cz**. The whole team of Memorix Histology wishes you effective time spent with the book and the microscope:

Jan Balko, Zbyněk Tonar, Ivan Varga
Prague, Pilsen, Bratislava, 11. 6. 2018

Due to the content and terminological demands of histology, we need to learn it very effectively. It is therefore useful to create **a system** that **makes revising faster and easier**. Although each student has their own system of learning, we have created the so–called **Memorix learning system** which can serve as a good inspiration. But since you are studying medicine (or a related field), you are bound to know that even the best system does not replace hundreds of hours you have to devote to learning. **Besides Memorix, your studies will need a "steel skull and lead bottom"**.

Steps of the Memorix Education System

1. **Syllabus and introductory texts** – at the beginning of a chapter or a unit, make a simple overview of its content
   – read the introductory spreadsheets of the contextual text that will tell you the story of the chapter and introduce the main terms
   – browse subchapter names, read the sentences in the opening windows of subchapters, and take a quick look at the main texts and pictures
   – write a few questions the text should answer (you can find an inspiration in the questions at the end of the chapter)
   – create a learning plan according to the scope of the chapter (how many hours you spend with one page, how many days you will learn for, etc.)

2. **Main contents** – scroll through the main contents of all subchapters to the smallest detail
   – read the introductory sentences once again and go through the main texts with pictures where you can find answers to your questions
   – underline what matters to you, make excerpts, redraw images, create mind maps

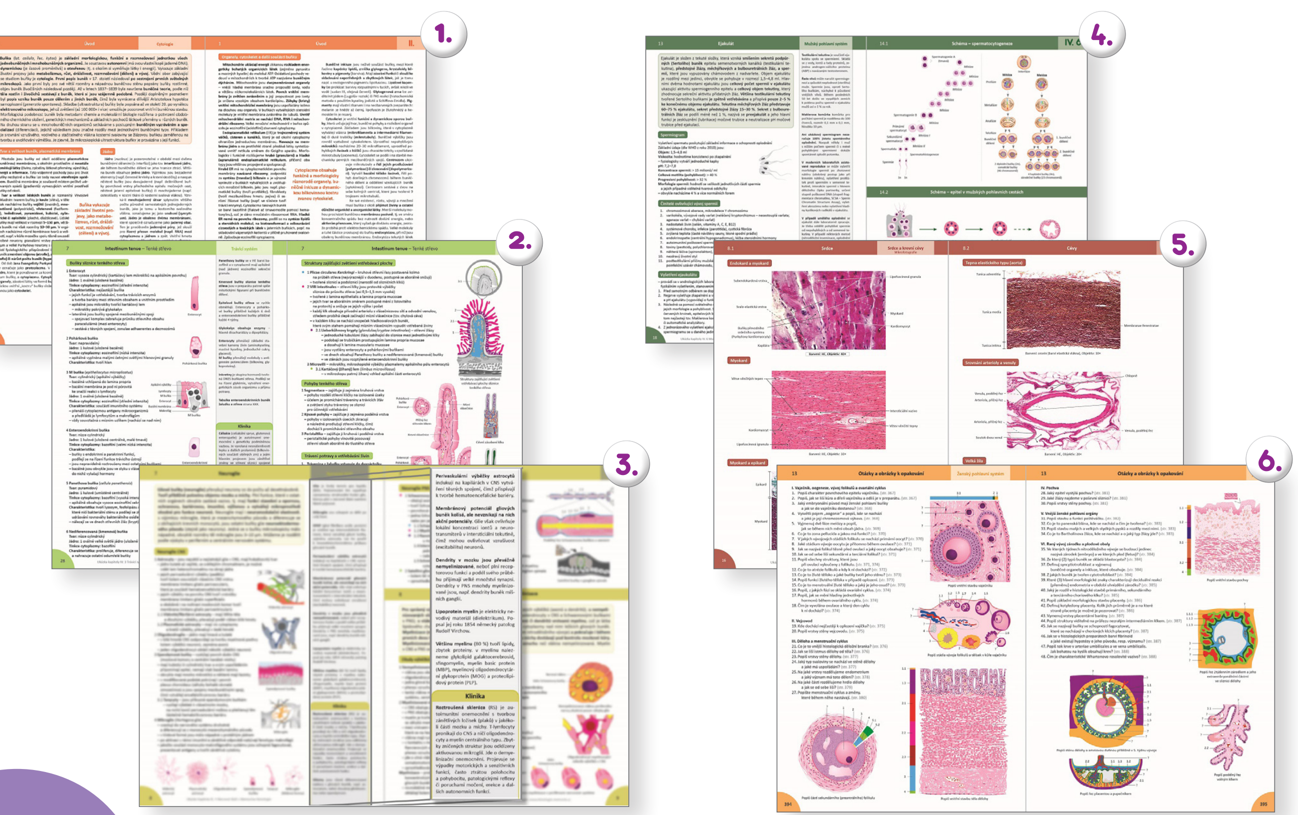
3. **Points of interest and clinical information** – after browsing the main content, see the information in the middle column
   – less important information, examples and outdated terms can make it easier for you to memorize your curriculum
   – read the clinical correlations to know which knowledge you will need the most as a physician

4. **Schemes, tables, and decision algorithms** – look at the clearly arranged information after the main text
   – decision algorithms will help you find the right way to search for cells or tissues in light microscope

5. **Electronograms a micrographs** – electronograms at the end of the Cytology chapter, micrograph in all other chapters
   – large annotated images will show you a real picture of histological structures seen in electron and light microscopy

6. **Questions and images to revise** – review questions and images to revise and make sure you understand the topic well

7. **Present the acquired information** – aloud and systematically, present the information you have learned to yourself or your classmates



Histology is not only intended to educate students about the microscopic body structures and research purposes. This is a **science with a wide practical use**. All tissues collected from patients must be histologically examined – these procedures are performed by doctors **at the pathology department who draw histopathological conclusions**, i.e. **examination of tissues obtained** from diseased, but **predominantly from living patients**. Definitive **diagnosis of malignant and many non–malignant diseases comes from pathologists**, although the lay public generally has no idea about the necessary processes. Collected materials include the tissues of almost all organs of the body in very different scale – **from cytological smears and puncture or lavage of effusions, through endoscopic sampling, curettage and excision, to surgical removal (resections) of any scale**. **Almost all medical fields** cooperate with the pathology daily and thus **come into contact with histopathologic terminology**. Therefore, it is necessary to learn it if we want to understand the findings in our patients.

I. Nature of material

Histopathology examinations on pathology departments are divided according to the nature of the acquired material – **necropsy, biopsy and cytology**. The results of all these methods go to the clinician who requested (indicated) them.

1. **Necropsy indicates tissue samples of dead patients** collected by a pathologist at autopsy to help determine the cause of death and to clarify the circumstances.
2. **Biopsies include any samples collected from living patients**, representing a wide range of materials from e.g. excised skin moles, through endoscopically removed material and curettage to the biopsy of whole organs (routine example is the appendix, uterus or gall bladder during the most common surgical procedures), and organ units (e.g. transplantation, amputation and cancer). Biopsy diagnostics is the predominant part of the workload of a pathologist and allows the definitive diagnosis of a number of diseases, especially tumors. Depending on the findings, the clinician continues to follow up on the patient's progress and when deciding about the treatment.
3. **Cytologic diagnosis** indicates the methodology that evaluates **individual cells isolated from tissues**. This discipline extends to other specializations and is used e.g. in the departments of gynecology and pneumology. Collected materials include a variety of cell surface swabs, cells aspirated using needles, punctuates or lavage of exudates and body cavity contents and cysts. Since cytology only evaluates cells without their tissue relationships, it does not inform about the microscopic structure of respective organs or their layers.

II. Sampling

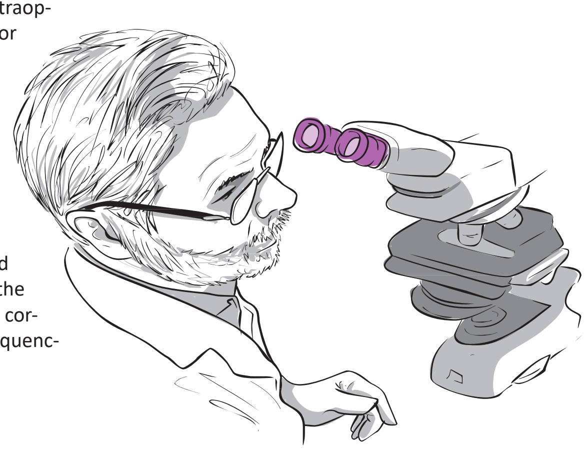
For the clinicians, the familiarity with the preparation of histological specimens is particularly useful **during the collection of the material**. It is imperative to know the medium, the collected tissue should be put into to ensure the preservation and enable the transfer, and to know how it is to be treated. All of this can be illustrated in an example of surgically removed appendix (appendix vermiformis caeci) in common inflammation (appendicitis).

After removing it in appendectomy, the surgeon must have it subsequently **fixed in formaldehyde solution in an appropriate volume (optimum volume ratio of 1:10 – tissues to formol)** and sent to the pathology department. Conversely, **other material should be sent to non–fixed, or frozen** (e.g. intraoperative biopsy) or stored in other media (for electron microscope examination, genetic tests). Any error in this process leads to the degradation of the material and further hinders the diagnosis with the corresponding consequences.

III. Diagnostics

Standard preparations, encountered during histology studies (clear staining with hematoxylin–eosin) are usually used in the histopathology diagnostics. If necessary and in cytological methods, useful staining may be added, which is also discussed in the chapter **V. Microscope techniques**. In many cases, **immunohistochemical and histochemical methods** are commonly used.

1. **Immunohistochemistry** mainly helps **decode cancers,** which has a fundamental role in determining their prognosis and treatment.
2. **Histochemical methods** allow to clarify **pathological processes of metabolism**.
3. **Other special procedures** , used mainly in the pathology of nerves and muscles, include **polarization and electron microscopy**.



Pathologist during biopsy diagnostics

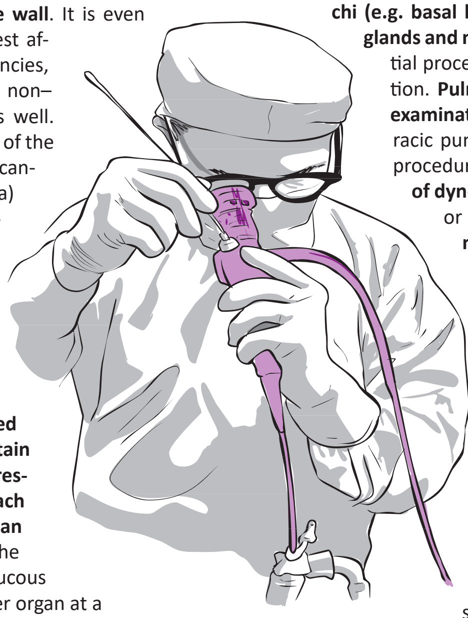
The above–described text implies another, also important significance of histology, especially for medical students. Histology is crucial for the subsequent study of pathology and other subjects in the following difficult years**.** Pathology **deepens the acquired knowledge about the physiological body structure at the microscopic level.** It shows morphological changes of tissues in disease states**. The success at the pathology examination in many institutes includes** the recognition of preparations with the basic pathological findings**. Other preclinical disciplines, where you will** work with histological terms, are embryology, physiology and pathophysiology**. As for the clinical subjects, particularly** oncology, hematology, internal medicine and gynecology.

As already indicated, **clinical medicine widely uses microscopic diagnosis of living patients** in the collaboration with the department of pathology. **Many histopathological findings are routine for pathologists** and clinicians come into contact with the resulting findings very often. The understanding of the descriptions of microscopic characteristics of disease states requires **good understanding of the histological structure of the organs**. We have prepared several examples of frequent cases categorized by clinical disciplines with a description of the basic knowledge in histology a clinician must cover.

Internal medicine

Almost all internal fields **abundantly use biopsy, particularly oncology and hematology,** but also pneumology, gastroenterology, nephrology, endocrinology, hepatology and others. **The physician in this field must know the histological structure of the organs he/she is specialized in** to fully utilize the results of the pathological evaluation to determine the extent of the damage and the next steps.

Gastroenterology is one of the most common referents for biopsy thanks to the introduction of endoscopy. It is necessary to know the wall structure of the entire digestive tract, because the penetration of local tumor affects the prognosis and treatment**. A** tumor affecting only the epithelium (carcinoma in situ) behaves and is managed in a different way than **invasive adenocarcinomas infiltrating the wall**. It is even necessary to accurately state the deepest affected layer of the wall. Besides malignancies, **precancerous (preceding cancers)** and non–tumorigenic processes are examined as well. E.g. goblet cells in the esophagus instead of the squamous epithelium are a high–risk precancerous condition (intestinal metaplasia) **and the patient should be further monitored (follow–up). Histology is used to determine the presence and type of inflammation of the esophagus, stomach and intestines (Crohn's disease, ulcerative colitis, microscopic colitis and others), including their severity (degree of esophagitis, gastritis, enterocolitis, proctitis) based on the degree of inflammation in certain layers of the organ wall. The eventual presence of a causative pathogen in stomach inflammation (Helicobacter pylori) can also be proven microscopically.** Also, the examination of polyps, ulcers, ectopic mucous membranes (mucosa presence of another organ at a specific location of the examined organ), and other conditions are the common problems biopsy helps solve. Without the knowledge of histology, the internist cannot truly understand **the description**.



The gastroenterologist performs biopsy using an endoscope

Hepatologists perform **percutaneous liver biopsy** requiring **various special staining method in the microscopic examination** (**PAS** to confirm glycogen storage disorder, **Berlin blue** for iron accumulation, **trichrome** for fibrosis and others) to help diagnose a wide range of disorders from inflammations, cirrhosis, tumors to complex metabolic diseases and storage disorders.

In pulmonology, the most common indications are **bronchial and lung tumors,** which again have different prognosis based on the affection of the bronchial walls. Likewise, asthma (asthma bronchiale) and other obstructive lung diseases are characterized by their findings with various **changes in the microscopic structure of the bronchi (e.g. basal lamina widening, increased number of glands and muscle layer in asthma)**. Also, all interstitial processes require histopathological examination. **Pulmonology also widely utilizes cytology examination of pleural effusion,** obtained in thoracic punctures. An example of very specialized procedures is **electron microscope examination of dynein arms in cilia** in Kartagener syndrome or **lamellar bodies in the granular pneumocytes** in defective synthesis of surfactant.

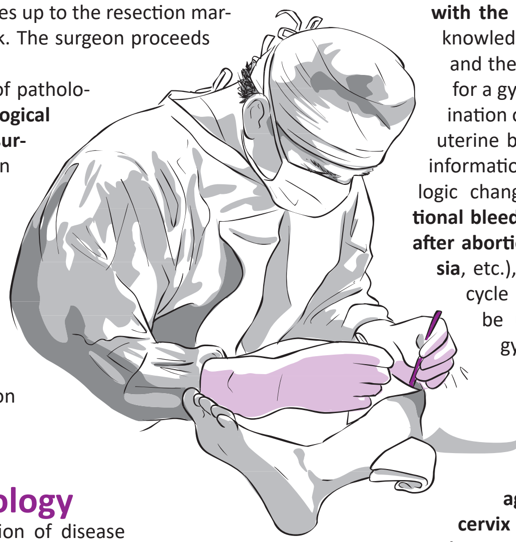
Nephrology frequently requires the help of pathologists, including the use of highly specialized techniques **(electron and polarization microscopy)**. This happens mostly in the **diagnostics of glomerulopathies, which cannot be understood without the knowledge of the structure of renal corpuscles**. **Transmission electron microscope** (TEM) specifically helps reveal **the damages to the filter barrier and is also used before the transplantation of kidney**. Also, endoscopic cold biopsy of the urinary bladder and urinary cytology are the "daily bread" of a pathologist.

Endocrinology calls for pathologists especially in the resection of **thyroid gland due to the hyperplasia (goiter), inflammations and tumors**. Endocrinologists always receive the description of the structure and **lining of the thyroid gland follicles,** helping them clarify the process.

Surgery

The requirements for histopathological examinations performed by surgeon overlap partially with the internal ones due to the similar use of endoscopic techniques. Further, surgeons supply biopsy station with numerous **resection samples of organs and tissues from all body parts**. As already said, each excised and resected tissue or organ sample must be examined. Whether **the appendix in the inflammation** (appendicitis), **gallbladder affected by gallstones** (cholelithiasis), **limb in case of amputation, or in major procedures in transplantations and oncological affections**. The surgeon will then receive extensive descriptions of the resected samples with information about the microscopic form of the process and the resulting diagnosis. This description is particularly important **in tumor diseases**, where the **depth of penetration, and metastatic affection of lymph nodes and distant organs are evaluated**. The results are reflected in the **TNM classification of** the extent of tumor spread: T – the extent of the tumor, N – metastases in regional lymph nodes, M – distant metastases, determining the type of the management. It also evaluates whether the disease process reaches up to the resection margins or whether the surgeon has removed the whole bulk. The surgeon proceeds based on all the reported information.

Another service offered to surgeons by the department of pathology is the **intraoperative biopsy**. This is a **rapid histopathological evaluation of the disease process directly during the surgery of the patients**. It enables to clarify whether it is an inflammatory or cancerous tissue change and informs the surgeon **whether he/she has resected the whole** bulk, or whether the process still exceeds the border of the removed sample**. Once the result is reported, the procedure may be completed or continued, extending its scope (more radical approach).** The technique of frozen sections is used during intraoperative biopsy. It significantly speeds up the tissue processing, because the sections are sliced and dyed without the need for fixation and embedding into paraffin blocks.


Surgeon during tissue resection

Gynecology

Another pillar in histopathological diagnostics is gynecology. The most commonly investigated samples include **curettage of the cervix and uterine body**. The cervix can be affected by a wide range of pathological processes which differ **by location (exo– or endocervix)**. **Each of these areas is lined by a different type of epithelium** and their interface is subject to various pathological changes. **The border of the epithelium moves with the age (ectropium)**. The knowledge of these linings and their changes is essential for a gynecologist. The examination of the curettage of the uterine body mucosa provides information on both the pathologic changes (**mostly dysfunctional bleeding, embryo remains after abortion, polyps, hyperplasia**, etc.), as well as menstrual cycle dating, which must be understood by every gynecologist at the histological level. As for more extensive gynecological examination, let's state **the diagnostics of uterine cervix conization samples (resection of the affected part of the cervix in the shape of a cone)**, **placenta after birth and resected uterus with the uterine tubes and ovaries (adnexa) after hysterectomy with eventual adnexectomy**. Other organs of internal and external female reproductive system are sent for histopathological examination. Routine gynecological examination includes the **cytological diagnosis of cervical smear**, which is useful for the early detection of metaplasia and precanceroses, often preceding the developing tumor.

Oncology

Oncology comprises a large **region of the tumor issue** within the internal fields. There are many types of tumors, which are divided **based on their microscopic morphology,** which matches their histogenesis. **Each tumor stems from certain cells of the tissue of various organs**. It often at least partially retains its original morphological features. Describing these histological features and determining the type (and possibly the subtype) of the tumor allows for an accurate diagnosis, which can be used by the oncologist to initiate an appropriate and targeted treatment regimen. As already indicated, **the extent of the cancer in the affected organ and its surroundings** (staging) **and its microscopic differentiation** (grading) are evaluated. A more accurate cancer diagnosis is often based on **specialized staining (mucicarmine, PAS, trichrome, Congo red)** , **immunohistochemical examination** and in many cases **even genetic testing**. The knowledge of histological terminology and microscopic anatomy helps oncologists navigate through the findings.

Hematology

The recognition of disease processes in hematology is an extension of pathology. Blood disease diagnostics is complex and requires laboratory testing in cooperation with microscopic examination**. The histopathological diagnosis often necessitates specialized methods** – flow cytometry, immunohistochemical and genetic analyzes**. Specialized staining is always used in** trepanobiopsy (bone marrow aspiration)(cholesterol acetate esterase, Giemsa staining and silver reticular fibers).

Pediatrics

Children can also undergo **biopsy examination** similar to adults. The spread of the disease is different, but not less important, so the pediatrician should be familiar with descriptions of the histopathological findings. **Organ structure of the smallest children shows a range of histological differences when compared to an adult**.

Dermatovenerology

Skin excisions are also histopathologically confirmed. Macroscopic evaluation is inaccurate in many cases; often, the diagnosis is difficult to determine even microscopically. The **cooperation of the histopathologist and a clinician is really important for proper diagnosis**. Routine cases include **excised birthmarks (nevi), inflammatory diseases of the skin and small skin tumors**.

Designing the concept, creating curriculum and dealing with the publishers were only a fraction of the work at the beginning of the development of our textbook. All this was followed by **writing the texts, drawing the pictures** and the **professional typesetting**. At the end, we went through **dozens of reviews from histologists, pathologists, clinicians, students, as well as laboratory technicians and other academician** primarily from medical schools and hospitals in the Czech and Slovak Republic. On this long journey we needed a lot of help, so at this point, we would like to **thank everyone** who stood at the development of this revolutionary histology textbook.

First of all, we would like to thank the chief coordinator of the English version of the Memorix Histology **René Novysedlák** and the co-authors who sacrificed an incredible amount of time and energy with us to create this unique histological book. Co-author **Richard Adamčík** brilliantly created and edited texts in the Muscle tissue and Senses and skin chapters, where he focused on the skin section. **Bětka Blanková** perfectly described the Male reproductive system, Female reproductive system and Endocrine system chapters, but also contributed to sections devoted to glands in the Epithelial tissue chapter. **Martin Gavač** has systematically elab- orated on most of the chapter on Epithelial tissues and further creat- ed the comprehensive chapter on the Digestive system. We are immensely grateful to **David Kachlík**, who, in addition to writing the Respiratory system chapter and most of the chapter of Senses and skin chapter, actively participated in the creation of all other chapters. His contribution consisted mainly in the unification of histological terminology, which was not an easy task at all.

As for graphic design, we would like to thank the chief illustrator **Jan Balko** and the graphic artist **Šárka Zavázalová** who contributed a number of illustrations in the epithelial, connective and nervous tissue chapters, and also created the pictures in the Nervous system chapter.

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Our appreciation goes also to **our predecessors and teachers** for their work in the field of histology, for the education of genera- tions of physicians and scientists and for the records on which we may count on.

We are also thankful to the **authors of the referred textbooks, atlases and scientific articles and our colleagues** for their ideas, consultation, advice and constructive criticism. Thank you to our associations and scientific fields, such as the **Czech Anatomical Society, Slovak Anatomical Society, Czech Cyto– and Histochemical Society and Czechoslovak Microscopy Society** for organizing congresses, support of scientific work and mobil- ity of young researchers, organizing training courses, providing the space for discussion of the morpholo- gy courses and other activities.

From the depth of our histological heart we sincerely thank everyone, who helped us bring Memorix Histology to reality.

We also thank the Memorix PR team, **Ľuboš Repka** and **Slávka Sotáková**, Memorix mobile app coordinator **Ester Bartl** and managers **Avetis Švamberk, René Novysedlák, Martin Mikeš** for the very important work they are doing in Memorix company.

Thank you to **Stanislav Juhaňák** and all employees of the publishing house Triton, who take care of successful printing the book and getting it to retail shelves.

Last but not least, our thanks go to the rector of Charles University **Tomáš Zima** and vice–dean of the 2nd Faculty of Medicine, **Roman Kodet**, for being the godparents of our textbooks, thus expressing recognition and support to our work.

And with the greatest love, we thank our friends, families and beloved ones for their patience, tolerance and support, which enabled us to work on this textbook. Thanks to our girlfriends or wives, namely **Gabriela Holubová, Kristína Demjanovičová, Martina Tonarová and Mária Vargová** for standing at our side even in the moments when we, instead of romantic walks and a joint dinner, spent days and nights working with microscopes and computers to write “some pink book” for you.

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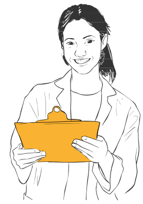
68 Academics and clinicians



59 Medical students

20 Other contributors

... worked hard creating MEMORIX HISTOLOGY for You!

If I learn all the time, I will know much and I will become a great doctor**. And because there is a lot to learn in medicine, I cannot waste time with other activities. This is one view of the study of medicine. The second one says that** it is not just knowledge which makes a successful doctor**.** The expertise gained during the study is an important building block, but certainly not the only one**. A good doctor has to master** professional **communication, time management, but also the management of the entire health care team. Only after the school, many graduates find out how difficult it is to coordinate the investigation of dozens of patients over several hours, or** how strenuous it is to clearly explain the diagnosis and subsequent treatment to the patient**.** Student clubs **provide excellent conditions during the study for the development of these** so called soft skills**.** By organizing projects, **you can learn** to manage your time, improve your communication skills **but also meet** a number of complications that you have to solve**. I spent many years in Motolák and IFMSA CZ, and they helped me much gain experience and contacts**. **Without this stage of life, I would probably never go into large projects such as the creation of books Memorix Anatomy and Memorix Histology**.

Radovan Hudák

Motolák is the student heart of the 2nd Faculty of Medicine. Each year, it organizes more than 40 projects focused on culture, sport, study, arts and volunteering. Musical group Ježci or volunteers in the Week of reading regularly make the long moments of children and seniors in the hospital more pleasant. The exhibition of pictures and photos of students and teachers called MotolArt presents the artistic talent of future and current doctors. (The main graphic artist and both graphic artists of Memorix also exhibit their paintings at MotolArt). The Faculty ball and the Steamer for graduates are among the biggest cultural events at the faculty. The project promoting science in a café called Medicafé gradually spread from Motol, thanks to IFMSA CZ, to most of the faculties of medicine in the Czech Republic.

IFMSA CZ is a part of the largest student organization in the world (IFMSA). In the Czech Republic, it has local branches at all medical faculties. Projects such as Teddy bear hospital, World AIDS Day, World Diabetes Day, 4Life, Medicafe, and Smokefree Party allow medical students to get to the issue of public health and education during their studies. Thanks to its membership in the multinational organization, the support of faculties and clinical departments, it facilitates exchange scholarships throughout the world. Every year more than 300 Czech medical students are sent to a clinical or research internship.

Trimed makes the 3rd Faculty of Medicine what it is – family–like and friendly. It strengthens the relationship between the students and educators at various events, such as the Representation ball, Steamer and many others, it extends the horizons of medical students through various study projects and adventure courses, and helps prospective graduates find employment at the annual work fair. Younger students are helped with seamless entry to the faculty, and the older ones can enjoy nice movements between the study sessions.

The Association of Czech Medical Students is the oldest student organization in the country with more than 150 years of tradition. Still, it has a young beating student heart – the purpose of the association is to care for the cultural, social and scientific life of the medical students of the 1st Faculty of Medicine, Charles University. Traditional activities include Mikuláš in the General University Hospital, a picnic in the garden of the Department of Psychiatry or the care for foreign students.

The Association of Medical Students at the Masaryk University is a student organization with more than ninety–year history. Traditionally, it organizes the Representation ball of the Faculty of medicine with Matriculation, the Student Scientific Conference, various lectures and social evenings with guitar.

The Association of Medical Students at the Palacký University organizes the project You do not know, you will not save!, which allows participants to virtually practice the basics of first aid. The night sports tournament of medical students always shakes stiff limbs with the slogan "healthy body, healthy spirit."

SloMSA, as a member of the international organization (IFMSA), mediates clinical and research internships for more than 150 Slovak medical students every year worldwide. In addition to internships, it also organizes interesting projects such as First gynecological screening, Stop AIDS, Men's Issues, Teddy Bear Hospital and many others.

The Association of physicians of SZU mediates voluntary internships at SZU departments clinics and surgical suturing seminars. It also focuses on projects for the general public through lectures at secondary schools or the project 5 minutes for your health.

The Association of Medical Students in Bratislava (BSM) is an association of more than 300 medical students at the Medical Faculty of Komenský University in Bratislava. The association supports the medical students in their studies, personality growth, and enhances the possibilities of education by organizing courses, seminars and lectures in various fields, not only in medicine.

The Association of Medical Students in Martin (MKM) is an association with a long tradition that helps students develop in many projects ranging from sports activities, lectures at schools, education courses to medical students.

The Association of Medical Students in Košice (SMMK) is an interest organization for students and graduates of the Faculty of Medicine of Šafárik University in Košice, who are interested in developing the scientific, cultural, social and sports life at the faculty. The mission of the association is to provide spiritual growth, cultural and social life as well as to increase the professional level of students and thus contribute to enriching the personality of the future physician.

The Association of Dentistry Students of the Czech Republic (SSSČR) is intended for all the students of dentistry. It publishes the StuDent magazine, organizes projects in Healthy Czech Republic with Healthy Teeth, International Dental Student Congress and sends students for foreign internships.

The Association of Physiotherapy Students brings together all students of physiotherapy in the Czech Republic, it organizes the projects as FyzioCafé, Physiocamps, Physiomeetings and other conferences and workshops. It provides foreign internships for students of physiotherapy.

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www.motolak.org

IFMSA CZ
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www.ifmsa.cz

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SSSČR
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www.ssscr.cz

Radovan Hudák managing editor and author

Impossible – what is it? For everyone it's different, and **that's the problem**. When I was at elementary school, I loved basketball so much that I wanted to play it professionally. **I was told I could not make it, but I did not believe them.** I went to Košice for sports grammar school and I played junior extraliga. Then I wanted to go from a sports school in the eastern Slovakia **to the 2nd Medical Faculty of Charles University in Prague** and once again, everybody laughed at me, that I cannot make it. **Once again, I worked hard, and I made it**. When I was putting together the team of Memorix Anatomy five years ago, **I only smiled when someone said that what we want to do is virtually impossible**. Because what is impossible? Just what **does not motivate us to create the "possible"**. I'm filling my dreams, no matter how real they are for others, and that's what I want. **Believe in yourself, work hard, and you can even make the impossible work**.

Jan Balko editor and chief illustrator

It is said that there are two kinds of textbooks. **"American model"** is a book that tries to sell itself to the reader and attract him/her **with readable text with numerous pictures and diagrams**, **so that his studies go smoothly**. **The second model is the so–called "Russian" –** textbooks that simply provide the material and "**who does not understand it, has got nothing to do here**". I firmly believe that we have managed to create the first model. I do not want to describe **the incredible amount of work at length we devoted to it**. I'd rather find a spot in silence somewhere in the corner, and I believe that **all texts and pictures** which we have prepared with co–authors, **will make your studies of this beautiful, yet underrated science, histology, simpler**. As **a pathologist**, I also know that **histology is not an unnecessary discipline, but rather a fundamental building block for understanding the pathology** – associated science, every physician will work with. And do not look for anything cynical in this statement.

Zbyněk Tonar editor

It was embryology that brought me to histology. For the thesis at the end of my studies as a biology teacher, **I needed to learn to cut, stain, work with microscope and photograph histological sections** and embryos of various mammals. **Teachers and researchers from the Faculty of Medicine in Plzeň** helped me, advised and **inspired me for this field** so much that I graduated from the faculty. **As a medical student I was involved in research and in lecturing at the Institute of Histology and Embryology and I do so until today**. **I still enjoy working with the microscope.** With its help, histology provides a unique insight into many medical disciplines and **enables me to find answers to unanswered questions**. I focus **on quantitative histology of blood vessels of humans and microscopic evaluation of experiments in animals** where we want to understand **the nature of certain diseases** and to test whether it is possible to treat the conditions. I like music, books and sports.

Ivan Varga editor

It's now been almost four years since I got the first chapter of Memorix Anatomy to review. The team of authors consisted **mostly of medical students, which was revolutionary!** I thought **how wonderful it would be to write in a histology book in similar spirit**. We managed to inspire the Rado Hudák to organize a team of authors from several medical faculties from the Czech Republic and Slovakia. It was a formidable task, and **in addition to the actual creation of chapters, we spent weeks with discussion over the accuracy of different views. Our graphic designers repeatedly edited pictures based on our requests**... Today, however, it seems that **my wish was fulfilled**. **Neurohistologist Ramon Y Cajal compared the various cells of the neural tissue to "fragile and elegant butterflies of the soul"** in 1937. I believe that **you will also see similar gorgeous cells in your microscopes** and that the exploration of the human body will bring you more joy than trouble.

Richard Adamčík
author

I got my first **microscope at the age of 10** and this moment **probably predestined my whole further journey**. My whole youth was accompanied by the verve for all natural sciences and a dream to become a scientist. **My heart drew me, for some reason, to the medicine** where I reopened that magical window into the microscopic world. **From the second year of my studies, I work as a lecturer at the Department of Histology and Embryology** of the Faculty of Medicine in Hradec Králové and precisely **this desire to share my knowledge** brought me to **the team of this revolutionary textbook**.

Alžběta Blanková
author

My journey to histology was not a straight and not planned at all. A chance brought me to her and my direction **was gradually shaped by meeting with people who taught me to see the beauty of the micro–cosmos.** They gave me the opportunity **to develop the ability and participate in scientific projects**. I was lucky because they became great friends and **histology has become a passion I have tried to pass on to my students**. I hope I at least partially succeeded and that **Memorix can not only improve the studies, but also seduce the reader to the same path that we took**.

Martin Gavač
author

Unlike Rado, I **I'm no workaholic**. **I did not want to go for medical studies,** because medicine requires hard work. But eventually, the other professions seemed so boring, that I filed the application. **After the histology examination, I got an offer to work as a lecturer**. Even if against my nature to minimize my efforts, I accepted the offer. **It is similar to the philosophy of Memorix**: **the information is given simply, clearly and understandably**. Thanks to the excellent figures, histology studies are from now a piece of cake**. Enjoy learning from it!**

David Kachlík
author

Anatomy is my love. During the study, I found that **without histology and embryology, it is not well understood** and I decided that **as a teacher, I will pass on the information about the structure of the human body through functional and clinical morphology** that highlights **the context and meaning of each part of the human body**. **Histology plays an irreplaceable part here,** similarly to the **scientific research**, which fills the other half of my career. **The cell rules the world,** whether we want it or not, so let us subdue it to make it serve us well.

Šárka Zavázalová
illustrator

I confess that in the first year of medical school in histology, I **enjoyed only drawing the histological slides into my notebooks during the class**. It was supposed to help us **remember the observed structure**. Though it would certainly be much easier, if the schematic images had already been created. **During the development of Memorix, I was trying to help in this area**. And though I **thought that I will never meet microscopes in medical practice,** I have another confession to make – I like using them, when, as **an ENT specialist, I look into the ears of my patients**.

"If you cannot explain it simply,
you do not understand it well enough."

Albert Einstein

Memorix histology

I. Introduction to histology

Ivan Varga
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Histology is the study of the microscopic structure of organisms. It is one of the biological sciences and is divided into plant histology and animal histology. From the medicine point of a view, the study of the **microscopic structure of the human body**, both in physiological conditions (**histology**) and during pathologic changes (**histopathology**), is of importance. Histology in the context of a medical school curriculum is usually classified within anatomy and physiology.

Histology and anatomy, as morphological sciences, examine the shape and structure of the organism. As opposed to gross anatomy, we use **light** (or other) **microscopy** in histology when studying human body structure, and therefore histology is sometimes called "**microscopic anatomy**". Understanding the structure of the human body at a histological level greatly facilitates the subsequent study of physiology. Due to this reason, the presented textbook follows the concept of "**functional histology**", in which the description of the **morphology of individual structures is at least briefly connected with their function**. The importance of knowledge of histology for the study of pathology (pathological anatomy) is indisputable. The world-renowned German pathologist **Rudolf Virchow** has found that **most of the pathologic changes begin at the cellular level**. One of Virchow's main legacies, still valid today, is the call to **"think microscopically"**. This means the knowledge and understanding of the structure and function of physiological ("healthy") tissues at such a level that we can subsequently diagnose pathologic alterations and other deviations from the norm. That is why **Rudolf Virchow was a pioneer of the mandatory use of light microscopes in medical faculties**. At present, knowledge of pathological histology is closely linked to the molecular-biological properties of the examined tissues.

In Memorix histology, we follow the concept of "functional histology" where the morphology of individual structures is at least briefly related to their significance and function.

At the beginning of the curriculum, students of most medical schools learn about the **histological techniques**. Before any part of an organ or tissue is examined with a microscope, it undergoes rather complex processing, using the knowledge of histological techniques. The second area of histology is the study of the cell called cytology. **Cytology** examines the **basic structure and function of cellular organelles, membrane structures, supramolecular complexes**, cell division patterns, and unique morphology of cells with special functions (e.g. cells responsible for the production of proteins, or mucus). This is followed by the study of **general histology**, which deals with tissues. **There are over 200 morphologically and functionally identifiable cell types in the human organism.** However, these occur at different stages of embryonic development**, and therefore estimates and opinions on the number of cell types of the human body are still evolving making the provision of a full list beyond the scope of contemporary knowledge.** The cells of the human body can be divided into four large groups, which together with the extracellular matrix compose the **tissues** (epithelial, connective, muscle and nervous tissue**). There are not artificially created groups; they** describe the common origin, characteristics, structure and functions of the cells and the extracellular matrix **in the individual types of tissues. Even in pathological conditions, tumors originating from a certain type of tissue share some similar biological properties.** The perfect study of the structure and function of the tissues is followed by the last (and probably the most extensive) part of histology, which is **special histology, i.e. the microscopic anatomy of the organs.**

Definitions

Morphology (Gr. *morphé* – shape, *logos* – science, word and reason) – is a scientific branch of biology, which deals with the structure of organisms
– medical disciplines include anatomy, histology, embryology and pathology
Histology (Gr. *histos* – tissue) – study of tissues and microscopic structure of organisms
Cytology (Gr. *kytos* – cell) – study of structure, function and composition of cells

Histopathology (Gr. *pathos* – disease) – part of pathology, the study of changes at the tissue level
Cytopathology – part of pathology, the study of changes at the cellular level

Terminologia Histologica – a complete edition of the official Latin nomenclature for the description of the microscopic structures of the human body according to the Federative International Committee on Anatomical Terminology (2008)
Eponyms – anatomical terms called by real or fictional persons; usually by the person, who described it or discovered it, but sometimes only in his/her honor
– in clinical medicine, some eponyms are commonly used instead of Latin terms

Microscope (Gr. *mikros* – small, *skopein* – observing) – a device for observing an enlarged image of objects to be seen by human eye
Resolution – the smallest distance between two points that are still distinguishable as separate
Histological technique – a set of laboratory procedures used for the preparation of histological slides (from sampling to sectioning and staining)

Histology is a **descriptive science**, whose **basis are terms** originating most commonly **from Latin or Greek language**. They are uniform **nearly in the whole world**. *The terms associated with microscopes and microscopy techniques are described in chapter **V. Microscopy techniques**.*

Important terms

Acinous: – grape–shaped formation with a narrow lumen
Alveolar – shape of arched pouch with wider lumen
Adhesion – adherence of cells to extracellular matrix or to the surfaces
Apical – related to the free surface (sometimes called domain) of epithelial cells; the term is of importance in shape–polarized cells, which are basically bound to the basal lamina and the free apical surface is turned into free space
Apposition – applying new layers of cells and extracellular matrix, e.g., apposition growth of cartilage or bone to increase thickness
Cell – basic structural, functional and reproductive unit of cellular organisms (bacteria and cyanobacteria, protozoa, fungi, plants, animals); we distinguish two types – prokaryotic and eukaryotic cells
Basal – related to the part of the cell resting on the basal lamina
Basement membrane – layer of extracellular material under the basal surface of epithelium; consists of basal lamina secreted predominantly by epithelial cells, and reticular lamina produced by the cells of connective tissue
Basal lamina – gel–like layer of extracellular matrix surrounding the cell; consists of layers distinguishable by an electron microscope (lamina densa, lamina rara); present as a part of the epithelial basement membrane or even independently, under the lining of vessels
(endothelium), around muscle cells and fibers, adipose cells
Distal – more distant, marginal
Electron dense – structures that appear dark in the transmission electron microscopy (they absorb electrons)
Electron microscopic – related to a fine structure visible in electron microscopy (*see also ultrastructural*)
Fibrillar – formed or fibers or with fiber–like appearance
Granular – with granular appearance or granular structure
Chromophobic – conventional stains produce no staining, and therefore, with bright color appearance in microscopy
Chromophilic – stainable by conventional staining methods
Chromaffin – stained using solutions containing chromium salts in various oxidation numbers
Inclusion – material accumulation (e.g. fat or pigment) inside the cells
Interstitium – connective tissue or a mixture of connective tissue proper and muscle interposed between epithelial glands or trabeculae
Interstitial – in between
Brush border – a set of densely stacked microvilli e.g. on the apical surface of the epithelial lining of the small intestine
Cohesion– coherence between cells
Longitudinal – running parallel with the long axis of the structure
Lumen – a hollow space inside blood vessels or organs
Organ – structural and functional unit of the human body consisting of multiple types of tissue
Organelle – microscopic structure inside the cell, most often delimited by a membrane
Organoid – organelle–like structure without its own biomembrane
Parenchyma – epithelial component of organs; e.g. “liver parenchyma”; refers to liver cells (hepatocytes), but not to the vascular and connective tissue stroma between hepatocyte trabeculae
Plasmatic – related cellular cytoplasm
Polarity (cellular) – presence of apparent differences between the basal and apical (or lateral) parts of the cell and its surface
Polar – located close to the poles of the cell nucleus
Proximal – closer
Reticular – mesh–like
Absorption – a route by which substances can enter the cell or body
Secretion – production of products of cell metabolism, consists of the precursor intake, synthesis and extrusion of matter from the cell to the ducts or to the free surface (exocrine secretion) or to the tissue fluid and then to the blood circulation (endocrine secretion)
Stroma – connective tissue of organs, usually scattered between epithelial glands or trabeculae
Sustentacular cells – supporting cells that provide other cells with mechanical or metabolic support
Terminal – associated with the end portion
Tissue – a set of cells (usually of the same kind) and extracellular material forming the basic building part of organs and body
Tubular – tube–like
Ultrastructural – related to fine structure under the resolution of the light microscope; observable by the electron microscope
Striated – fine annealing, i.e. alternating of lighter and darker areas; striated interlobular duct in the parotid gland, where the straited form is the multiple wrinkling of the cell membrane (with cytoplasmic folds with mitochondria) of the epithelium of ducts

Abbreviations

A-band – optically anisotropic region of the sarcomere, made up of overlapping actin and myosin filaments; in a microscope, it appears to be a darker area alternating with the I–band
ACTH – adrenocorticotropic hormone
ADH – antidiuretic hormone
APC – antigen presenting cells
ATP – adenosine triphosphate
BALT – bronchus–associated lymphoid tissue
BM – basement membrane
C – the number of chromatids that made up chromosomes of the nucleus (1C – a chromosome with one chromatid, 2C – chromosome consisting of two chromatids)
CD molecules – surface features of white blood cells and other cells, formed by integral membrane proteins, used in typing the developmental and functional stages of the cells (cluster of differentiation)
CFC or CFU – progenitor cells of individual lines of hematopoiesis; formed from hematopoietic stem cells (colony forming cells or colony forming units)
COP I – a protein encapsulating vesicles directed from the *cis*–end Golgi complex back into the endoplasmic reticulum (coating protein I)
COP II – a protein encapsulating vesicles directed from rough endoplasmic reticulum to the Golgi complex (coating protein II)
CRH – corticoliberin (corticotropin–releasing hormone)
DNA – deoxyribonucleic acid
DNES – diffuse neuroendocrine system, more recently under the more general abbreviation DES
DES – diffuse endocrine system
ENS – enteric nervous system of autonomic plexuses in the wall of the digestive tract
F-actin – actin in the form of a fibrous double helix; formed by G-actin polymerization
FSH – follicle stimulating hormone
G0 phase – entry into the resting phase of the cell cycle in differentiated cells that have ceased to divide
G1 phase – a part of the cell cycle, when proteins and RNAs are intensively produced
G2 phase – a part of the cell cycle that corrects DNA errors; duplication to form centrosome and preparation of proteins required for cell division
G-actin – basic globular form (monomer) of actin
GALT – gut–associated lymphoid tissue
RER – rough endoplasmic reticulum
GH – growth hormone, also STH
GnRH – gonadoliberin (gonadotropin releasing hormone)
H-band – the inner, lighter area of
Hb – hemoglobin
Hct – hematocrit
SER – smooth endoplasmic reticulum
HLA – leukocyte antigens of the major histocompatibility complex (MHC) of the human (human leukocyte antigens)
HSC – hematopoietic stem cells
Ig – immunoglobulins, antibodies neighboring sarcomere; formed by actin; visible by a microscope, appears to be a lighter area alternating with the A–band
ICSH – hormone stimulating testicular interstitial cells, former name for luteinizing hormone (interstitial cells stimulating hormone)
Leu – the number of leukocytes in the blood count
LH – luteinizing hormone (also known as ICSH in men)
M-phase – the mitotic part of the cell cycle, in which cell division takes place
M-line – a darker area in the middle of a sarcomere; cross–links neighboring myosin filaments (from German Mittellscheibe)
M1 macrophages – a subgroup of macrophages that participate in chronic inflammatory responses and activate cellular immunity
M2 macrophages – a subgroup of macrophages with a rather anti–inflammatory effect on wound healing; they activate anti-body immunity
MALT – mucosa–associated lymphoid tissue
MCH – mean corpuscular hemoglobin
MCHC – mean corpuscular hemoglobin concentration
MCV – mean corpuscular volume
MHC – major histocompatibility complex, also called HLA in humans
MSH – melanocyte stimulating hormone
N – the number of haploid sets of chromosomes in the cell nucleus (1N – haploid, 2N – diploid)
NK cells – natural killers; a group of lymphocytes capable of killing target cells infected with a virus or a tumor–altered cell that does not carry the correct combination of the MHC–features of an individual
p53 protein – protein with the role of a transcription factor, which affects genes controlling cell growth, apoptosis and DNA repairs; prevents the formation of some tumors (the name was based on the molecular weight of 53 kilodalton, which is actually lower)
PALS – periarteriolar T–lymphocyte sheath around the arteries of the white pulp of spleen (periarteriolar lymphatic sheath)
POMC – proopiomelanocortin
PRL – prolactin
PTL – platelets in the blood count
RNA – ribonucleic acid
S-phase – the synthetic part of the cell cycle, when DNA duplication occurs
STH – somatotropin, or growth hormone (also GH)
T3– triiodothyronine
T4 – tetraiodothyronine, also thyroxine
TCR – T–cell receptor
TDLU – terminal ductolobular units; the smallest functional units (lobules) of the mammary gland
TSH – thyroid stimulating hormone
TRH – thyrotropin–releasing hormone
Z-line– glycoprotein barrier forming the boundary of two neighboring sarcomeres of skeletal and cardiac muscle, anchoring of actin (from German Zwischenlinie)

Specialized terms named **usually according to the scientist** who described or discovered that particular structure or region. **They are used in clinical medicine** when they are **often preferred to the official terms**.

1. AUERBACH **Auerbach's nerve plexus** – autonomic nerve plexus between the circular and longitudinal muscle layer of the digestive tract
2. BILLROTH **Cords of Billroth** – bundles of reticular connective tissue in the red pulp of spleen; wide blood capillaries (sinusoids) are located between them
– cells of the cords actively participate on removing damaged or old blood cells in the spleen
3. BETZ **Betz cells** – large pyramidal neurons in the motor area of the cerebral cortex
– axons of Betz cells form the pyramidal (corticospinal and corticonuclear) tracts, which lead to the somatomotor neurons of the cranial nerve nuclei and to the motor neurons in the anterior spinal horns
4. BIRBECK **Birbeck's bodies/granules** – rod–like organelles visible in electron microscopy only in the Langerhans dendritic cells of skin and mucosa, probably a part of the endosomal system
5. BOWMAN **Bowman's capsule** – double layer envelope surrounding the glomerulus, forming the renal body
Bowman's membrane – layer of extracellular matrix under the anterior epithelium of the cornea
Bowman's glands – glands in the olfactory area of the nasal mucosa
6. BRUCH **Bruch's membrane** – the innermost layer of the ocular uvea; substances are transported between the retinal cells and the uvea with good blood supply
– width of 2–4 µm, consists of basement membrane of the pigmented epithelium of the retina, from inner collagen layer, elastin layer, outer collagen layer and basal lamina of uveal capillaries
– during aging, it thickens, thus slowing the nourishment of retinal photoreceptors
7. BRUNNER **Brunner's glands** – mucus–secreting glands in the submucosa of the duodenum
8. CAJAL **Interstitial cells of Cajal** – cells in the wall of the digestive tract, they help control peristaltic movements (so called pacemakers)
Cajal–Retzius horizontal cells – bipolar neurons of cerebral cortex with horizontal direction of the processes
9. CLARA **Clara cells** – exocrine cells of bronchial epithelium producing glycosaminoglycans, which is a part of pulmonary surfactant; the term "club cells" is used as well
10. CLAUDIUS **Claudius cells** – columnar supporting cells of the organ of Corti in the inner ear
– their tight junctions delimit the area filled with endolymph
11. CLOQUET **Cloquet's canal** – the majority of adults have a microscopic canal (*canalis hyaloideus*) running through the vitreous body of the eye between the posterior surface of the eye lens and the optic nerve papilla with the central retinal artery
– it is a residue of the space, where the temporary hyaloid artery used to run through the eye during embryonic development, which nourished the growing lens
12. COHNHEIM **Cohnheim's areas** – group of myofibrils visible on a cross–section of the skeletal muscle fibers
– polygonal shape, mostly artefacts emerging due to uneven contraction of sarcoplasm and myofibrils during chemical fixation
13. CORTI **Organ of Corti** – group of sensory and supporting cells of the membranous labyrinth of the inner ear
Tunnel of Corti – part of the organ of Corti; space between the outer and inner supporting pillar cells
Ganglion of Corti – spiral ganglion of the cochlear nerve inside the bony cochleae
14. ČERMÁK/ CZERMAK **Czermak's lacunas** – different staining in the interglobular dentine
– found in the superficial layer of dentine, where the hydroxyapatite crystals are sometimes connected only incompletely; these less mineralized spaces remain after them
15. DEITERS **Deiters cells** – outer supporting cells (phalangeal) of the organ of Corti in the inner ear
– support the sensory hair cells, connect them with the basilar membrane and allow them to perceive shear movements between the basilar and the tectorial membrane
16. DESCEMET **Descemet's membrane** – basal lamina of the posterior epithelium of the cornea
17. DISSE **Perisinusoidal space of Disse** – microscopic space between the vascular pole of the hepatocyte and the endothelium of hepatic blood sinusoids, where microvilli of hepatocytes absorb substances filtered from the blood
18. DUA **Dua's layer** – approximately 15 µm thick layer separating fibrous stroma of the cornea
19. from the basement membrane of Descemet of the posterior corneal epithelium
20. EBNER **(von) Ebner's glands** – serous minor salivary glands of the tongue in the vicinity of vallate and foliate papillae; their watery secretory product wash the surface of the taste buds
21. GIANUZZI **Lunula of Gianuzzi** – group of basophile serous cells, with conspicuous crescent appearance in formaldehyde–fixated sections of mixed glands; contrasting with the adjacent brighter mucous–secreting cells
22. GLISSON **Glisson's capsule** – fibrous capsule of liver
Glisson's triad – term for the interlobular artery, vein and bile duct in the portal area of liver
23. GOLGI **Golgi's complex/system** – cellular organelle
Golgi type I neuron – a neuron with a long axon; **Golgi type II neuron** – neuron with a short axon
Golgi tendon organ – a proprioceptor in the tendon in the vicinity of the connection of the tendon to the muscle
24. GRAAF **Graafian follicle** – mature follicle in the ovarian cortex, whose wall ruptures during ovulation (approximately in the half of the ovarian cycle)
Graaf's ducts – excretory canals of the testis in the head of the epididymis

25. **HASSALL** **Hassal's bodies** – concentric corpuscles in the medulla of the thymus, consisting mainly of epithelial reticular cells probably important in the control of lymphopoiesis (the full role has not been elucidated)
26. **HAVERS** **Haversian canal** – part of the osteon in the compact bone
contains the central vessel of osteon; the canal is surrounded by bone lamellas
Haversian system – osteon formed by the Haversian canal surrounded by bone lamellas
Haversian bone – lamellar bone, where the layers of bone cells alternate with the layers consisting of extracellular bone mass
27. **HENLE** **Loop Henle** – part of the nephron tubule running through the renal medulla
Henle layer – outer layer of cells of the inner sheath of a hair root
Henle sheath – connective tissue capsule of a neural fiber
28. **HENSEN** **Cells of Hensen** – group of outer supporting cell of the organ of Corti in the inner ear
Canal of Hensen – narrow canal connecting the scala media (*ductus cochlearis*) and saccule of the membranous labyrinth in the inner ear
Node of Hensen – primitive node, ending of the primitive streak of epiblast in the stage of the bilaminar embryonic germ disc
29. **HERING** **Canals of Herring** – biliary canals with epithelial lining in a hepatic lobule
30. **HERRING** **Bodies of Herring** – expansion terminal parts of axons of neurosecretory neurons in the neurohypophysis containing hormones arriving here via axonal transport from the hypothalamic nuclei
31. **HOFBAUER** **Hofbauer cells** – macrophages of placenta contributing to the suppression of the immune responses between the tissues of the mother and the fetus; also support the growth of the chorionic villi of placenta
32. **HORTEGA** **Hortega's glia** – microglia, one of the types of neuroglia in the central nervous system responsible for phagocytosis, important in immune reactions
33. **HOWSHIP** **Howship lacunes** – small cavities in bone tissue created by the enzymatic resorption activity of osteoclasts (multi–nucleate cells derived from monocytes)
34. **HUXLEY** **Huxley's layer** – middle epithelial layer of cells of the inner sheath of a hair root
35. **ITO** **Ito cells** – stellate cells in the perisinusoidal space of liver (of Disse)
– thanks to the ability of lipophagy, they store vitamin A in their lipid droplets
– simultaneously, they are able to stimulate the regeneration of liver tissue thanks to their ability to produce growth factors and lead to an excess production of connective tissue (fibrotization) in the liver during pathologic conditions
36. **KOHN** **Pores of Kohn** – openings in the interalveolar septa, which communicate through individual pulmonary alveoli
– they facilitate the equilibration of the pressure between individual alveoli; they enable the passage of alveolar macrophages
37. **KORFF** **Korff dentine** – area of less mineralized dentine on the border with the cement or enamel
38. **KRAUSE** **Krausse bodies** – ovoid sensory capsulated thermoreceptors,
– occur in the connective tissue of the conjunctiva, mucosa of the tongue, dermis of the lips
39. **KUPFFER** **Kupffer cells** – liver macrophages in the luminal surface of the endothelial lining of hepatic blood sinusoids; part of the mononuclear–phagocytic system
– capture microorganisms, damaged blood elements and foreign bodies from the blood circulation
40. **LANGER** **Langer's lines** – notional lines on the surface of the skin corresponding to the direction of skin cleavage in that area
– defined by the prevailing directions of collagen and elastic fibers in the dermis
– skin incisions parallel to these lines heal with a minimal scar by only pulling edges without tension
41. **LANGERHANS** **Langerhans islets** – endocrine tissue of the pancreas
Langerhans dendritic cells – antigen–presenting cells in the spinous layer of the epidermis of skin
– a part of the immune system of the skin and some mucous membranes, contain Birbeck's granules
42. **LANGHANS** **Langerhans cells** – cells of the cytotrophoblast in the wall of the chorion villi
Langerhans giant multinucleated cells (foreign–body giant cells) – fused macrophages in the vicinity of a foreign material form giant multinucleated (up to 100 nuclei) cells
43. **LANTERMANN** **Schmidt–Lantermann's clefts** – incisures running in an oblique direction through the myelin sheath of a myelinated nerve fiber; remains of the cytoplasm of a Schwann cell after myelination
– function as a communication microscopic area in the multiple rotations of the Schwann cell
44. **LEYDIG** **Leydig cells** – interstitial cell of the testes producing male sex hormones (androgens)
45. **LIEBERKÜHN** **Crypts of Lieberkühn** – simple tubular glands in the intestinal mucosa
46. **MALPIGHI** **Malpighian corpuscles** – renal bodies consisting of Bowman's capsule and glomerulus
Malpighian corpuscles – lymph nodules of the white pulp of spleen
Malpighian layer – germinal layer of the epidermis of skin
– it consists of the basal layer and the spinous layer, where keratocytes are mitotically active
47. **MARTINOTTI** **Martinotti cells** – small multipolar neurons mainly with inhibitory function
– scattered in most of the six layers of the brain cortex
– short dendrites, but long axons, which are oriented perpendicularly to the cerebral cortex
48. **MEIBOM** **Meibomian glands** – greater sebaceous glands in the tarsal plate of the eyelid
49. **MEISSNER** **Meissner's nerve plexus** – autonomic nerve plexus in the submucosa of the digestive tract
Meissner's bodies – type of tactile bodies in the dermis

50. MERKEL **Merkel's cells** – part of the basal layer of the epidermis of skin and epithelium of some mucous membranes, mainly in the finger tips and the face
– connected via nerve endings and form the tactile Merkel's bodies

51. MOLL **Glands of Moll** – apocrine glands on the edges of eyelids
– they contribute to the secretion of a lipid layer protecting excessive evaporation of the lacrimal film

52. NASMYTH **Nasmyth's membrane** – temporary, about 1 µm thick membrane covering the surface of the tooth enamel
– it disappears shortly after tooth eruption

53. NISSL **Nissl substance / tigroid** – basophilic aggregates of cisterns of the rough endoplasmic reticulum and free ribosomes in the cytoplasm of nerve cell bodies (when stained using basic dyes)

54. NUEL **Space of Nuel** – microscopic canal between the outer pillar cells and inner supporting cells of the organ of Corti in the inner ear

55. PACINI **Vater–Pacini bodies** – nearly macroscopically visible mechanoreceptors with layered structure, quick adaptation, sensitive to vibration and pressure

56. PANETH **Paneth cells** – type of cells of the epithelium in the intestine and the appendix of large intestine, located on the bottom of intestinal glands (crypts of Lieberkühn)
– creating antimicrobial peptides (e.g. lysozyme, alpha–defensine), which are part of the innate immunity

57. PEYER **Peyer's patches** – aggregates of lymphatic follicles in the wall of the aboral part of the small intestine
– nearly 50% of Peyer's patches are concentrated in the last 25 cm of ileum, where they create a ring of lymphatic tissue

58. PURKYNĚ / PURKINJE **Purkinje cells** – large multipolar neurons of pear–like (bottle–like) shape in the middle layer (*stratum purkinjese*) of the cortex of cerebellum
Purkinje fibers – terminal part of the electrical conduction system of the heart specialized cells of cardiac muscle running through the subendocardial connective tissue layer of ventricles

59. RANVIER **Nodes of Ranvier** – gaps between two consequent myelin sheaths of nerve fibers
– area between two nodes of Ranvier is called internodium (segment of Ranvier)

60. RATHKE **Rathke's pouch** – temporary embryonic structure; it separates the roof of the primitive mouth cavity (stomodeum) of the embryo; it gives rise to the adenohypophysis

61. REINKE **Reinke's space** – loose connective tissue of mucosa under the epithelium of vocal cords

62. RENSHAW **Renshaw cells** – inhibitory interneurons in the gray matter of the anterior horns of the spinal cord
– via a collateral from the axon of somato–motor alpha–motor neuron of the anterior horns of the spinal cord, they receive information about motor stimuli travelling to the skeletal muscles and simultaneously send an inhibitory signal to the body of a specific alpha motor neuron

63. RETZIUS **Striae of Retzius** – alternating lighter and darker incremental lines in an enamel section

64. REXED **Rexed laminae** – structure of ten layers of grey matter of the spinal cord; areas are numbered using Roman numerals I–IX in a direction from the posterior horns to the anterior horns; the area no. X lies around the central spinal canal

65. RUFFINI **Ruffini bodies** – slowly reacting encapsulated mechanoreceptors of the subcutaneous tissue; they detect pressure as they bend

66. SHARPEY **Sharpey's fibers** – bundles of collagen fibers, which run from the dense collagenous connective tissue of periosteum to the superficial (subperiosteal) bone layer

67. SCHWANN **Schwann cells** – supporting neuroglial cells of the peripheral nervous system responsible for the myelination of fibers and protection of non–myelinated nerve fibers
Schwann sheath – layer of cytoplasm of Schwann cells on the myelin sheath of a peripheral nerve

68. SERTOLI **Sertoli cells** – supporting cells in the seminiferous tubules of the testicle; nourishing the developing spermatogonia, spermatocytes and spermatids; sensitive to follicle stimulating hormone endocrine activity and their intercellular contacts form the blood–testicle barrier

69. SCHLEMM **Schlemm's canal** – venous sinus running on the outer surface of the iris at its interface with the cornea and sclera
– through netted trabeculae of the ventricular angle, it collects the aqueous humor and leads it to the major veins of the sclera of the eye

70. SCHREGER **Hunter–Schreger striation** – spiraled alternating light and dark lines on an enamel section
– caused by the fact, that the section alternately captures the lateral, oblique or anterior surfaces of enamel prisms which diffract light in a different way

71. TOMES **Tomes fibers** – projections of odontoblasts, which run inside the dentinal tubules
72. perpendicularly to the surface of the tooth

73. VOLKMANN **Volkmann's canals** – narrow canals in the compact bone containing vessels; oriented in perpendicular or oblique direction to the osteons; interconnecting individual Haversian canals

74. von WILLEBRAND **von Willebrand's factor** – adhesive glycoprotein produced by endothelial cells and megakaryocytes
– important for blood clotting in case of a damage to the endothelium of blood vessels

75. WEBER **Weber's glands** – mucous–secreting minor salivary glands at the radix of the tongue

76. WEIBEL **Weibel–Palade bodies (granules)** – storage granules in endothelial cells
– for storing and releasing of von Willebrand's factor and P–selectin

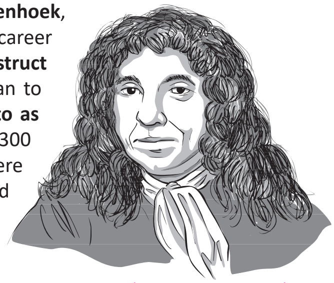
77. WHARTON **Wharton's jelly** – mucous connective tissue of the umbilical cord with high content of hyaluronic acid

78. WOLFRING **Wolfring's glands** – accessory lacrimal glands present in the middle part of the upper eyelid in some individuals

79. ZEIS **Sebaceous glands of Zeis** – holocrine glands of the upper eyelid, end in the sheaths of the eyelashes
– their sebum forms a stabilizating surface preventing excessive evaporation of the tear film

History of histology is **tightly bound to the construction of the light microscope**, and therefore, compared to some other disciplines, is relatively short. For example, **in 1882 histology was taught at Charles University in Prague only as a part of anatomy**. The first Czech associate professor of histology and embryology, **Jan Janošík**, defended his thesis in 1884 and an **independent histological institute was founded at Charles University in Prague in 1886**. *In this subchapter, we present a mosaic of selected personalities. For a comprehensive historical overview, refer to the used literature.*

In the biomedical sciences, the first use of a microscope is not attributed to university researchers, but to a Dutch tradesman without biologic or medical higher education. His name was **Anthony van Leeuwenhoek**, and he excelled, among other things, in optical lens grinding. Self-taught, he began his scientific career in his 40s, when he began making hundreds of tiny single-lens microscopes. He was able to **construct a microscope with approximately 200x magnification**, which allowed him to be the first human to see red blood cells**. In other samples,** he observed bacteria and protozoa, **which he referred to as** animalcules, and striated muscle fibers. Over 50 years of his scientific carieer, he wrote more than 300 letters to renowned scientists of the Royal Society with his discoveries. More than a hundred were published and translation in the Royal Society's Philosophical Transactions. Leeuwenhoek guarded his microscopes in an extraordinary way, and the only other person who could secretly get access to those microscopes was Ham, an assistant in a canvas shop. He is also considered to be the first to describe sperm.

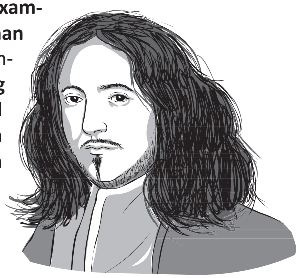


Antonie van Leeuwenhoek
(1632 – 1723)

The term "**cell**" (cellula) in the biological sense was first used by the English scientist **Robert Hooke**. In his work "**Micrographia**", published in 1665, he used this term for **tiny hollows in tree cork** (the dead outer layer of the plant rhytidome under the bark). **Hooke built a microscope with his own light source** - **oil lamp flame**. Due to the imperfections of the 17th century microscopes, animal cells, which are generally smaller than plant cells and lack a conspicuous cell wall, became a subject of interest much later.

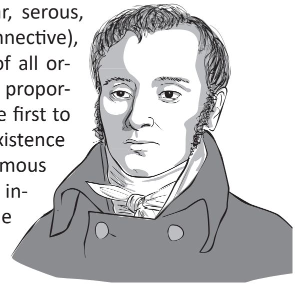
Robert Hooke (1635 – 1703)

Marcello Malpighi was an Italian physician, also called "**the father of microscopic anatomy**." **He examined the microscopic structure of the human body,** vertebrates, invertebrates including insects, and plants. **During the study of frog lung parenchyma, he discovered blood capillaries,** which, until then, had only been thought of as hypothetical links between arterial and venous blood system. For example, **he described the taste buds of the tongue, glomeruli of the kidney, the follicles of the white pulp of the spleen, :and the development of the chicken embryo.**



Marcello Malpighi
(1628 – 1694)

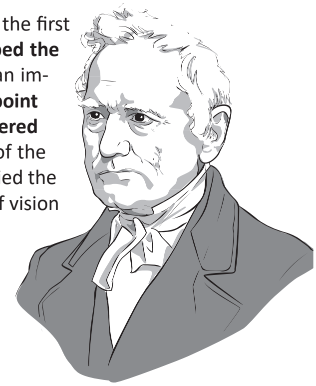
Marie François Xavier Bichat was a French anatomist. Although he did not use a microscope for his work, **he introduced the term "tissue" as the first**. Based on autopsies, **he assumed that the human body consists of 21 different types of tissues** (e.g. nervous, vascular, serous, mucinous, connective), which are part of all organs in different proportions. He was the first to assume the existence of an autonomous nervous system independent of the brain.



Xavier Bichat
(1771 – 1802)

The Dutch anatomist, **Regnier de Graaf**, is considered to be the founder of **reproductive biology**. In 1668, he published a **monograph on anatomy of the male genital system**, and in 1672 a similar **book about the female genital system**. Although he did not have an access to a microscope (he died in the same year that Leeuwenhoek published his first microscopic observations), the detailed autopsy and numerous experiments with rabbits enabled him to reveal **the importance of the uterine tubes**. He was the first **to describe the obstruction of the uterine tubes and extrauterine pregnancy in the uterine tube due to post-inflammatory mucosal adhesions. Mature follicles** in the cortex of the ovary, whose development he documented, bear his name. In his work, de Graaf also made some mistakes, for example **he supposed that the fertilization occurs in the ovary or that sperm is stored in seminal vesicles.**

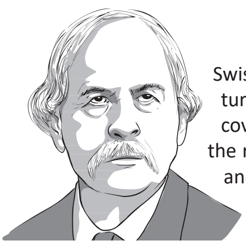
Regnier de Graaf (1641 – 1673)



The discovery of the nucleus of the animal cells is credited to a **Czech scientist of the world format**, the first professor of physiology at Charles University in Prague, Jan Evangelista Purkyně**. In 1825, he described the** cell nucleus in a bird egg: under the name **vesicula germinativa** ***(germinal vesicle).*** He introduced an important concept of "protoplasm" from cytological aspects **(1839) and was among the first ones to point out the fact that** the bodies of plants and animals are made of cells**. Using a microscope, he discovered pear-shaped** neurons in the cerebellum cortex (Purkinje cells) **and** a part of the conduction system of the heart (Purkinje's fibers)**. He found that nerve fibers were not hollow**, but contained an axon. He studied the microscopic structure of bones, teeth, skin and stomach mucosa. He also dealt with the physiology of vision and hearing. At the same time, he was an active participant in Prague's patriotic life.

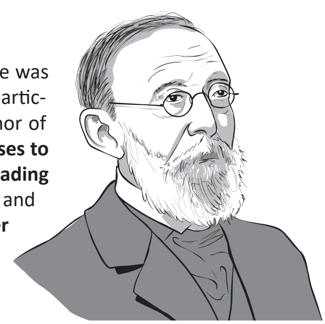
In 1837, Purkyně presented a lecture (hereinafter unpublished) at the Natural Sciences Congress in Prague, in which he described the granular structure of nervous tissue. These granules were cells. However, the cell theory is now attributed to **Matthias Schleiden** (1804–1881) and **Theodor Schwann** (1810–1882). Schleiden, as a botanist, labelled the cell as the basic structural unit of the plant. Schwann, in his paper "Microscopical Researches into the Accordance in the Structure and Growth of Animals and Plants" (1839)**, more clearly expressed the unity between the cells of all living organisms.**

Jan Evangelista Purkyně
(1787 – 1869)



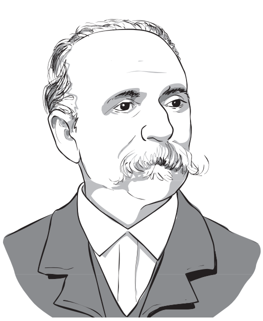
Swiss comparative anatomist, **Rudolf Albert von Kölliker**, considered to be one of the doyens of the nineteenth-century histology, :introduced **new methods of histological techniques into embryological research.** His greatest discoveries include the **demonstration of connection of the neuronal projection (axon) with the body of the neuron**, the results of the study of **spermiogenesis**, the **description of the development and differentiation of blood cells**, and the importance of **germinal layers during the development of the embryo**. In 1852, he published **the first modern textbook of histology** (Handbuch der Gewebelehre des Menschen), and in 1861, he published the textbook of animal and human embryology (Entwicklungsgeschichte des Menschen und der Höheren Tiere).

Albert von Kölliker
(1817 – 1905)



German pathologist, **Rudolph Carl Virchow**, is considered to be the "**father of cellular pathology**". He was the first to **prove the practical importance of microscopic examination of tissues in medicine** and participated in the **introduction of histopathology to other medical examination methods**. He is the author of the famous statement **"Omnis cellula e cellula**" (all cells come from other cells). **He considered diseases to be disorders of the normal structure and function of cells and tissues.** He described **the factors leading to thrombosis** (the so-called **Virchow triad** involving a hypercoagulable state, blood flow decrease, and damage to the vascular wall endothelium) and **metastatic propagation of tumors**: **Virchow-Troisier lymph nodes** *(*nodi lymphoidei supraclaviculares sinistri**), where stomach tumors often metastasize. To the classical four Celsus signs of inflammation (**dolor – **pain,** calor – **elevated temperature,** rubor – **redness,** tumor – **swelling), he added the fifth sign** – functio laesa – function disruption. In addition to pathology, he also focused on anthropology and social medicine.

Rudolph Virchow
(1821 – 1902)



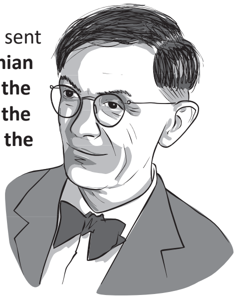
Camillo Golgi
(1843 – 1926)

Nobel Prize in physiology and medicine in 1906 was awarded to two histologists: Italian **Camillo Golgi** and Spanish **Santiago Ramón y Cajal**. Both received this award for their contribution to the **research of microscopic anatomy of the central nervous system**. It can even be said that, before the work of Golgi and Cajal, the discipline known today as **neuroscience** almost did not exist. Ramón y Cajal, using and refining Golgi's method for the visualization of neurons, **detailed the structure of the central nervous system and correctly defined the neurons as the basic, separate morphological and functional units of the nervous system.**

Ramón y Cajal
(1852 – 1934)

On June 27, 1919, the National Assembly in Prague approved the Act No. 375, which established the **Czechoslovak State University** in Bratislava. During the initial years, teaching took place only in the higher clinical years. **The first Institute of Histology and Embryology in Slovakia was founded at the Faculty of Medicine of Comenius University in Bratislava in 1922**. Its founder was **Zdeněk Frankenberger**.

Frankenberger previously worked at the Medical Faculty of Charles University in Prague from where he was sent to build a histology oriented institute to Slovenian Ljubljana, **and he is still considered the founder of Slovenian histology. Between 1922 and 1938, he worked at the Faculty of Medicine in Bratislava as the head of the** Institute of Histology and Embryology**, and from 1933 to 1936, professor Frankengerber was the head of the Institute for Normal and Topographic Anatomy. His versatility and profound knowledge is evidenced by the fact that at one time he has** lectured both on histology and embryology, as well as on anatomy and general biology. **From 1930 to 1931, he held the position of the Dean of the Faculty of Medicine in Bratislava.**



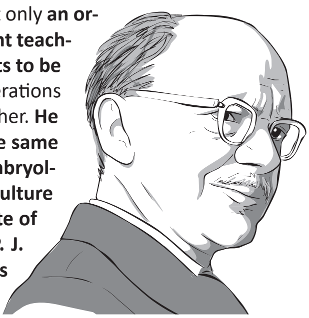
Zdeněk Frankenberger

(1892 – 1966)

The **second head of the Institute of Histology and Embryology (1933–1936)** was **Jan Florian** (1897–1942) from Brno, a fellow of František Karel Studnička. After returning to Brno**, he became the Dean of the Medical Faculty in Brno**. He severely condemned fascism, and in 1938 he made a sharp protest against the closure of Czech universities and engaged in an illegal anti-fascist resistance. He was executed in Mauthausen on 7. 5. 1942. He left his students a living and valid legacy: **to live in the truth and not to hesitate to give one's own life for it**. During the Second World War in the years 1939–1943, the Institute was led by **Július Ladziansky-Ledényi** (1903–1943) an **excellent staff of the Slovak anatomy**. He made pioneering work on the field of **Slovak anatomical terminology**.

According to a preserved text, **Frankenberger began his first lecture on biology by considering the necessary qualities of a good physician.** For the physician to prove himself/herself in practice**, he/she must have not only a deep-rooted attitude** to the profession but also **extensive professional knowledge**. No matter what's the field of expertise, he/she must always base the work on theoretical scientific ground of foundations. When comparing the work of a mid-level healthcare staff (nurses) and a physician, he explained to the students the need for a long, comprehensive and profound study of medicine. **The physician must be able to decide independently and very responsibly the care of the patient.** This creative approach to right decisions is based on theoretical fields.

From 1945 to 1972, **Ivan Stanek**, was the head of the Institute of Histology and Embryology in Bratislava. He was a member of the Slovak Academy of Sciences, was one of the most prominent staff of the Slovak histology and embryology. Stanek was not only **an organizer and a prominent scientist but, above all, an excellent teacher**. **He regarded the training of new physicians and scientists to be his mission in life**. His fellows, co-workers, and several generations of medical studens recall him as an excellent university teacher. **He was famous, in particular, by its comprehensible and at the same time engaging lectures and graphic drawings of human embryology**. As a scientist, he **introduced methods of in vitro cell culture in Slovakia**. **He also participated in establishing the Institute of Histology and Embryology at the Faculty of Medicine of P. J. Šafárik University in Košice** (1949/50) **and at the Jessenius Medical Faculty in Martin** (1966/67).



Ivan Stanek

(1915 – 1972)

Karol Kapeller

(*1926)

Karol Kapeller was the head of the Institute of Histology and Embryology in Bratislava in 1980–1991 and achieved remarkable results in **electron microscopy**. In the 1960s, he published a **series of articles on axonal transport of noradrenaline in sympathetic nerve fibers and ultrastructure of autonomic nerves**.

Kapeller worked on part of his research on axonal transport during his study stay in Sheffield, England, from 1964 to 1965.

Similarly, to the world scale, **the development of histology in the countries of Bohemia, Moravia and Silesia also emerged from anatomy and** general zoology. For a half century before Bichat's classification of tissues, **Jan Křtitel Boháč** (1724–1768), dean of the Faculty of Medicine of Charles University, published a study **"De Partibus machinae humanae similaribus**", where he attempted for a scientific **specification of tissues**. *In this subchapter, we present a mosaic of selected personalities.*

Gabriel Valentin
(1810 – 1883)

After the already mentioned **Purkyně**, one cannot omit his vision, who provided for **further development and dissemination of the microscopic understanding of the structure of the tissues of animals** and plants. Purkyně's assistant, **Gabriel Valentin**, described in his thousand-page study, "Histiogeniae plantarum atque animalium inter se comparatae**" (1835), that plant cells and animal "**granules**" (Purkyně's term for animal cells)** are the same in their primary origin, but vary in their further differentiation**. It brings a** developmental view into the understanding of tissues, differentiating bases", **i.e.** blastemas**, as a specific counterpart to static conception of cells.**

Purkyně's friend, an anatomist **Wáclav Staněk** (1804–1871), incorporated into his Czech anatomy textbook called "**Pitwy**" a part on **tkanivosloví**, **the old Czech term for histology**. A part of the world's development of the knowledge of the cell in the 19th century is grounded on the contribution of the professor of zoology **František Vejdovský** (1849–1939) in the form of the **discovery of centrosome in a fertilized egg** (1878). Vejdovský correctly described the **spermatic origin of the centrozome** and published the first Czech textbook of general zoology.

Jan Janošík
(1856 – 1926)

The first Czech habilitated histologist and embryologist and the head of the Institute of Histology and Embryology at the Czech Medical Faculty, **Jan Janošík**, published the first Czech textbook entitled **"Histology and Microscopic Anatomy**" (1892). Janošík **discovered *pronefros*** in early human embryos. The next head of the independent histological-embryological institute after Janošík was **Josef Viktor Rohon**. In addition to his paleontological discoveries, we can select the description of the **preotic and postotic head segments of the embryo, or the description of the Rohon-Beard sensory ganglionic cells** from the dorsal part of the spinal cord of the lancelet (they have an important role in explaining the origin of neural crest and spinal ganglia of vertebrates).

Josef Viktor Rohon
(1845 – 1923)

The next head after Rohon was **Otakar Srdínko**. In histology, he contributed to the understanding of the relation of the **exocrine and endocrine part of the pancreas, adrenal development and histogenesis of connective tissue**. In the political and social sphere, he contributed in the foundation of universities in Brno and Bratislava in the Czechoslovakia. His textbooks **"Histology", "Fundamentals of Histological Techniques"** and **"Embryology Textbook"** are still valued for their modern concepts and documentation.

Otakar Srdínko
(1875 – 1930)

After Srdínko, **František Karel Studnička** came from Brno to the institute of histology in Prague. He is the world famous for the **studies of the organization of a living mass as multicellular organisms**. There, in the framework of the so-called **exoplasmic theory**, he pointed out the **formational, differentiating and functional significance of the extracellular matrix**, which provides informational and communicational connection of the cells of an organism into a functional unit.

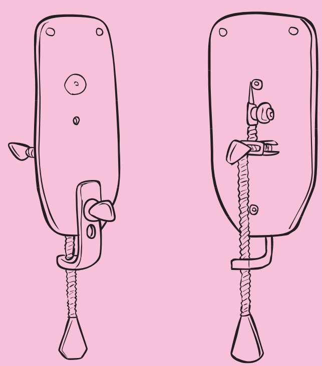
František Karel Studnička
(1870 – 1955)

Jan Wolf
(1894 – 1977)

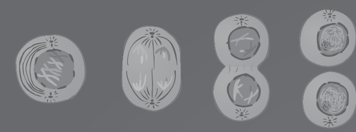
After Studnička, the independent institute of histology was led by **Jan Wolf** and the institute of embryology by **Zdeněk Frankenberger**. Wolf published **several histology textbooks**, the most famous of which is "Histology" (1966), following the previous textbooks written in collaboration with Studnička. Wolf **contributed to the development of histological techniques, the introduction of electron microscopy and the understanding of the remineralization of the surface layer of the enamel**. Frankenberger was widely educated and active in the field of comparative embryology, phylogeny and evolutionary morphology. Their fellows helped in establishing institutes of histology-embryology at other newly founded faculties after the Second World War. Of many followers, let's mention e.g. **Zdeněk Lojda**. Lojda devoted his career in studying the **histochemistry of enzymes** and became a world-recognized and sought-after authority in this field. In his honor, the conference of the Czech Society of Histochemistry and Cytochemistry is called the **Lojda's symposium".**

Zdeněk Lojda
(1927 – 2004)

15+ milestones of histology



The first microscope with approximately 200x magnification made by Antonie van Leeuwenhoek.



„Omnis cellula e cellula"

"All cells come from other cells"

– Rudolph Carl Virchow –

1 Zacharias and Hans Janssen constructed the **first microscope** at the end of the 16th century, combining two objective lenses and an eyepiece lens in a common optical tube. The microscope provided a blurry image with a maximum magnification of 10×.

2 Around 1670, Antony van Leeuwenhoek perfected the quality of the lenses so much that his **light microscope** had a **200-fold magnification** at **approximately 1 micrometer resolution**. He was the first to observe and draw protozoa, bacteria and red blood cells.

3 In 1665, Robert Hooke used the term *"cell"* (**cellula**) in his work "*Micrographia*" to designate microscopic cavities in tree cork, which resembled small "chambers" (*cellae*).

4 In the second half of the 17th century, Marcello Malpighi discovered a capillary bed, pulmonary alveoli and taste buds. He became the first **microscopic anatomist (histologist)**.

5 By the end of the 18th century, Marie François Xavier Bichat introduced the term **"tissue"** (from the French tissu, i.e. fabric, canvas). Based on his naked-eye observation, he distinguished up to 21 "different tissues".

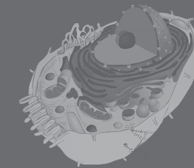
6 In 1838, Matthias Jakob Schleiden and Theodor Schwann came with the hypothesis that became the basis of **cell theory**. According to it, the bodies of animals and plants consist of similar basic structural blocks (cells) and their products.

7 The Czech scientist Jan Evangelista Purkyně is also considered to be **the author of cell theory**. In the first half of the 19th century, he was the first to describe the cell nucleus, the contents of living cells (protoplasm), structure of bone, dentine, stomach and many glands, axons in the nerves, Pear-shaped neurons of the cerebellar cortex and the endings of the cardiac conduction system bear his name.

8 German pathologist Jacob Henle published the **first histology textbook** called "*Allgemeine Anatomie*" in 1841 (General anatomy). He introduced the current classification of four types of tissues (epithelial, connective, muscle and nerve).

"Granules"

the name Purkyně gave to animal cells



9 In the 19th century, Albert von Kölliker described the hematopoiesis, the development of sperm and the importance of germinal layers during embryogenesis. He was probably the first to observe **mitochondria**.

10 Rudolf Virchow supplemented the cellular theory by rejecting spontaneous cell production, saying that **each cell originated only from an already existing cell** (1855). He introduced the use of microscopes to the study of medicine and as a "father of cellular pathology" drew the attention of physicians to the importance of microscopic examination of tissue samples.

11 After 1858, Joseph von Gerlach's work (carmine staining) contributed to the expansion of staining methods in histology. In 1878, H. Busch described the most commonly used histological staining – a combination of hematoxylin and eosin.

12 Following the accidental discovery of Ferdinand Blum (1894), formalin (40% formaldehyde solution, previously used for disinfection) started to be routinely used for **tissue fixation**.

13 The Nobel Prize for Physiology and Medicine in 1906 was awarded to two neurohistologists, Camillo Golgi and Santiago Ramón y Cajal. Golgi developed a new impregnation technique for visualization of the nerve tissue parts. Cajal correctly explained the interconnection of cells through projections. Both belong to the foundation of **neuroscience**.

14 In the 1930s, Ernst Ruska and Max Knoll built the first **transmission electron microscope** in Germany, in which Ruska was awarded the Nobel Prize in Physics in 1986 for. The **first scanning electron microscope** was built in 1937 by Manfred von Arden.

15 Albert Coons and his coworkers first used the method of direct **immunohistochemistry** to detect pneumococci in tissues in 1941. Later, the method expanded rapidly in specific antigen detection in histology.

\+ The ongoing development of histology may be seen e.g. in the Nobel Prize in Chemistry awarded to Eric Betzig, Stephan Hell and Edward Moser in 2014 for the discovery and development of the **super resolved fluorescence microscopy**. By concentrating the image with two different lenses at one point, they improved the spatial resolution of the light microscope above the so-called diffraction limit, described by Ernst Abb in 1873 as the resolution limit of light microscope (half of the visible wavelength, cca. 200 nm). The discovery enables observing nanoscopic changes at the molecular level in living cells.

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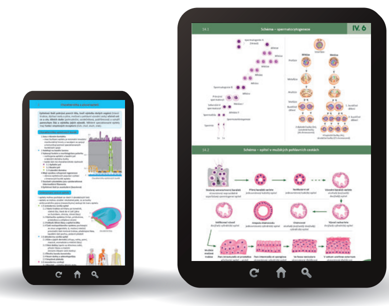

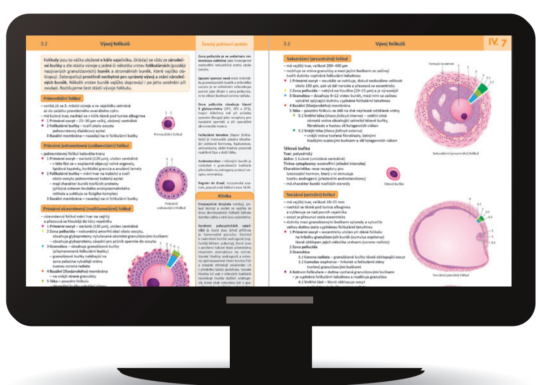

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